

# Kazmis

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## ALOPECIA AREATA

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## INTRODUCTION

### BACKGROUND

Alopecia areata is a recurrent nonscarring type of hair loss that can affect any hair-bearing area. Clinically, alopecia areata can manifest many different patterns. Although medically benign, alopecia areata can cause tremendous emotional and psychosocial distress in affected patients and their families.

### PATHOPHYSIOLOGY

The exact pathophysiology of alopecia areata remains unknown. The most widely accepted hypothesis is that alopecia areata is a T-cell-mediated autoimmune condition that is most likely to occur in genetically predisposed individuals.<sup>[1]</sup>

### Autoimmunity

Much evidence supports the hypothesis that alopecia areata is an autoimmune condition. The process appears to be T-cell mediated, but antibodies directed to hair follicle structures also have been found with increased frequency in alopecia areata patients compared with control subjects. Using immunofluorescence, antibodies to anagen-phase hair follicles were found in as many as 90% of patients with alopecia areata compared with less than 37% of control subjects. The autoantibody response is heterogeneous and targets multiple structures of the anagen-phase hair follicle. The outer root sheath is the structure targeted most frequently, followed by the inner root sheath, the matrix, and the hair shaft. Whether these antibodies play a direct role in the pathogenesis or whether they are an epiphenomenon is not known.

Histologically, lesional biopsy findings of alopecia areata show a perifollicular lymphocytic infiltrate around anagen-phase hair follicles. The infiltrate consists mostly of T-helper cells and, to a lesser extent, T-suppressor cells. CD4<sup>+</sup> and CD8<sup>+</sup> lymphocytes likely play a prominent role because the depletion of these T-cell subtypes results in complete or partial regrowth of hair in the Dundee experimental bald rat (DEBR) model of alopecia areata. The animals subsequently lose hair again once the T-cell population is replete. The fact that not all animals experience complete regrowth suggests that other mechanisms likely are involved. Total numbers of circulating T lymphocytes have been reported at both decreased and normal levels.

Studies in humans also reinforce the hypothesis of autoimmunity. Studies have shown that hair regrows when affected scalp is transplanted onto SCID (severe combined immunodeficiency) mice that are devoid of immune cells. Autologous T lymphocytes isolated from an affected scalp were cultured with hair follicle homogenates and autologous antigen-presenting cells. Following initial regrowth, injection of the T lymphocytes into the grafts resulted in loss of regrown hairs. Injections of autologous T lymphocytes that were not cultured with follicle homogenates did not trigger hair loss.

A similar experiment on nude (congenitally athymic) mice failed to trigger hair loss in regrown patches of alopecia areata after serum from affected patients was injected intravenously into the mice. However, the same study showed that mice injected with alopecia areata serum showed an increased deposition of immunoglobulin and complement in hair follicles of both grafted and nongrafted skin compared with mice injected with control serum, which showed no deposition.

In addition, research has shown that alopecia areata can be induced using transfer of grafts from alopecia areata-affected mice onto normal mice. Transfer of grafts from normal mice to alopecia areata-affected mice similarly resulted in hair loss in the grafts.

Clinical evidence favoring autoimmunity suggests that alopecia areata is associated with other autoimmune conditions, the most significant of which are thyroid diseases and vitiligo (see History).

In conclusion, the beneficial effect of T-cell subtype depletion on hair growth, the detection of autoantibodies, the ability to transfer alopecia areata from affected animals to nonaffected animals, and the induction of remission by grafting affected areas onto immunosuppressed animals are evidence in favor of an autoimmune phenomenon. Certain factors within the hair follicles, and possibly in the surrounding milieu, trigger an autoimmune reaction. Some evidence suggests a melanocytic target within the hair follicle. Adding or subtracting immunologic factors profoundly modifies the outcome of hair growth.

## Genetics

Many factors favor a genetic predisposition for alopecia areata. The frequency of positive family history for alopecia areata in affected patients has been estimated to be 10-20% compared with 1.7% in control subjects.<sup>[1]</sup> The incidence is higher in patients with more severe disease (16-18%) compared with patients with localized alopecia areata (7-13%). Reports of alopecia areata occurring in twins also are of interest. No correlation has been found between the degree of involvement of alopecia areata and the type of alopecia areata seen in relatives.

Several genes have been studied and a large amount of research has focused on human leukocyte antigen. Two studies demonstrated that human leukocyte antigen DQ3 (DQB1\*03) was found in more than 80% of patients with alopecia areata, which suggests that it can be a marker for general susceptibility to alopecia areata. The studies also found that human leukocyte antigen DQ7 (DQB1\*0301) and human leukocyte antigen DR4 (DRB1\*0401) were present significantly more in patients with alopecia totalis and alopecia universalis.<sup>[2,3,4]</sup>

Another gene of interest is the interleukin 1 receptor antagonist gene, which may correlate with disease severity. Finally, the high association of Down syndrome with alopecia areata suggests involvement of a gene located on chromosome 21.

In summary, genetic factors likely play an important role in determining susceptibility and disease severity. Alopecia areata is likely to be the result of polygenic defects rather than a single gene defect. The role of environmental factors in initiating or triggering the condition is yet to be determined.

### **Cytokines**

Interleukin 1 and tumor necrosis factor were shown to be potent inhibitors of hair growth in vitro. Subsequent microscopic examination of these cultured hair follicles showed morphologic changes similar to those seen in alopecia areata.

### **Innervation and vasculature**

Another area of interest concerns the modification of perifollicular nerves. The fact that patients with alopecia areata occasionally report itching or pain on affected areas raises the possibility of alterations in the peripheral nervous system. Circulating levels of the neuropeptide calcitonin gene-related peptide (CGRP) were decreased in 3 patients with alopecia areata compared with control subjects. CGRP has multiple effects on the immune system, including chemotaxis and inhibition of Langerhans cell antigen presentation and inhibition of mitogen-stimulated T-lymphocyte proliferation.

CGRP also increases vasodilatation and endothelial proliferation. Similar findings were reported in another study, in which decreased cutaneous levels of substance P and of CGRP but not of vasoactive intestinal polypeptide were found in scalp biopsy specimens. The study also noted a lower basal blood flow and greater vasodilatation following intradermal CGRP injection in patients with alopecia areata compared with control subjects. More studies are needed to shed light on the significance of these findings.

### **Viral etiology**

Other hypotheses have been proposed to explain the pathophysiology of alopecia areata, but more evidence is needed to support them. Alopecia areata was believed to possibly have an infectious origin, but no microbial agent has been isolated consistently in patients. Many efforts have been made to isolate cytomegalovirus, but most studies have been negative.<sup>[5]</sup>

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## FREQUENCY

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### UNITED STATES

Prevalence in the general population is 0.1-0.2%. The lifetime risk of developing alopecia areata is estimated to be 1.7%. Alopecia areata is responsible for 0.7-3% of patients seen by dermatologists.<sup>[6,7]</sup>

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### INTERNATIONAL

Worldwide prevalence of alopecia areata is the same as that in the United States.

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## MORTALITY/MORBIDITY

Alopecia areata is a benign condition and most patients are asymptomatic; however, it can cause emotional and psychosocial distress in affected individuals. Self-consciousness concerning personal appearance can become important. Openly addressing these issues with patients is important in helping them cope with the condition.

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## RACE

All races are affected equally by alopecia areata; no increase in prevalence has been found in a particular ethnic group.

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## SEX

Data concerning the sex ratio for alopecia areata vary slightly in the literature. In one study including 736 patients, a male-to-female ratio of 1:1 was reported.<sup>[8]</sup> In another study on a smaller number of patients, a slight female preponderance was seen.

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## AGE

Alopecia areata can occur at any age from birth to the late decades of life. Congenital cases have been reported. Peak incidence appears to occur from age 15-29 years. As many as 44% of people with alopecia areata have onset at younger than 20 years. Onset in patients older than 40 years is seen in less than 30% of patients with alopecia areata.

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## CLINICAL

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### HISTORY

The natural history of alopecia areata is unpredictable. Extreme variations in duration and extent of the disease occur from patient to patient. Alopecia areata most often is asymptomatic, but some patients (14%) experience a burning sensation or pruritus in the affected area. The condition usually is localized when it first appears. Of patients with alopecia areata, 80% have only a single patch, 12.5% have 2 patches, and 7.7% have multiple patches. No correlation exists between the number of patches at onset and subsequent severity. Alopecia areata most often affects the scalp (66.8-95%);

however, it can affect any hair-bearing area. The beard is affected in 28% (males; see first image below), eyebrows in 3.8%, and extremities in 1.3% of patients (see second image below). More than one area can be affected at once.



ALOPECIA AREATA AFFECTING THE BEARD.



#### ALOPECIA AREATA AFFECTING THE ARMS.

- Localized alopecia areata: Episodes of localized (<50% involvement) patchy alopecia areata usually are self-limited; spontaneous regrowth occurs in most patients within a few months, with or without treatment.
- Extensive alopecia areata: Extensive (>50% involvement) forms of alopecia areata are less common. Alopecia totalis or alopecia universalis are reported to occur at some point in 7% of patients; alopecia areata involving more than 40% hair loss is seen in 11%. The proportion of patients with alopecia totalis appears to decrease with every decade of life.
  - In 30% of patients with alopecia totalis, complete hair loss occurred within 6 months after onset of disease. Sharma et al<sup>[9]</sup> reported a mean progression period to alopecia totalis of 4 months after onset. The natural evolution of alopecia totalis is unpredictable, but recurrences of alopecia areata (not necessarily alopecia totalis) are expected.
  - In a study involving 736 patients,<sup>[8]</sup> the relapse rate was 90% over 5 years. One percent of children and 10% of adults can experience long-lasting regrowth. Forty-four percent of children and 34% of adults experience a significant period of normal or near-normal hair growth. Twenty-two percent of children and 34% of adults do not experience regrowth.
- Associated conditions: Because some of the entities associated with alopecia areata occur uncommonly in the general population, a large number of patients with alopecia areata need to be examined to confirm whether an increased prevalence of these conditions exists among patients with alopecia areata. Unfortunately, most studies are performed on small groups; therefore, the data should be interpreted carefully.

- Atopic dermatitis is seen in 9-26% of patients with alopecia areata. In the general population, the prevalence of atopic dermatitis in children in temperate developed countries varies from 5-20%. In adults, the prevalence decreases to 2-10%. Some authors have found atopy to be a poor prognostic factor for alopecia areata.
- Vitiligo is seen with an incidence varying from 1.8-3% compared with 0.3% in control subjects. Also see Vitiligo.
- Clinically evident thyroid disease was found in 0.85% of 1700 patients with alopecia areata.<sup>[10]</sup> The prevalence of thyroid disease determined on a clinical or laboratory basis varies among studies from 0.85-14.7%. The incidence of thyroid disease in control subjects is estimated to be 0.17-2%. The presence of microsomal antibodies is found in 3.3-16% of patients. Antibodies can be found with or without signs or symptoms of thyroid disease, but patients with positive autoantibodies have a higher incidence of functional abnormalities found on thyroid-releasing hormone tests (26% vs 2.8%). The incidence of thyroid microsomal and thyroglobulin antibodies in control subjects is 7%. Other studies have not supported these results. A study in 100 patients with alopecia areata failed to find an increased incidence of circulating autoantibodies, including mitochondrial and thyroglobulin antibodies.
- Collagen-vascular diseases have been found in 0.6-2% of patients with alopecia areata, while the incidence in control subjects is 0.17%. The incidence of alopecia areata in 39 patients with lupus erythematosus was 10% in a study by Werth et al,<sup>[11]</sup> in contrast to 0.42% of general dermatologic patients.
- Diabetes mellitus was found to be more common in control subjects (1.4%) than in patients with alopecia areata (0.4%).<sup>[12]</sup> The occurrence of alopecia areata may protect against the appearance of type I diabetes mellitus. However, the incidence of type I diabetes mellitus was significantly higher in relatives of patients with alopecia areata compared with the general population.
- Alopecia areata is seen in 6-8.8% of patients with Down syndrome, but only 0.1% of patients with alopecia areata have Down syndrome. The high frequency of alopecia areata in patients with Down syndrome suggests that a genetic linkage for alopecia areata may exist on chromosome 21.
- Anxiety, personality disorders, depression, and paranoid disorders are seen with increased prevalence varying from 17-22% of patients, and the lifetime prevalence of psychiatric disorders is estimated to be 74% in patients with alopecia areata. Psychiatric problems are seen in both children and adults. No association has been made between the severity of the psychiatric disorder and that of alopecia areata.
- Stressful life events within the 6-month period preceding episodes of alopecia areata were significantly higher in patients with alopecia areata compared with patients with androgenetic alopecia or tinea capitis.<sup>[13]</sup> Major stress factors (eg, death in family) were reported in 12% of patients.
- Others associations in some studies include pernicious anemia, myasthenia gravis, ulcerative colitis, lichen planus, and *Candida* endocrinopathy syndrome.
- Precipitating factors: A precipitating factor can be found in 15.1% of patients with alopecia areata. Major life events, febrile illnesses, drugs, pregnancy, trauma, and many other events have been reported, but no clear conclusions can be drawn. Despite these findings, most patients with alopecia areata do not report a triggering factor preceding episodes of hair loss.

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## PHYSICAL

The presence of smooth, slightly erythematous (peach color) or normal-colored alopecic patches is characteristic. The presence of exclamation point hairs (ie, hairs tapered near proximal end) is pathognomonic but is not always found. A positive result from the pull test at the periphery of a plaque usually indicates that the disease is active, and further hair loss can be expected. Additionally, hair loss

on other hair-bearing areas also favors the diagnosis. The most common presentation is the appearance of one or many round-to-oval denuded patches. No epidermal changes are associated with the hair loss.

Alopecia areata can be classified according to its pattern. Hair loss most often is localized and patchy (see image below).



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#### PATCHY ALOPECIA AREATA.

A reticular pattern occurs when hair loss is more extensive and the patches coalesce. An ophiasis pattern occurs when the hair loss is localized to the sides and lower back of the scalp (see image below).



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#### OPHIASIS PATTERN OF ALOPECIA AREATA.

Conversely, sisaipho (ophiasis spelled backwards) pattern occurs when hair loss spares the sides and back of the head (see image below).



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SISAIPHO PATTERN OF ALOPECIA AREATA.

Alopecia totalis occurs with 100% hair loss on the scalp (see image below).



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#### ALOPECIA TOTALIS.

Alopecia universalis occurs with complete loss of hair on all hair-bearing areas. Alopecia areata usually is focal; however, it can be diffuse, thereby mimicking telogen effluvium (TE) or the type of androgenetic alopecia seen in women (see image below).



## DIFFUSE ALOPECIA AREATA.

See also Androgenetic Alopecia and Telogen Effluvium.

- Dermoscopy
  - Dermoscopic findings have been reported to be helpful in the diagnosis of difficult cases of alopecia areata.
  - The presence of yellow dots seems to be a specific feature of alopecia areata and has been reported to be present in 95% of patients, regardless of their disease stages. Following histopathological correlation, these yellow dots represent degenerated follicular keratinocytes and sebum contained within the ostium of hair follicles. Although occasionally seen in advanced male-pattern hair loss, yellow dots are not seen in cases of female-pattern hair loss, scarring alopecia, or telogen effluvium.
  - Other dermoscopic signs reported include black dots, tapering hairs, broken hairs, and clustered short vellus hairs.
- Nail involvement
  - Nail involvement is found in 6.8-49.4% of patients and most commonly is seen in patients with severe forms of alopecia areata.
  - Pitting is the most common finding.
  - Several other abnormalities have been reported (eg, trachyonychia, Beau lines, onychorrhexis, onychomadesis, koilonychia, leukonychia, red lunulae).
  - Fingernails predominantly are affected.

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## CAUSES

The true cause of alopecia areata remains unknown. The exact role of possible factors needs to be clarified (see Pathophysiology).

- No known risk factors exist for alopecia areata, except a positive family history.
- The exact role of stressful events remains unclear, but they most likely trigger a condition already present in susceptible individuals, rather than acting as the true primary cause.

## DIFFERENTIAL DIAGNOSES

Androgenetic Alopecia  
Pseudopelade, Brocq  
Syphilis  
Telogen Effluvium  
Tinea Capitis  
Trichotillomania

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## OTHER PROBLEMS TO BE CONSIDERED

- Trichotillomania: Alopecic patches have unusual shapes and sizes and show broken hairs; no inflammation or epidermal change occurs. A scalp biopsy can be helpful if the diagnosis is difficult clinically.
- Tinea capitis: The diagnosis is suggested by erythema, scaling, and crusting locally on the scalp.
- Scarring alopecia and posttraumatic alopecia: These can be differentiated by the absence of follicular ostia or some degree of atrophy.
- Syphilis: Syphilis rarely is seen but should be suspected in patients at high risk or with other signs or symptoms.
- Telogen effluvium and androgenetic alopecia: Exclude these when hair loss is diffuse. In androgenetic alopecia, hair loss is patterned and usually is slowly progressive rather than acute. Differentiating telogen effluvium from diffuse alopecia areata is difficult in the absence of an obvious precipitating factor that can result in telogen effluvium. Noting hair loss on other hair-bearing areas can be helpful and favors a diagnosis of alopecia areata.

## WORKUP

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## PROCEDURES

Diagnosis usually can be made on clinical grounds; a scalp biopsy seldom is needed, but it can be helpful when the clinical diagnosis is less certain.

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## HISTOLOGIC FINDINGS

A histologic diagnosis of alopecia areata can be made when characteristic features are present. Horizontal sections usually are preferred to vertical sections because they allow examination of multiple hair follicles at different levels.

The most characteristic feature is a peribulbar lymphocytic infiltrate, which is described as appearing similar to a swarm of bees. The infiltrate often is sparse and usually involves only a few of the affected hairs in a biopsy specimen. Occasionally, no inflammation is found, which can result in diagnostic difficulties. A significant decrease in terminal hairs is associated with an increase in vellus hairs, with a ratio of 1.1:1 (normal is 7:1). Other helpful findings include pigment incontinence in the hair bulb and follicular stellae.

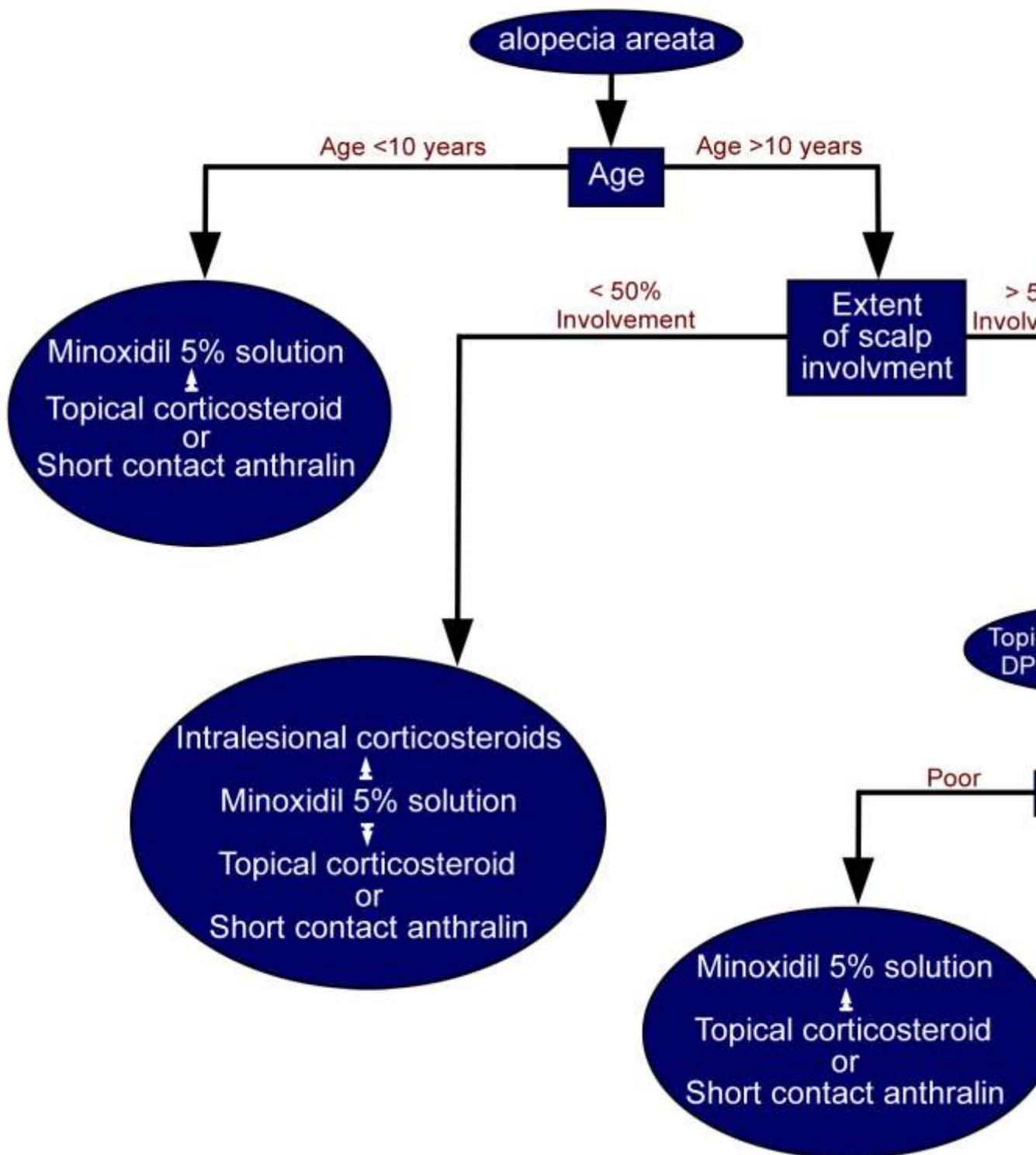
A shift occurs in the anagen-to-telogen ratio, which is not specific. The normal ratio is approximately 90% anagen phase to 10% telogen phase hair follicles; in alopecia areata, 73% of hairs are found to be in the anagen phase and 27% in the telogen phase. In long-standing cases of alopecia areata, the percentage of telogen-phase hairs can approach 100%. Degenerative changes of the hair matrix can be found but are uncommon. Eosinophils may be present in fibrous tracts and near hair bulbs.

## TREATMENT

### MEDICAL CARE

See the treatment algorithm below.

## Treatment protocol for alopecia areata



TREATMENT ALGORITHM FOR ALOPECIA AREATA.

Treatment is not mandatory because the condition is benign, and spontaneous remissions and recurrences are common. Treatments used are believed to stimulate hair growth, but no evidence indicates they can influence the ultimate natural course of alopecia areata. Treatment modalities usually are considered first according to the extent of hair loss and the patient's age.

Assessment of the efficacy of a treatment must be considered with care because the condition is highly unpredictable in presentation, evolution, and response to treatment. Little data exist regarding the natural evolution of the condition. For example, in patients with less than 40% scalp involvement, a study showed no benefit with treatment (minoxidil 1% and topical immunotherapy) over placebo.<sup>[14]</sup> The high spontaneous remission rate makes clearly assessing the true efficacy of a therapy difficult unless appropriate controls with placebo treatment are studied.

For patients with extensive alopecia areata (>40% hair loss), little data exist on the natural evolution. The rate of spontaneous remission appears to be less than in patients with less than 40% involvement. Vestey and Savin<sup>[15]</sup> reviewed 50 patients with extensive alopecia areata. Of the 50 patients, 24% experienced spontaneous complete or nearly complete regrowth at some stage during the observation period of 3-3.5 years. The relapse rate is high in patients with severe forms of alopecia areata.

Patients with alopecia totalis or alopecia universalis usually have a poorer prognosis, and treatment failure is seen in most patients with any therapy.

Because alopecia areata is believed to be an autoimmune condition, different immunomodulators have been used to treat this condition. Additional treatment options for alopecia areata include minoxidil and other treatment modalities.

## **Topical treatments**

### *Corticosteroids*

Corticosteroid therapies can include intralesional injections or topical application.

- For intralesional steroids, few studies are available regarding efficacy; however, they are used widely in the treatment of alopecia areata.
  - Intralesional steroids are the first-line treatment in localized conditions.
  - In a study including 84 patients, regrowth on treated areas was present in 92% of patients with patchy alopecia areata and 61% of patients with alopecia totalis. Regrowth persisted 3 months after treatment in 71% of patients with patchy alopecia areata and 28% of patients with alopecia totalis. Regrowth usually is seen within 4-6 weeks in responsive patients. Patients with rapidly progressive, extensive, or long-standing alopecia areata tend to respond poorly.
  - Another study showed regrowth in most patients (480) treated with intralesional steroids, except in 2 patients with alopecia universalis.
  - Hair growth may persist for 6-9 months after a single injection.
  - Injections are administered intradermally using a 3-mL syringe and a 30-gauge needle.
  - Triamcinolone acetonide (Kenalog) is used most commonly; concentrations vary from 2.5-10 mg/mL. The lowest concentration is used on the face. A concentration of 5 mg/mL is usually sufficient on the scalp.

- Less than 0.1 mL is injected per site, and injections are spread out to cover the affected areas (approximately 1 cm between injection sites; see image below).
- 



#### CORTICOSTEROID INJECTION.

- Adverse effects mostly include pain during injection and minimal transient atrophy (10%). The presence of atrophy should prompt a reduction in the triamcinolone acetonide concentration and avoidance of the atrophic site.
- Injections are administered every 4-6 weeks.
- Although intralesional injections of triamcinolone acetonide are usually recommended for alopecia areata with less than 50% involvement, a report showed that 6 of 10 patients had regrowth.<sup>[16]</sup> Although injections may work in extensive alopecia areata, results are unlikely if no response is observed at 6 months (personal observation).
- For topical steroids, again, few studies have been performed regarding efficacy in the treatment of alopecia areata; they can however be useful, especially in children who cannot tolerate injections.
  - Fluocinolone acetonide cream 0.2% (Synalar HP) twice per day induced a satisfactory-to-excellent response in 61% of patients, which was maintained in 71% of patients. Children younger than 10 years responded better, as did patients with a duration of hair loss of less than 1 year.
  - Betamethasone dipropionate cream 0.05% (Diprosone) showed similar efficacy.
  - A 2005 study by Tosti et al<sup>[17]</sup> in patients with alopecia totalis or alopecia universalis showed that the use of 2.5 g of clobetasol propionate under occlusion with a plastic

film 6 d/wk for 6 months induced regrowth in 8 (28.5%) of 28 patients. Regrowth was seen 6-14 weeks after the onset of therapy. Regrowth was maintained for at least 6 months after cessation of therapy in 5 (62.5%) of 8 patients. Even though only 17.8% of patients showed long-term benefits from that treatment, it should be kept in mind that the study was performed in a subgroup of patients that is usually refractory to treatment.

- Treatment must be continued for a minimum of 3 months before regrowth can be expected, and maintenance therapy often is necessary.
- Despite these data, the authors do not believe that monotherapy with a topical steroid has been of great benefit in the authors' practice.
- The most common adverse effect is local folliculitis, which appears after a few weeks of treatment. Telangiectases and local atrophy also have been reported. No systemic adverse effects have been reported.

### *Immunotherapy*

Topical immunotherapy<sup>[18]</sup> is defined as the induction and periodic elicitation of an allergic contact dermatitis by topical application of potent contact allergens.

- Commonly used agents for immunotherapy include squaric acid dibutylester (SADBE) and diphencyprone (DPCP).<sup>[19]</sup> These 2 sensitizers are not present in the natural or industrial environment. Dinitrochlorobenzene (DNCB) has become less popular as a result of reports that it is mutagenic in the Ames assay (a bacterial assay).
- No rigorous toxicologic and pharmacologic studies have been performed on the use of these agents in humans.
- Although DPCP and SADBE have not been found mutagenic in the Ames assay, neither is approved by the US Food and Drug Administration, and unknowns still exist concerning their safety profiles.
- No contaminants have been found in SADBE. Acetone solutions and alcohol solutions of SADBE are equally stable for 2 months under storage conditions.
- DPCP occasionally can contain mutagenic contaminants; therefore, it should be screened periodically to ensure purity. No formal data are available on DPCP regarding its longevity in solution.
- Cosmetically acceptable regrowth with topical immunotherapy rates in patients with severe alopecia areata (>50% involvement) varies from 22-68%. Most studies have a success rate of 30-50%. Wiseman et al<sup>[20]</sup> retrospectively reported the results of a large cohort of 148 consecutive patients treated with DPCP.
  - Their analysis showed that the cumulative patient response at 32 months was 77.9%.
  - The response rate varied with the extent of the alopecia. Cosmetically acceptable regrowth was seen in 17.4% of patients with alopecia totalis or alopecia universalis, 60.3% in patients with 75-99% hair loss, 88.1% in patients with 50-74% hair loss, and 100% regrowth in those with 25-49% hair loss.
  - Age at onset was also a significant variable, with older age at onset leading to a better prognosis. A lag period of 3 months was usually present between the onset of therapy and the presence of regrowth.
  - The median time to achieve significant regrowth was 12.2 months. Some patients showed regrowth on the treated side after 18 months of therapy.
  - No benefit is achieved with continuing therapy after 24 months in the absence of regrowth.
  - The relapse rate after reaching significant regrowth was 62.6%.
- In a report of a 5-year experience with the use of DPCP, 97 subjects received continued therapy with DPCP. A response rate of greater than 75% was seen in 15% at 6 months, 49% at 12 months, 53% at 18 months, and 56% at 24 months. The only variable that seemed to

affect response to treatment was the baseline extent of the alopecia areata. A greater than 75% response rate was seen in 100% of patients with 25-49% hair loss at baseline, 77% of those with 50-74% loss at baseline, 54% of those with 75-99% loss at baseline, 50% of alopecia totalis patients, and 41% of alopecia universalis patients demonstrated a response. Maintenance treatment (once every 1-4 wk) appeared to reduce the risk of relapse (>25% hair loss). Only 18% of patients experienced relapse on maintenance therapy, compared with 57% in those who discontinued treatment<sup>[21]</sup>

- The type of alopecia areata before treatment, duration of the disease, and the presence of nail changes were found to predict a lower response to treatment. Age at onset and sex of the patient do not appear to influence the prognosis. Controversy exists concerning whether atopy is an adverse prognosis factor.
- Topical immunotherapy has been used for almost 20 years; no serious adverse effects have been reported.
- The most common side effect, which is desired, is a mild contact dermatitis (redness, scaling, itching).
- Adverse effects include cervical lymphadenopathy and pigment changes. Vitiligo developed on the application site in 6.7-7.5% of patients. Transient leukoderma on a distant untreated area has been reported. Of patients who develop vitiligo, 31% (4 of 13) had a history of vitiligo. Only 0.75% of patients developed hyperpigmentation. Confetti-type dyschromia (ie, hyperpigmentation, hypopigmentation) has been described as an adverse effect of DPCP treatment and occurred in 1.6% of 243 patients treated. Less common adverse effects include erythema multiforme-like eruptions and urticaria, which were reported in 3 patients treated with DPCP.
- The mechanism of action of topical immunotherapy is unknown. Antigenic competition has been hypothesized. That is, the introduction of a second antigen can initiate a new infiltrate containing T-suppressor cells and suppressor macrophages that may modify the preexisting infiltrate and allow regrowth.
- Because topical immunotherapy involves the production of contact sensitivity in a previously naive patient, it is best to seek approval for the treatment by the ethics review board and to have the patient sign an informed consent.
- Both SADBE and DPCP appear to be equally effective. Acetone-based solutions usually are preferred because they evaporate quickly, allowing patients to wear a hat or wig immediately after treatment. Quick drying also decreases the chances of dissemination to other body parts by contact.
- Treatment is provided weekly.
- The patient first is sensitized directly on the scalp with a 2% concentration on a small area (2 cm).
- The following week, a low concentration (0.0001%) is applied.
- The concentration is increased slowly every week as needed until a mild tolerable allergic contact dermatitis is elicited. Many concentrations are available that achieve this goal.
- Treating only half of the head allows the physician to use the untreated half as a control. Once regrowth occurs on the treated half, treatment can be applied to the entire scalp. If regrowth initially occurs on both sides, spontaneous remission is likely, although treatment cannot be excluded as the cause.
- Avoid severe contact dermatitis. Patients are advised to avoid light exposure on the scalp for 48 hours because light degrades the chemical. Patients also are advised not to wash the scalp for 48 hours.
- Initial regrowth may be seen at weeks 12-24. Once cosmetically acceptable regrowth is achieved, the treatment can be tapered gradually. Almost all patients relapse if the treatment is discontinued, and maintenance treatment is needed.

### *Anthralin*

The efficacy of anthralin was assessed in 3 studies, which unfortunately were uncontrolled.

- Both short-contact and overnight treatments have been used. Anthralin concentrations varied from 0.2-1%.
- A 2004 study by Tang et al<sup>[22]</sup> showed no benefit in using anthralin. Other studies showed a response rate of 20-75%, respectively, for patchy alopecia areata and a 25% response rate for alopecia totalis. The mean time to response was 11 weeks, and the mean time to cosmetic response was 23 weeks. Anthralin was used by Tang et al in balding C3H/HeJ mice, which is one animal model for alopecia areata. Half the body was treated with anthralin 0.2%, while the other side was treated with the vehicle ointment. Regrowth was seen on the treated side in 64% of mice after 10 weeks. Four mice had almost complete regrowth. The untreated side showed either no regrowth or continued hair loss. Cytokine studies performed with an RNase protection assay showed that tumor necrosis factor-alpha and -beta were inhibited in mice that responded to treatment.
- Most patients experienced irritant contact dermatitis. Whether the dermatitis is necessary for efficacy remains under debate.
- Cosmetically acceptable regrowth was maintained during therapy in 71% of responders. No correlation exists between duration of the current episode and response to treatment.
- Adverse effects include pruritus, erythema, scaling folliculitis, local pyoderma, and regional lymphadenopathy. Withholding treatment for a few days results in rapid disappearance of adverse effects. Treatment then can be reinstated, but anthralin should be left on for shorter periods. Staining of clothes and skin can be a concern.
- The mechanism of action of anthralin is unknown. Most likely, it creates inflammation by generating free radicals, which have antiproliferative and immunosuppressive actions.

### *Minoxidil*

Minoxidil appears to be effective in the treatment of alopecia areata in patients with extensive disease (50-99% hair loss). Response rates in that group vary from 8-45%. Minoxidil was of little benefit in patients with alopecia totalis or alopecia universalis.

- The 5% solution appears to be more effective.
- No more than 25 drops are applied twice per day regardless of the extent of the affected area.
- Initial regrowth can be seen within 12 weeks, but continued application is needed to achieve cosmetically acceptable regrowth.
- Minoxidil usually is well tolerated. Adverse effects include distant hypertrichosis (5%) and irritation (7%).
- The exact mechanism of action of minoxidil remains unclear. Minoxidil does not appear to have either a hormonal or an immunosuppressant effect. Minoxidil most likely has a direct mitogenic effect on epidermal cells, both in vitro and in vivo. Anagen-phase hair bulbs plucked from men applying minoxidil showed a significant increase in proliferation index as measured by DNA flow cytometry. Minoxidil also has been shown to prolong the survival time of keratinocytes in vitro. Finally, minoxidil may oppose intracellular calcium entry. Calcium influx normally enhances epidermal growth factors to inhibit hair growth. Minoxidil is converted to minoxidil sulfate, which is a potassium channel agonist and enhances potassium ion permeability, thus opposing the entry of calcium into cells. Local vasodilatation does not appear to play a primary role in hair growth associated with minoxidil.

### **Systemic treatments**

#### *Psoralen plus UV-A*

Many studies have been performed regarding the efficacy of psoralen plus UV-A (PUVA) in the treatment of alopecia areata, and the initial response rate varies from 20-73%. The relapse rate, unfortunately, is high (50-88%). Most patients relapse within a few months (mean 4-8 mo) after treatment is stopped.

- Both systemic and topical PUVA therapies have been used.
- The number of treatments required for regrowth varies, but 20-40 treatments usually are sufficient in most cases.
- A younger age at onset, a longer duration of disease, and the presence of alopecia totalis or alopecia universalis appear to indicate a poorer outcome.
  - Taylor and Hawk<sup>[23]</sup> published 10 years of experience with PUVA. The initial response rate (>90% regrowth) was comparable to other studies and was 43.8% for partial alopecia areata and 50% for alopecia totalis and alopecia universalis. However, after excluding patients with vellus hair regrowth and patients who relapsed rapidly in the follow-up period (approximately 4 mo), they found the success rate to be, at best, 6.3% for partial alopecia areata and 12.5% for alopecia totalis and alopecia universalis. They concluded that PUVA generally is not an effective long-term treatment for alopecia areata.
  - PUVA is a relatively safe treatment modality; adverse effects include burning and, possibly, an increased risk of skin cancer.

### *Prednisone*

The use of systemic steroids for the treatment of alopecia areata is sometimes justifiable, but hair loss frequently follows discontinuation of the medication and benefits must be carefully weighed against long-term risks. Some authors support a beneficial role of systemic steroids in halting the progression of alopecia areata,<sup>[24]</sup> but many others have had poor results with this form of therapy.

- The rate of regrowth varies greatly (27-89%), and many dose regimens have been used in these studies.
- Although the initial regrowth appears promising, the prednisone dose necessary to maintain cosmetic growth usually must be high enough that adverse effects are inevitable, and most patients relapse after therapy is discontinued.
- Some benefit was shown using minoxidil 2% solution applied twice per day following a 6-week taper of prednisone, but the relapse rate remained at a minimum of 50% at 4 months in the treated group.
- Adverse effects from systemic therapy were common in these reports and included diabetes, weight gain, hypertension, psychological changes, osteoporosis, suppression of the adrenocorticotrophic axes, striae, acne, hypertrichosis, and purpura.
- Systemic steroids most likely are effective via their immunosuppressive effects.
- An initial benefit may occur by using systemic prednisone in some patients, but the relapse rate is high, and it does not appear to alter the course of the condition.
- Systemic prednisone is not an agent of choice for alopecia areata because of the adverse effects associated with both short- and long-term treatment.

### *Cyclosporine*

Cyclosporine has been used both topically and systemically in the treatment of alopecia areata.

- Topical cyclosporine has not proven to be effective in severe alopecia areata because no patient (0 of 10) showed benefit with application of a 10% cyclosporin A (CsA) solution twice per day for 12 months.

- Another study of 14 patients using a 5% solution of cyclosporine twice per day for 4-6 months reported vellus growth in 3 of 14 patients and normal hair growth in 3 patients with patchy alopecia areata. No regrowth was seen in 8 of the patients.
- Neither study showed systemic absorption of CsA, and routine blood examination showed only a transient increase of hepatic enzymes in 1 patient.
- Oral cyclosporine was effective in the DEBR model for alopecia areata. All rats had a full pelage by 5 weeks of treatment with 10 mg/kg/d, 5 d/wk for 7 weeks. Studies in humans also have proven efficacy with doses of 6 mg/kg/d for 3 months in 6 patients. All patients experienced regrowth, and cosmetically acceptable regrowth was seen in 3 of 6 patients. Unfortunately, all patients relapsed within 3 months of discontinuation of cyclosporine. No evidence indicates that CsA can prevent hair loss during an active episode because reports have described patients taking CsA who developed alopecia areata while they were under treatment for unrelated conditions.
- The mechanism of action of cyclosporine remains unclear. It may act through its immunosuppressive effect, because, in patients who regrew hair, clearance of immune cells from the hair follicles and alteration in the balance of regulatory lymphocytes occurred (ie, decrease of the CD4/CD8 ratio). Cyclosporine causes hypertrichosis in patients treated for conditions unrelated to hair loss. The mechanism by which cyclosporine stimulates hair growth remains unknown.
- In conclusion, topical cyclosporine has shown limited efficacy. Although systemic CsA appears to be effective in alopecia areata, the adverse effect profile, the recurrence rate after treatment discontinuation, and thus, the inability to produce long-term remissions, make CsA unattractive for the treatment of alopecia areata.

### *Tacrolimus*

Regrowth was shown on the application site of topical tacrolimus in 2 studies using the DEBR model. Oral tacrolimus was ineffective. No benefit was shown in the use of topical tacrolimus for alopecia areata in a small 2005 study by Price et al that included 11 patients.<sup>[25]</sup>

### *Interferon*

A study of 11 patients with alopecia areata ranging from patchy alopecia areata to alopecia universalis showed no benefit using intralesional interferon alfa-2 (1.5 million IU, 3 times per wk for 3 wk).

### *Dapsone*

Dapsone at 50 mg twice per day was used in a 6-month, double-blind, placebo-controlled study. Of patients in the study, 54% (7 of 13) withdrew from the dapsone group because of adverse effects such as malaise. Of the remaining 6 patients, 3 experienced generalized growth of terminal hair, compared with 4 (4 of 13) patients in the placebo group, who experienced only sparse patchy regrowth of vellus hair. The authors concluded that although dapsone showed some efficacy, the high incidence of adverse effects rendered it unacceptable. Another study showed a rate of success comparable to the occurrence of spontaneous regrowth reported in the literature.

### *Methotrexate*

Joly<sup>[26]</sup> reported 22 patients with long-standing, severe alopecia areata who responded well to methotrexate, with or without systemic corticosteroids. Although the results from that study are surprisingly good, a more standardized study involving more patients is needed because other dermatologists have not had such good efficacy with methotrexate.

## Other treatment modalities

Many other modalities have been reported to have variable response rates in small studies. These include latanoprost,<sup>[27]</sup> nitrogen mustard, massage and relaxation, isoprinosine, acupuncture, and aromatherapy, among others. The efficacy of these treatments needs to be demonstrated in larger, placebo-controlled trials before they can be recommended.

### *Biological agents*

The majority of studies, including prospective, randomized placebo controlled studies<sup>[28,29]</sup> and case reports published in the last few years regarding the use of biologic agents (including adalimumab, alefacept, etanercept and infliximab) in the treatment of alopecia areata did not show efficacy, and some patients developed alopecia areata while under treatment with biologic agents for other conditions.

### *Nonpharmacologic methods*

A systematic MEDLINE search could not find any study with sufficient validity to provide scientific evidence of benefit with complementary and alternative medicine therapies for alopecia areata.<sup>[30]</sup>

A study on hypnosis for refractory alopecia areata did not show efficacy of regrowth, but it did show that hypnosis can improve depression, anxiety, and quality of life in affected patients.<sup>[31]</sup>

Cosmetic treatments for patients with alopecia areata include dermatography and hairpieces. Dermatography has been used to camouflage the eyebrows of patients with alopecia areata. Follow-up visits at 4 years showed that 30 of 39 of patients demonstrated excellent cosmetic results and 3 had good results. On average, 2-3 sessions lasting 1 hour each were required for each patient. No adverse effects were reported. Hairpieces are useful for patients with extensive disease and allow them to carry on their usual social life. Reassure patients about the natural look provided by hairpieces.

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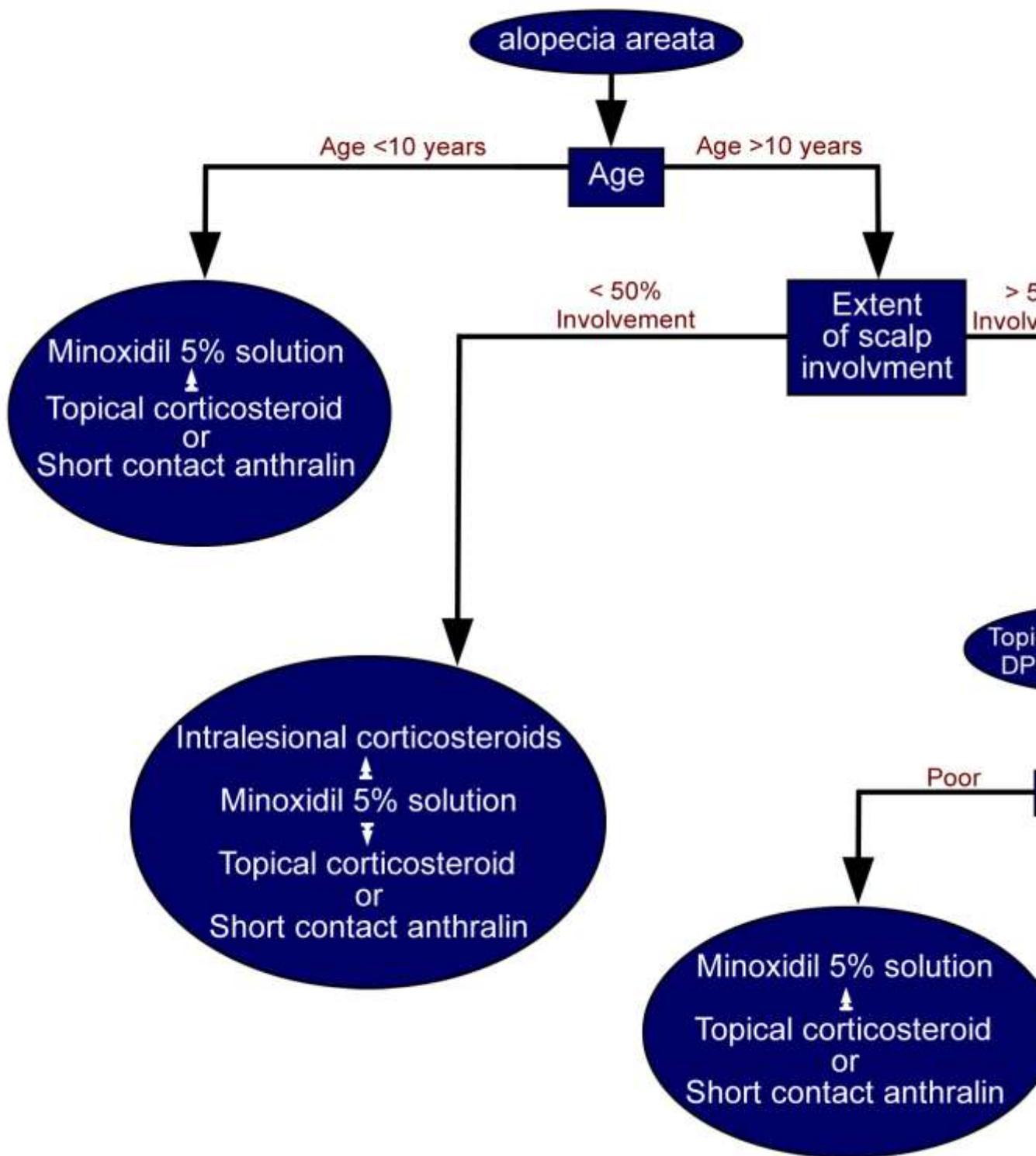
## SURGICAL CARE

Surgical intervention has no role in the treatment of alopecia areata.

## MEDICATION

Therapies most commonly include corticosteroid injections, corticosteroid creams, minoxidil, anthralin, topical immunotherapy, and phototherapy. The choice of one agent over the others depends on patient age (children do not always tolerate adverse effects), extent of condition (localized vs extensive), and the patient's personal preference. The University of California (San Francisco) and University of British Columbia have devised a treatment algorithm that can guide the physician in the treatment of alopecia areata (see image below).

## Treatment protocol for alopecia areata



TREATMENT ALGORITHM FOR ALOPECIA AREATA.

For patients younger than 10 years, options include corticosteroid creams, minoxidil, and anthralin. For adults with less than 50% scalp involvement, the first option usually is an intralesional corticosteroid, followed by corticosteroid cream, minoxidil, and anthralin. For adults with greater than 50% scalp involvement, topical immunotherapy and phototherapy are additional options.

---

## IMMUNOMODULATORS

Because alopecia areata is believed to be an autoimmune condition, different immunomodulators have been used to treat the condition. Exact mechanism of action of topical immunotherapy is unknown. Antigenic competition was hypothesized (ie, introduction of a second antigen can initiate a new infiltrate containing T-suppressor cells and suppressor macrophages that may modify preexisting infiltrate and allow regrowth).

Commonly used agents for immunotherapy include SADBE and DPCP.

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## SQUARIC ACID DIBUTYLESTER AND DIPHENCYPRONE

May modulate key factors of the immune system.

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## DOSING

### ADULT

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First, sensitize patient directly on scalp using 2% concentration on small area (2 cm); the following wk, apply lowest concentration (0.0001%); slowly increase concentration each wk thereafter prn until mild tolerable allergic contact dermatitis is elicited.

### PEDIATRIC

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<12 years: Not established  
>12 years: Apply as in adults

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## INTERACTIONS

None reported.

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## CONTRAINDICATIONS

Documented hypersensitivity, documented anaphylaxis, pregnancy, breastfeeding

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## PRECAUTIONS

## PREGNANCY

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C - Fetal risk revealed in studies in animals but not established or not studied in humans; may use if benefits outweigh risk to fetus

## PRECAUTIONS

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Local common adverse effects include burning, itching, blistering, crusting, urticaria, eczema, and cervical lymphadenopathy; less common adverse effects include vitiligo, dyschromia in confetti, erythema multiforme-like eruptions, and urticaria

---

## CYCLOSPORINE (SANDIMMUNE, NEORAL)

Used both topically and systemically for the treatment of alopecia areata. Topical cyclosporine has shown limited efficacy. Although systemic CsA appears to be effective in alopecia areata, the adverse effect profile, recurrence rate after treatment discontinuation, and inability to produce long-term remissions make CsA unattractive for the treatment of alopecia areata.

Mechanism by which cyclosporine stimulates hair growth remains unknown. May act through its immunosuppressive effect because patients who regrew hair had clearance of immune cells from the hair follicles and alteration in the balance of regulatory lymphocytes (ie, decreased CD4/CD8 ratio). Causes hypertrichosis in patients treated for conditions unrelated to hair loss.

---

## DOSING

### ADULT

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Topical cyclosporine: Apply 5-10% formulations bid  
Systemic cyclosporine: 1-6 mg/kg/d PO in 2 divided doses

### PEDIATRIC

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Not established; see note in Contraindications

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## INTERACTIONS

Erythromycin, clarithromycin, azithromycin, norfloxacin ciprofloxacin, cephalosporins, doxycycline, ketoconazole, itraconazole, fluconazole, ritonavir, indinavir, saquinavir, nelfinavir, diltiazem, verapamil, nifedipine, cimetidine, methylprednisolone, dexamethasone, thiazides, furosemide, allopurinol, bromocriptine, danazol, amphotericin B, metoclopramide, oral contraceptive pills, warfarin, and grapefruit juice increase CsA levels

Rifampin, rifabutin, nafcillin, carbamazepine, phenobarbital, phenytoin, valproate, octreotide, and ticlopidine decrease CsA levels

Tobramycin, gentamicin, ketoconazole, azapropazone, TMP-SMZ, vancomycin, sulindac, amphotericin B, indomethacin, naproxen, cimetidine, ranitidine, diclofenac, tacrolimus, and melphalan

potentiate renal toxicity

Because of decreased renal clearance, coadministration with digoxin may lead to digitalis toxicity, coadministration with lovastatin may lead to myositis, and coadministration with methylprednisolone or prednisolone may lead to convulsions; coadministration with ACE inhibitors, potassium supplements, and potassium-sparing diuretics increases risk of hyperkalemia

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## CONTRAINDICATIONS

Absolute: Significantly decreased renal function, uncontrolled hypertension, hypersensitivity, clinically cured or persistent malignancy (except nonmelanoma skin cancer)

Relative: Age <18 or >64 (however, CsA at 5 mg/kg/d for 6 wk shown to be safe and effective for patients aged 2-16 y with severe atopic dermatitis), controlled hypertension, planning to receive a live-attenuated vaccine, active infection or evidence of immunodeficiency, concurrent phototherapy, coal tar, methotrexate (or other immunosuppressive agents), pregnancy or lactation, unreliable patient, severe hepatic dysfunction

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## PRECAUTIONS

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### PREGNANCY

C - Fetal risk revealed in studies in animals but not established or not studied in humans; may use if benefits outweigh risk to fetus

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## PRECAUTIONS

Evaluate renal and liver function often by measuring BUN, serum creatinine, serum bilirubin, and liver enzyme levels; may increase risk of infection and lymphoma; reserve IV use for patients who cannot take PO

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## METHOXSALLEN (8-MOP, OXSORALEN)

Inhibits mitosis by binding covalently to pyrimidine bases in DNA when photoactivated by UV-A.

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## DOSING

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### ADULT

0.6-0.8 mg/kg PO, 1-2 h prior to UV-A exposure; can be administered topically (cream, lotion, soak)  
Supplied as methoxsalen 10 mg cap (generic) or a 1% lotion (Oxsoralen lotion) for topical use

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### PEDIATRIC

Not established

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## INTERACTIONS

Toxicity increases with phenothiazines, griseofulvin, nalidixic acid, tetracyclines, thiazides, or sulfanilamides; bacteriostatic soaps and organic staining dyes

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## CONTRAINDICATIONS

Documented hypersensitivity, history of melanoma or squamous cell carcinoma, photosensitive conditions (eg, lupus, porphyria), intolerance to heat, or claustrophobia, ingestion of photosensitizing drugs, hepatic disease, arsenic therapy

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## PRECAUTIONS

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### PREGNANCY

C - Fetal risk revealed in studies in animals but not established or not studied in humans; may use if benefits outweigh risk to fetus

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### PRECAUTIONS

Severe burns may occur from sunlight or UV-A if dose or treatment frequency exceeded; use only if response to other forms of therapy is inadequate; long-term use may increase risk of skin cancer

---

## ANTHRALIN (DRITHO-SCALP 0.5% CREAM, ANTHRA-DERM 1% CREAM, DRITHOCREME 1%, MICANOL 1% CREAM)

Synthetic derivative of a tree bark extract. Mechanism of action in alopecia areata is unknown. Most likely creates inflammation by generating free radicals, which have antiproliferative and immunosuppressive actions. Both short-contact and overnight treatments have been used. High concentration (1-3%) is used for short-contact treatments. Lower concentrations (0.1-0.4%) are used for overnight treatments. Applications in excessive amounts may stain clothing.

---

## DOSING

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### ADULT

Apply sparingly to affected areas; usually, short-contact treatments last a few h (depending on level of cutaneous irritation), then wash off with soap and water; overnight treatments apply hs and wash off in morning

---

### PEDIATRIC

Administer as in adults

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## INTERACTIONS

Long-term corticosteroid treatment withdrawal may cause complications of rebound phenomenon (allow 1-wk interval between discontinuation of corticosteroids and initiation of anthralin therapy)

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## CONTRAINDICATIONS

Documented hypersensitivity, acutely or actively swollen psoriatic lesions

---

## PRECAUTIONS

### PREGNANCY

---

C - Fetal risk revealed in studies in animals but not established or not studied in humans; may use if benefits outweigh risk to fetus

### PRECAUTIONS

---

Caution in renal disease; avoid eye contact; if redness develops, discontinue application; adverse effects include pruritus, erythema, scaling folliculitis, local pyoderma, and regional lymphadenopathy; caution on irritated skin because most likely aggravates preexisting condition; may discolor skin to brown-orange color (temporary)

---

## GLUCOCORTICOIDS

Have anti-inflammatory properties and cause profound and varied metabolic effects. In addition, these agents modify the body's immune response to diverse stimuli.

Topical corticosteroids (including intralesional corticosteroids) are safe and easy to use. They are acceptable cosmetically and allow patients to wear hats or wigs shortly after application. They also are relatively inexpensive. While the usefulness of high-potency topical corticosteroids is under debate, they remain a good (painless) option in children.

Intralesional steroids are first-line treatment in localized conditions.

Oral prednisone usually is reserved for patients with rapidly progressive alopecia areata. The relapse rate is high, and the potential for multiple severe adverse effects when used long term limits its usefulness.

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## CLOBETASOL PROPIONATE (TEMOVATE)

Class I superpotent topical steroid. Suppresses mitosis and increases synthesis of proteins that decrease inflammation and cause vasoconstriction. Treatment should continue until cosmetically acceptable regrowth is achieved or for a minimum of 3-4 mo.

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## DOSING

### ADULT

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Apply bid for up to 2 wk; not to exceed 50 g/wk

### PEDIATRIC

---

Not established

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## INTERACTIONS

None reported

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## CONTRAINDICATIONS

Documented hypersensitivity; viral or fungal skin infections

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## PRECAUTIONS

### PREGNANCY

---

C - Fetal risk revealed in studies in animals but not established or not studied in humans; may use if benefits outweigh risk to fetus

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## PRECAUTIONS

May suppress adrenal function in prolonged therapy; most common adverse effect is local folliculitis, which appears after few weeks of treatment; telangiectasias and local atrophy have been reported; dryness, burning, itching, and local irritation may occur; secondary infection is rare; no systemic adverse effects have been reported

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## PREDNISONE (DELTASONE, METICORTEN, STERAPRED)

Immunosuppressant occasionally used in rapidly progressive alopecia areata in an attempt to halt condition, but relapse rate is high. Use of systemic steroids for treatment of alopecia areata is under much debate. Stabilizes lysosomal membranes and suppresses lymphocytes and antibody production. Many drug doses and regimens have been used in treatment of alopecia areata, but no formal recommendation exists.

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## DOSING

## ADULT

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<60 kg: Not established

>60 kg: 40 mg PO for 1 wk, 35 mg PO for 1 wk, 30 mg PO for 1 wk, 25 mg PO for 1 wk, 20 mg PO for 3 d, 15 mg PO for 3 d, 10 mg PO for 3 d, and 5 mg PO for 3 d

## PEDIATRIC

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4-5 mg/m<sup>2</sup>/d PO or 0.05-2 mg/kg PO divided bid/qid; taper over 2 wk as symptoms resolve

---

## INTERACTIONS

Coadministration with estrogens may decrease clearance; concurrent use with digoxin may cause digitalis toxicity secondary to hypokalemia; phenobarbital, phenytoin, and rifampin may increase metabolism of glucocorticoids (consider increasing maintenance dose); monitor for hypokalemia with coadministration of diuretics

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## CONTRAINDICATIONS

Documented hypersensitivity; viral infection, peptic ulcer disease, hepatic dysfunction, connective-tissue infections, and fungal or tubercular skin infections; GI disease

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## PRECAUTIONS

## PREGNANCY

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B - Fetal risk not confirmed in studies in humans but has been shown in some studies in animals

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## PRECAUTIONS

Abrupt discontinuation of glucocorticoids may cause adrenal crisis; adverse effects from systemic therapy are common and include diabetes, weight gain, hypertension, electrolyte and fluid imbalance, psychological changes, osteoporosis, suppression of adrenocorticotrophic axes, striae, acne, hypertrichosis, and purpura; ocular or GI complaints, renal function impairment, immunosuppression, and avascular necrosis may occur

---

## TRIAMCINOLONE ACETONIDE SUSPENSION (KENALOG 10 MG/ML OR 40 MG/ML)

In alopecia areata, intralesional triamcinolone is believed to suppress the immune system locally and thereby allow hair to regrow. Injections are administered with 3-mL syringe and 30-gauge needle intralesionally.

Pediatric patients generally are less tolerant of intralesional injections because of local discomfort.

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## DOSING

### ADULT

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2.5- to 5-mg/mL concentrations typically administered, injected intralesionally, spread out to cover affected areas (approximately 1 cm between injection sites)

Alternatively, 60 mg IM followed by additional doses of 20-100 mg when symptoms recur

### PEDIATRIC

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Administer as in adults

---

## INTERACTIONS

Coadministration with barbiturates, phenytoin, and rifampin decreases effects

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## CONTRAINDICATIONS

Coadministration with barbiturates, phenytoin, and rifampin decreases effects

---

## PRECAUTIONS

### PREGNANCY

---

C - Fetal risk revealed in studies in animals but not established or not studied in humans; may use if benefits outweigh risk to fetus

### PRECAUTIONS

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Adverse effects include pain during injection and minimal transient atrophy (10%); rarely, atrophy is severe and permanent (avoid reinjecting area of denting to allow atrophy to revert); if large volume is injected per session, suppression of HPA axis may occur

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## BETAMETHASONE DIPROPIONATE CREAM 0.05% (DIPROSONE)

For inflammatory dermatosis responsive to steroids. Decreases inflammation by suppressing migration of polymorphonuclear leukocytes and reversing capillary permeability.

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## DOSING

### ADULT

---

Apply thin film bid until response

## PEDIATRIC

---

Administer as in adults

## INTERACTIONS

Effects decrease with coadministration of barbiturates, phenytoin, or rifampin; dexamethasone decreases effect of salicylates and vaccines used for immunization

## CONTRAINDICATIONS

Documented hypersensitivity; paronychia, cellulitis, impetigo, angular cheilitis, erythrasma, erysipelas, rosacea, perioral dermatitis, and acne

## PRECAUTIONS

### PREGNANCY

---

C - Fetal risk revealed in studies in animals but not established or not studied in humans; may use if benefits outweigh risk to fetus

### PRECAUTIONS

---

Not for use in skin with decreased circulation; can cause atrophy of groin, face, and axillae; if infection unresponsive to antibiotic treatment develops, discontinue until infection is controlled; do not use as monotherapy to treat widespread plaque psoriasis

## VASODILATORS

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Relax arteriolar smooth muscle, causing vasodilation; hair growth effects are secondary to vasodilation.

## MINOXIDIL TOPICAL (ROGAINE EXTRA STRENGTH)

Stimulates hair growth in general and is effective in many types of hair loss. Exact mechanism of action remains unclear, but does not appear to have either hormonal or immunosuppressant effects. The 5% solution appears to be more effective.

## DOSING

### ADULT

---

Apply <25 gtt bid regardless of extent of affected area.

## PEDIATRIC

---

Not established

## INTERACTIONS

Concurrent use with guanethidine, diuretics, or hypotensive agents may result in additive hypotension

## CONTRAINDICATIONS

Documented hypersensitivity, pheochromocytoma, coronary artery disease, cardiac dysrhythmias, congestive heart failure, or valvular heart disease, pregnancy, breastfeeding

## PRECAUTIONS

### PREGNANCY

---

C - Fetal risk revealed in studies in animals but not established or not studied in humans; may use if benefits outweigh risk to fetus

### PRECAUTIONS

---

May exacerbate angina pectoris; caution in pulmonary hypertension, congestive heart failure, coronary artery disease, and significant renal failure

## FOLLOW-UP

## DETERRENCE/PREVENTION

- Alopecia areata is highly unpredictable. No treatment is effective in preventing or halting progression of the condition. No trigger can be found to explain disease exacerbation in most patients.

## PROGNOSIS

- The natural history of alopecia areata is unpredictable. Most patients have only a few focal areas of alopecia, and spontaneous regrowth usually occurs within 1 year.
- Estimates indicate less than 10% of patients experience extensive alopecia and less than 1% have alopecia universalis.
- Patients with extensive long-standing conditions are less likely to experience significant long-lasting regrowth.
- Adverse prognostic factors include nail abnormalities, atopy, onset at a young age, and severe forms of alopecia areata.

---

## PATIENT EDUCATION

- Patient education is a key factor in alopecia areata. Inform patients of the chronic relapsing nature of alopecia areata. Reassure patients that the condition is benign and does not threaten their general health.
- Most patients try to find an explanation about why this is happening to them. Reassure these patients that they have done nothing wrong and that it is not their fault.
- Inform patients that expectations regarding therapy should be realistic.
- Support groups are available in many cities; it is strongly recommended that patients be urged to contact the National Alopecia Areata Foundation at 710 C St, Suite 11, San Rafael, CA 94901 or view the Web site.
- Many patients are reluctant to use hairpieces or take part in support groups because, at first, these often are perceived as last-resort options. Take the time to discuss the options with patients because they are of great benefit.

## MISCELLANEOUS

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## MEDICOLEGAL PITFALLS

- Failure to discuss at length realistic treatment expectations and treatments that have serious adverse effects or are not approved by the Food and Drug Administration (ie, topical immunotherapy)
- Medscape Medical Malpractice and Legal Issues Resource Center

## MULTIMEDIA



MEDIA FILE 1: ALOPECIA AREATA AFFECTING THE BEARD.



MEDIA FILE 2: ALOPECIA AREATA AFFECTING THE ARMS.



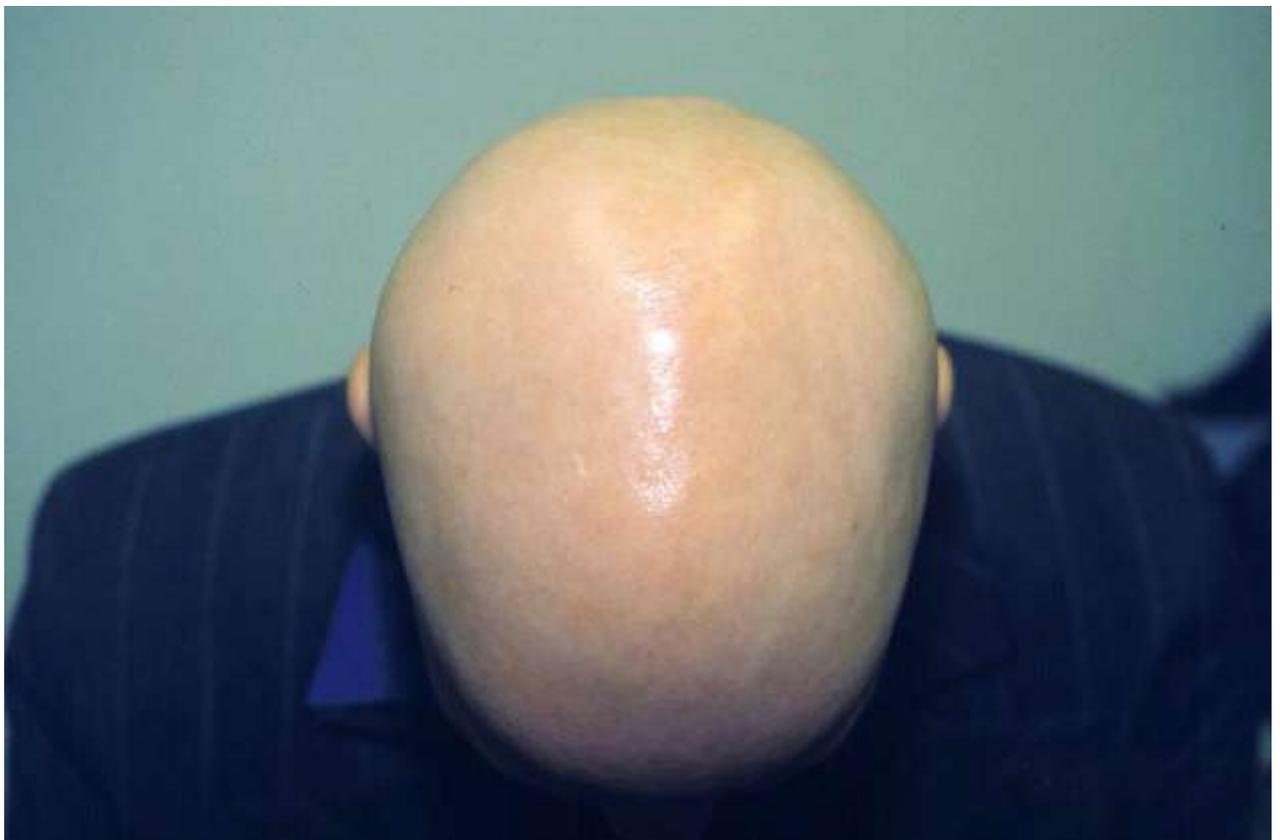
MEDIA FILE 3: PATCHY ALOPECIA AREATA.



MEDIA FILE 4: OPHIASIS PATTERN OF ALOPECIA AREATA.



MEDIA FILE 5: SISAIPHO PATTERN OF ALOPECIA AREATA.



MEDIA FILE 6: ALOPECIA TOTALIS.

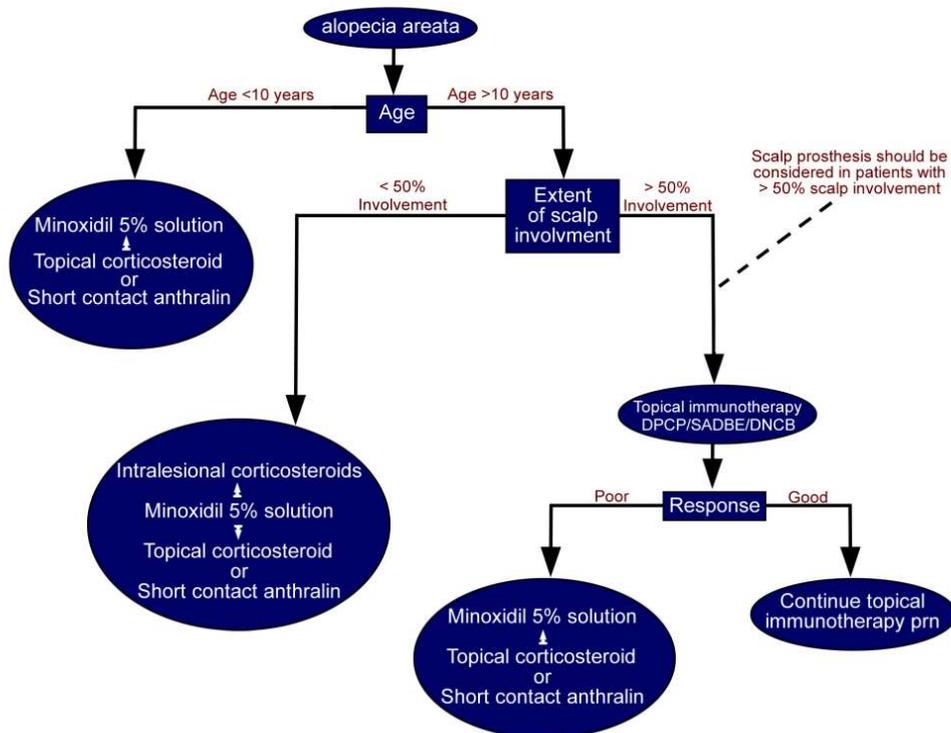


MEDIA FILE 7: DIFFUSE ALOPECIA AREATA.



MEDIA FILE 8: CORTICOSTEROID INJECTION.

**Treatment protocol for alopecia areata**



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## KEYWORDS

alopecia areata, hair loss, autoimmune alopecia, baldness

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