Chapter 120: Alopecia

Rebecca M. Law; Le Hanh Dung Do; Howard I. Maibach

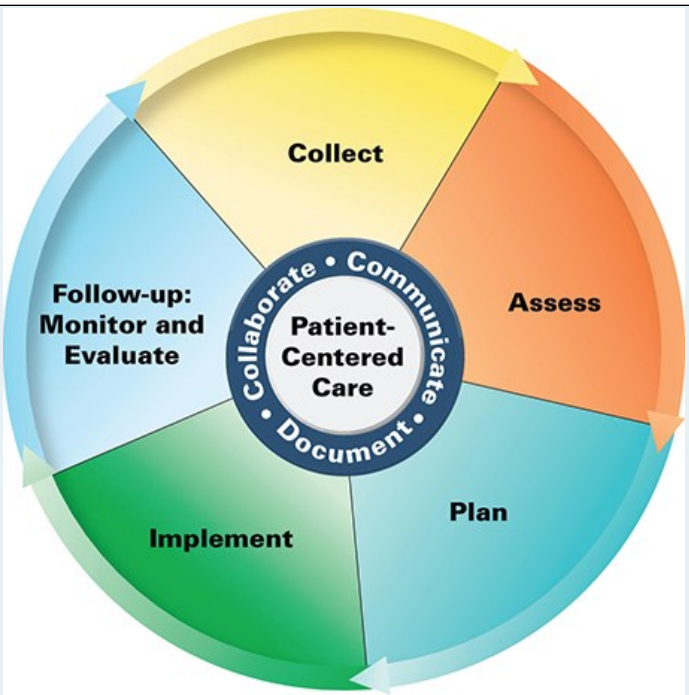
KEY CONCEPTS

KEY CONCEPTS

1. The hair cycle consists of three phases: anagen, catagen, and telogen. These are not synchronized across all hair follicles. Different factors regulate each phase of the hair cycle.
2. Pattern hair loss (or androgenetic alopecia) is an inherited condition in which androgens play a key role.
3. Inflammation plays an important role in alopecia. Inflammatory infiltrates are evident in androgenetic alopecia and alopecia areata. Alopecia areata is the most frequent cause of inflammation-induced alopecia. Chronic inflammation may lead to the destruction of the hair follicle, resulting in irreversible hair loss.
4. Scarring hair loss (or cicatricial alopecia) leading to irreversible hair loss can be caused by chronic inflammation or secondary to burns, cancer, trauma, radiation, or other diseases such as lichen planopilaris and chronic cutaneous lupus erythematosus.
5. Thinning of hair or hair loss is usually the only clinical sign of alopecia. Other symptoms (eg, itching, pain, burning, or prickly discomfort) would suggest other underlying disease conditions. Dermatologic diseases can cause hair loss, which varies from mild, nonscarring, and reversible to scarring and irreversible.
6. Alopecia can be distressing, affecting the quality of life and causing psychological problems. Psychosocial support and counseling must not be overlooked.
7. Treatment and management strategies of alopecia should be as cause-specific as possible. Identified causes (eg, iron deficiency, tinea capitis) should be treated and/or eliminated as soon as practically feasible.
8. Treatment for androgenetic alopecia includes topical minoxidil, oral 5α-reductase inhibitors (finasteride, dutasteride) for men, hormonal therapy for women, and miscellaneous therapies including nutritional supplements and laser light therapy with variable efficacy.
9. Treatment for alopecia areata includes intralesional corticosteroids, topical corticosteroids, high-dose oral corticosteroids, topical minoxidil, topical immunotherapy, topical and systemic biologic agents (in particular JAK inhibitors), azathioprine and other immunosuppressive agents, and other miscellaneous therapies.
10. Treatment of alopecia in patients of color should include cultural sensitivity for hair stigma (patient hair differs from perceived societal norm) and hair discordance (racial discordance between health professionals and patients seeking care for alopecia).

PATIENT CARE PROCESS

Patient Care Process for Androgenetic Alopecia



Collect

- Patient characteristics (eg, age, sex, pregnancy status if female)
- Patient medical history (personal and family)
- Patient description of history of the alopecia
- Signs associated with severity of androgenetic alopecia (eg, areas of involvement)
- Signs or symptoms of other conditions (ie, differential diagnosis—could this be a condition other than androgenetic alopecia? Symptoms such as itching, pain, burning, or prickly discomfort may suggest underlying conditions. If the alopecia is seen in a female, is polycystic ovarian syndrome [PCOS] or congenital adrenal hyperplasia present?)

Assess

- Severity of androgenetic alopecia—can quantify using hair counts, hair density measurements, and assessing the areas of involvement
- Relevant lab work, if needed (eg, check parameters that would rule out PCOS. Refer to the Acne case in the Casebook for discussion of relevant labs for PCOS.)
- Ability/willingness to pay for treatment options
- Emotional/psychological concerns

Plan

- Determine an appropriate treatment approach or various optional approaches (ie, topical vs systemic pharmacotherapy vs natural health products/nutritional supplements vs other approaches [mesotherapy, low-level laser light therapy, hair restoration surgery, cosmetic coverings]). Determine if psychosocial support is needed.
- Discuss with the patient various options to determine the most appropriate therapies (nonpharmacologic and pharmacologic) for the patient. Discuss options for psychosocial support if needed.

Implement*

- Provide patient education regarding all elements of treatment plan. Patient counseling points for various agents follow.
  - If topical therapy with minoxidil lotion is used: (1) Transient hair shedding may initially occur (indicating that minoxidil is stimulating hair follicles to re-enter a growth phase called anagen). This usually normalizes within a few weeks to months of starting therapy and treatment should be continued and not stopped. (2) To minimize drug contamination of the pillow and then inadvertent transfer to the face during sleep, use minoxidil lotion at least 2 hours before going to bed.
  - If systemic therapy with finasteride or dutasteride is used: (1) The medication must be swallowed whole and not chewed or crushed. (2) The medication may harm a growing fetus; pregnant women should not ingest or touch broken tablets. This also includes women seeking to become pregnant (including pharmacists, other health professionals, and caregivers). (3) The medication may cause sexual dysfunction. (4) Bloodwork may be needed (liver function tests) to monitor for potential side effects. (5) There are potential interactions with other medications—please check with your physician or pharmacist.
- Use motivational interviewing and coaching strategies to maximize adherence when needed.
- Provide information about prevention/minimization of further hair loss (eg, appropriate hair care). Provide information about psychosocial support options, if needed.

Follow-up: Monitor and Evaluate

- Contact patient in 3 and 6 months to follow-up about the efficacy of recommended therapies and any issues with the treatment regimen.
- Ensure that appropriate monitoring parameters for efficacy and potential adverse effects have been put in place. Ensure follow-up lab tests if needed are in place (eg, liver function tests when finasteride or dutasteride is used).
- Reinforce preventive measures including appropriate hair care.

****Collaborate with patient, caregivers, and other healthcare professionals.***

BEYOND THE BOOK

BEYOND THE BOOK

Read this continuing medical education article: "Hair Loss: Common Causes and Treatment," by T. Grant Phillips, W. P. Slomiany, and R. Allison.[1]

INTRODUCTION

Having a full head of hair is of some importance to most adults and children. Alopecia, defined in the Oxford Dictionary as "the partial or complete absence of hair from areas of the body where it normally grows," is a condition with a myriad of causes. This chapter reviews normal hair growth and physiology and discusses some of the known causes and types of alopecia.

ANATOMY AND PHYSIOLOGY OF THE HAIR FOLLICLE

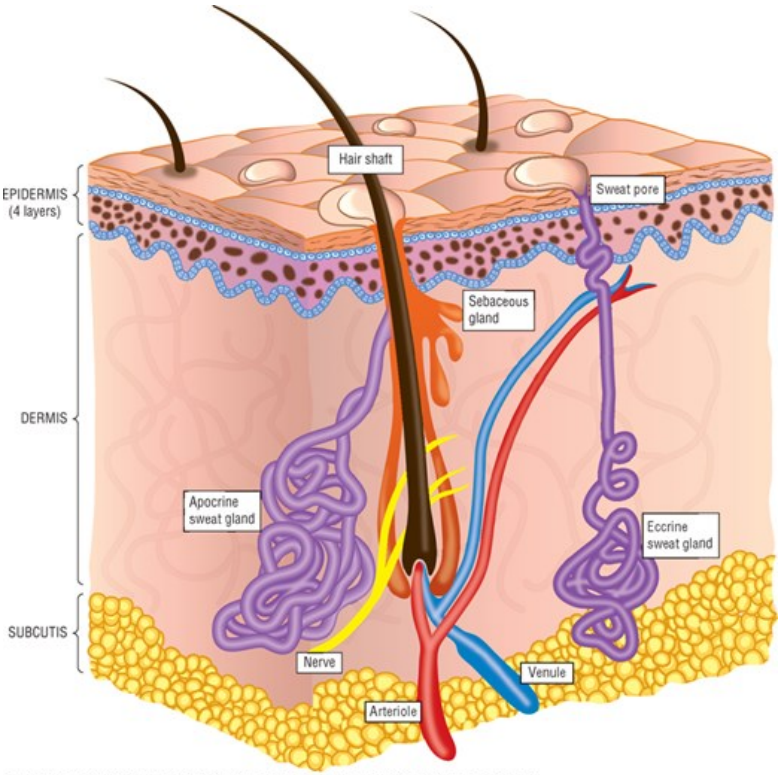
Hair covers most of the human body and grows both outside and inside of the skin. The external part is keratinized nonliving hair shaft, and the living follicles are located below the skin surface. The visible dead shaft mostly remains constant, while the living follicles continuously regenerate.[2,3]

The hair follicle is part of the human skin. It begins in the dermis with the hair bulb and the hair shaft, which extend through the epidermis and out into the external environment. The dermis provides support for the hair bulb, hair shaft, and other skin structures and appendages. The hair follicle and

the sebaceous gland form a pilosebaceous unit with a common duct opening into the environment (Fig. 120-1). (For discussions of other components in skin, refer to Chapter e121, "Drug-Induced Dermatologic Disorders.")

FIGURE 120-1

The hair follicle and its relationship to other structures and appendages of the human skin. Refer to Chapter e121, "Drug-Induced Dermatologic Disorders," for discussions about other components in skin. *(Original artwork courtesy of Rebecca Law, ©2018 by R Law, all rights reserved.)*



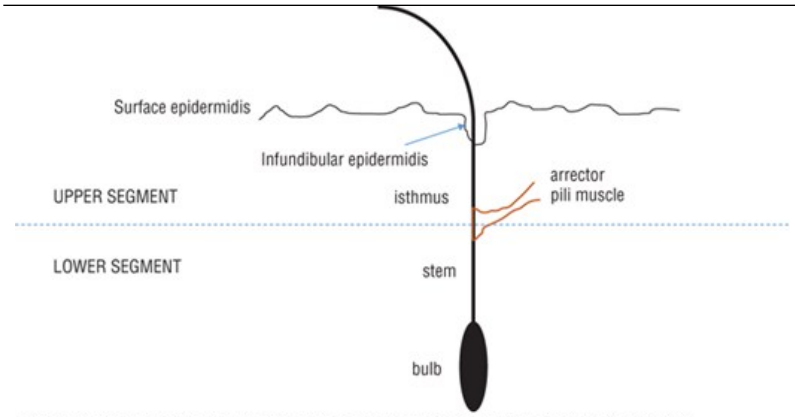
Source: Joseph T. DiPiro, Gary C. Yee, Stuart T. Haines, Thomas D. Nolin, Vicki L. Ellingrod, L. Michael Posey: *DiPiro's Pharmacotherapy: A Pathophysiologic Approach, 12e*
Copyright © McGraw Hill. All rights reserved.

The hair shaft comprises three layers from outside to inside: the cuticle, the cortex, and the medulla. The cuticle consists of hard, colorless cells that overlap. This outermost layer is responsible for elasticity and resiliency; it determines the general condition of the hair. The cortex contains melanin and thus determines hair color. It also contains keratin and determines whether the hair is straight or curly. The innermost layer is the medulla, which plays an important role in supporting the structure of hair.

Below the skin surface, the hair follicle is divided into upper and lower segments by the insertion site of the arrector pili muscle. The upper segment comprises the infundibulum and the isthmus (Fig. 120-2). The infundibulum is a funnel-shaped cavity that serves as a reservoir of the sebaceous gland. It is filled with sebum, and covered by an impermeable stratum corneum. The isthmus lies below the infundibulum, and it connects the duct of the sebaceous gland to the arrector pili muscle. The lower segment of the hair follicle contains the stem and the hair bulb. Adamson's fringe is the boundary between anucleate cells in the stem and nucleated cells in the bulb. The hair bulb contains nerve fibers, a capillary network, and loose connective tissue called the dermal papilla. Nerves and arterioles that supply the follicles are arranged as a plexus, arising from the subcutaneous fat to the dermis. The dermal papilla is a pear-shaped structure that consists of active cells and growth factors, which can induce hair growth and pigmentation.

FIGURE 120-2

The hair follicle.



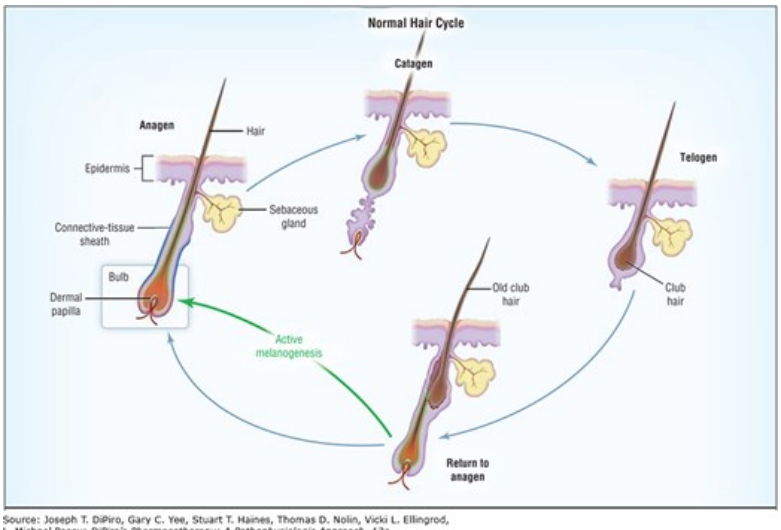
Source: Joseph T. DiPiro, Gary C. Yee, Stuart T. Haines, Thomas D. Nolin, Vicki L. Ellingrod, L. Michael Posey: *DiPiro's Pharmacotherapy: A Pathophysiologic Approach, 12e*

The Hair Cycle

1 The hair cycle consists of three phases; these are not synchronized among all hair follicles. The phases are the anagen, catagen, and telogen phases, followed by an intermediary "returning to anagen" phase (Fig. 120-3).[4]

FIGURE 120-3

The normal hair cycle. *(Reprinted with permission from Gilhar A, Etzioni A, Paus R. Alopecia areata. N Engl J Med. 2012;366(16):1515–1525.)*



Source: Joseph T. DiPiro, Gary C. Yee, Stuart T. Haines, Thomas D. Nolin, Vicki L. Ellingrod, L. Michael Posey: *DiPiro's Pharmacotherapy: A Pathophysiologic Approach, 12e*

Most of the hairs are in the *anagen phase* (also known as the growth phase). At the beginning of this phase, hair stem cells multiply, grow downward into the dermis, and differentiate into the hair shaft,[5] where the melanocytes start producing pigment. While the anagen phase of short hairs (eg, eyelashes, eyebrows, hairs on arms, and legs) lasts around 1 month, those of longer scalp hairs can last up to 6 years. Scalp hairs of an adult grow at a rate of about 1 mm per 3 days.

The anagen phase is regulated by factors as listed in column 1 of Table 120-1. Since hairs in this phase are growing, regulation is mostly by growth factors.

TABLE 120-1

Regulatory Factors of Three Phases in the Hair Cycle

Anagen Phase	Catagen Phase	Telogen Phase
Bone morphogenetic protein (BMP) Sonic hedgehog WNT proteins and receptors Insulin-like growth factor-1 (IGF-1) Fibroblast growth factor-7 (FGF-7) Hepatic growth factor (HGF) Vascular endothelial growth factor (VEGF)	FGF-5 Transforming growth factor β1 (TG F-β1) Interleukin 1b (IL-1b) Neurotrophins NT-3, NT-4 Bone morphogenetic protein BMP2/4 Tumor necrosis factor α (TNF-α)	Androgens Prolactin Adrenocorticotropic hormone (ACT H) Retinoids and thyroid hormones Estrogen FGF-5 BMP-4[6]

Overall, about 1% to 3% of hairs are in the *catagen phase* (also known as the transition phase). It begins when the anagen phase ends. The hair follicle starts to undergo apoptosis and reduces in size. The keratinocytes decrease proliferation, melanocytes decrease the production of pigments, and the hair shaft is no longer lengthened. The dermal papilla is transformed into a cluster of inactive cells along with the shrinking hair follicle. This phase lasts about 2 to 3 weeks.

The catagen phase is regulated by factors as listed in column 2 of Table 120-1.[7] Note that Interleukin 1b (IL-1b) and tumor necrosis factor α (TNF-α) aid the inhibition of growth factors, leading to a decrease in proliferation of hair follicles.

The *telogen phase* begins after the catagen phase ends and lasts for 1 to 3 months, with 10% to 15% of hairs. The hair and the dermal papilla go into a resting phase and melanocytes go into apoptosis.

This phase is regulated by various hormones (thyroid hormones, androgens, prolactin, ACTH, and others) as listed in column 3 of Table 120-1. In the end, the hair falls out (*exogen phase*) at a usual rate of 50 to 100 scalp hairs per day.

The follicle rests for a few weeks and then proceeds to the growth phase with the multipotent stem cells from the bulge area. Generally, hair grows until the fourth decade of life. After that age period, the majority of hair follicles are in the catagen and telogen phases, which leads to thinning of the hair, and baldness.

PATHOPHYSIOLOGY

Hormones

Androgens play a key role in pattern hair loss, which is an inherited condition characterized by scalp sensitivity to dihydrotestosterone (DHT). Testosterone is converted into DHT by the enzyme 5α-reductase. DHT binds to androgen receptors in the same manner as testosterone, but with much greater affinity. DHT shortens the telogen phase, leading to more rapid hair loss. With aging, new hairs become insufficient to replace the shed ones and contribute to alopecia. This mechanism is observed both in male and female pattern hair loss. Treatment protocols for alopecia using inhibitors of 5α-reductase are proven to be effective.[8]

Genetic Association

In the 1990s and early 2000s, observations that there is a resemblance between alopecia in fathers and sons led to suggestions that genes from some autosomal chromosomes were the cause of male pattern baldness. Postulated genes included the insulin gene, the 5α-reductase genes, and the hairless gene.[9] However, further investigations[10-12] found only a weak association between those genes and male pattern alopecia.

Maternal inheritance of male pattern alopecia with their investigation of variants of androgen receptor locus on the X chromosome was

demonstrated.[13] This implied that the phenotypic resemblance should be higher between affected males and their maternal grandfathers than between affected males and their fathers. However, the attributable risk from this case–control study was only 0.46, which indicated that the remaining risk fraction was due to other autosomal loci, which may explain the similarity of the alopecia pattern between fathers and sons.

Genetic predisposition has been shown for alopecia areata (AA) through a genome-wide association study that identified eight susceptibility loci and 139 single-nucleotide polymorphisms associated with the activation and proliferation of T-cells, IL-2 receptors, natural killer cell receptors, genes expressed in the hair follicle, and other factors.[14] A follow-up study established IL-13 and KIAA0350/CLEC16A as susceptibility loci for AA.[15] Research is ongoing.

Hair Cycle Dynamics

The hair cycle itself was one of the key factors in alopecia.[16] As mentioned above, maximal hair length is achieved in the *anagen phase*. If this phase is too short, patients may present with shortened hair. In some cases, the *anagen* duration may significantly decline, which may lead to empty follicular pores.[17] A shortened *anagen phase* leads to a premature progression to the *telogen phase*, which contributes to a decrease in hair diameter (clinically seen as fine hair) and hair loss. Patients also present with longer duration of the *telogen phase* and latency to the next hair cycle. This lag worsens the effect of alopecia.

Inflammation

3 Inflammation plays an important role in alopecia. Lymphohistiocytic infiltrate in the perifollicular area was shown, with collagen deposition four times higher in patients with male pattern alopecia than in normal controls.[18] Morphometric and ultrastructural analyses of the transitional zones in patients with male pattern alopecia were performed and found a significant increase in the number of mast cells and lymphocytes around the follicular epithelium.[19]

A study in 2012 also showed greater eosinophilic infiltration around lower hair follicles and mononuclear cell count in diffuse AA.[20] A 2012 review described AA as an autoimmune inflammatory disorder in which hair follicles are attacked by a mixed inflammatory cell infiltrate containing T-cells, natural killer cells, mast cells, and dendritic cells.[4]

Scarring

3 Chronic inflammation may lead to the destruction of the hair follicle and irreversible hair loss.[21] In this case, the hair follicle is replaced by fibrous tissue and the epithelial stem cells in the bulge are destroyed, leading to the hair follicle losing the ability to regenerate.[22]

4 Scarring alopecia (or cicatricial alopecia) leading to irreversible hair loss can be caused by chronic inflammation or secondary to burns, cancer, trauma, radiation, or other diseases such as lichen planopilaris and chronic cutaneous lupus erythematosus. This type of scarring alopecia is discussed further in the "Scarring Hair Loss" section.

CLINICAL PRESENTATION

5 Thinning of hair or hair loss is usually the only sign of alopecia. Other symptoms such as itching, pain, burning, or prickly discomfort may suggest other underlying conditions.

Anagen Hair Loss

Anagen hair loss or anagen effluvium usually has a sudden onset.[23] Patients present with the chief complaint of short hair and the inability to grow longer hair. The hair can be thin, sparse, but usually not fragile. Empty follicles can also be seen. Most cases of anagen effluvium are reversible and hair can regrow in 6 months. Common causes and presentations of anagen effluvium are listed in Table 120-2.

TABLE 120-2

Characteristics of Hair Loss in Anagen Effluvium

Causes	Presentations
Autoimmune disease—severe diffuse alopecia areata[20]	Diffuse and rapid hair shedding with exclamation point hairs, usually starts with a round patch, then spreads in a multilocular pattern.
Chemotherapy-induced alopecia[24]	Patients who recently received anticancer chemotherapeutic agents, radiation treatment, and other medications. Not all anticancer agents/treatments cause hair loss.
	Usually, recovery occurs within 6 months of treatment completion/drug discontinuation.
Inherited/congenital condition—loose anagen syndrome[25]	Predominantly seen in young girls between 2 and 6 years, but sometimes in boys. Diffuse or patchy alopecia often seen in the occiput.

Telogen Hair Loss

Telogen hair loss or telogen effluvium starts with thinning of hair, especially at the temples. It is a noninflammatory alopecia, usually of sudden onset.[2] Patients can lose 300 to 500 hairs a day, which is 2 to 3 times more than usual hair loss in a healthy individual. Hairs appear to be short, thin, and lacking melanin.

Telogen effluvium is usually seen 3 months after a medical condition that stops hair growth, such as childbirth, surgery, hormonal imbalance, or medications. The *telogen phase* normally lasts for about 3 months; if the condition is caused by drugs, hair can regrow after 4 months of drug withdrawal. The various systemic medical conditions affect the scalp, resulting in nonscarring alopecia. Medical causes include iron deficiency, thyroid hormone deficiency, systemic lupus erythematosus, syphilis, bacterial infections, and viral infection (herpes zoster). Medical and other causes are listed in Table 120-3.

TABLE 120-3

Causes of Telogen Effluvium

Pregnancy
Psychological stress
Fever, infection, hemorrhage, surgery
Weight loss
Autoimmune diseases (most common is systemic lupus erythematosus), thyroid hormone deficiency
Localized telogen effluvium following hair transplantation[26]
Vitamin or mineral deficiency—iron deficiency is a common cause of hair loss in women
Medications: contraceptives, anticoagulants, anticonvulsants, isotretinoin, warfarin

Androgenetic Alopecia

Distinct patterns of hair loss are seen in boys/men and girls/women (Table 120-4).

TABLE 120-4

Male and Female Pattern Hair Loss

Male Pattern Hair Loss	Female Pattern Hair Loss
Gradual loss of the frontal hairline early in the process.	The frontal hairline is often preserved. Gradual thinning leading to widening of the part line.
Gradual thinning in the vertex and temporal areas.	Thinning hair on the mid-frontal area of the scalp. Diffuse pattern. Hair loss is generally less severe than that which occurs in males.

2 Male pattern hair loss, or androgenetic alopecia (AGA), is the most common type of hair loss; it most often occurs in adult males.[23] AGA is caused by the effects of DHT in specific areas of the scalp such as the vertex and the temporal scalp. Patients usually have a vivid memory of a transitional time from having thick, long pigmented hairs to thinner, shorter hairs with less pigment.

A few women present with male pattern hair loss (AGA) caused by excessive levels of androgens, which leads to thinning hair on the mid-frontal area, but the condition is usually milder than in men. Polycystic ovarian syndrome (PCOS) and congenital adrenal hyperplasia are the common causes of male pattern hair loss in women.

Female pattern hair loss (FPHL or female AGA) usually presents with preservation of the frontal hairline with widening of the part line and reduced hair volume. These women are mostly losing their hair with age and hormone tests are normal. The Ludwig Classification is often used to describe FPHL, with Type I being minimal thinning that can be camouflaged with hair styling techniques and Type III being diffuse thinning with a see-through appearance on the top of the scalp.[27]

Dermatological Disease

3 4 5 Dermatological conditions on the scalp may result in scarring or nonscarring patchy hair thinning and alopecia. Table 120-5 provides some common diseases and their presentations.

TABLE 120-5

Dermatological Diseases That Can Cause Hair Loss

Diseases	Presentations
Tinea capitis[28]	Gray patch (scaling with patchy hair loss), black dot, and diffuseal opecia. But on occasions, severely inflammatory and raised lesions can occur.
Psoriatic alopecia[29]	Often nonscarring and regrows after a few months. Complete destruction of the follicle leads to the inability to regrow.
Seborrheic dermatitis of the scalp[30]	From mild desquamation to honey-colored crusts attached to scalp and hair leading to alopecia. May reach into forehead as scaly erythematous border known as “corona seborrheica.”
Allergic contact dermatitis of the scalp[31]	Mild hair loss 2-4 months after the episode of scalp dermatitis.
Pityriasis rubra pilaris[32]	Eczematous changes of the skin, ichthyosiform scale on lower extremities, coarse laminated palmoplantar keratoderma, and alopecia.
Erythroderma (a generalized disease)	Generalized erythema and exfoliation, patients sometimes present with malaise, fever or hypothermia, pruritus, diffuse alopecia, keratoderma, nail dystrophy, ectropion, pitting edema, lymphade nopathy, tachycardia, and high-output cardiac failure.[33]

Scarring Hair Loss

3 4 Scarring hair loss, or cicatricial alopecia, can be primary or secondary to indirect causes, such as burns, cancer, trauma, or radiation. Table 120-6 provides common causes of scarring hair loss and their presentations.

TABLE 120-6

Characteristics of Scarring Hair Loss

Causes	Presentations
Lichen planopilaris	<10% scalp involvement (localized) Generalized Rapidly progressing Itchy, multifocal, or central patches with follicular hyperke ratosis and perifollicular erythema; nonscalp areas may be affected
Chronic cutaneous lupus erythematosus	Single or multifocal patches with pronounced activity in the center of the patch, ulceration, follicular plugging, atrophy, and depigmentation
Frontal fibrosing alopecia	Band-like distribution around the frontal hairline; may be present in eyebrows
Central centrifugal cicatricial alopecia	Resembles lichen planopilaris; burning, scaling, and itchiness may occur
Brocq pseudopelade	Small and/or large, irregular patches of hair loss on the scalp with no detectable symptoms or inflammation; end-stage burnout
Folliculitis decalvans	Single patch of complete alopecia that expands circumferentially, slowly over years; typically found on hair-bearing p eriphery of scalp; pustules, honey-colored crusting, tufting; nonscalp involvement is rare
Dissecting cellulitis of the scalp	Multiple fluctuant nodules found across the scalp, often interconnected by sinus tracts; may be associated with acne conglobata: discharge is common and should be cultured

Alopecia Areata

Alopecia areata (AA) is the most frequent cause of inflammation-induced hair loss, affecting perhaps 4.5 million people in the United States.[4] AA affects both children and adults, with prevalence rates peaking between the ages of 20 and 40 years; up to 66% of AA patients are younger than 30 years and only 20% are older than 40 years.[4] Although AA generally occurs equally in males and females,[4,34] one study involving subjects 21 to 30 years found male dominance.[35]

AA is a nonscarring, autoimmune inflammatory disease that manifests in the hair follicles and can affect the nails in up to two-thirds of patients.[36] Due to the autoimmune nature of the disease, hair-follicle specific autoantibodies may be detected and other autoimmune conditions may be associated. There is a familial tendency with an especially high concordance rate in monozygotic twins, and genetic polymorphisms have been identified in multiple regions of the human genome.[34]

AA presents as an acute, patchy alopecia (with a well-circumscribed solitary or multiple patches) that is most commonly seen on the scalp but can be elsewhere in the body.[36,37] Patches up to 2 cm (~0.8 in.) in diameter can suddenly appear overnight then extend circumferentially at a rate of about 1 cm/week (0.4 in./week); the hair loss consists of hair breakage close to or just below the skin surface. As a result, black dots can be seen on dermoscopy, with characteristic “exclamation mark” hairs—that is, hairs where the distal hair shaft is broader than the proximal end—around the margins of the patch of hair loss.[4] Table 120-7 lists the types of AA.

TABLE 120-7

Classifications of Alopecia Areata

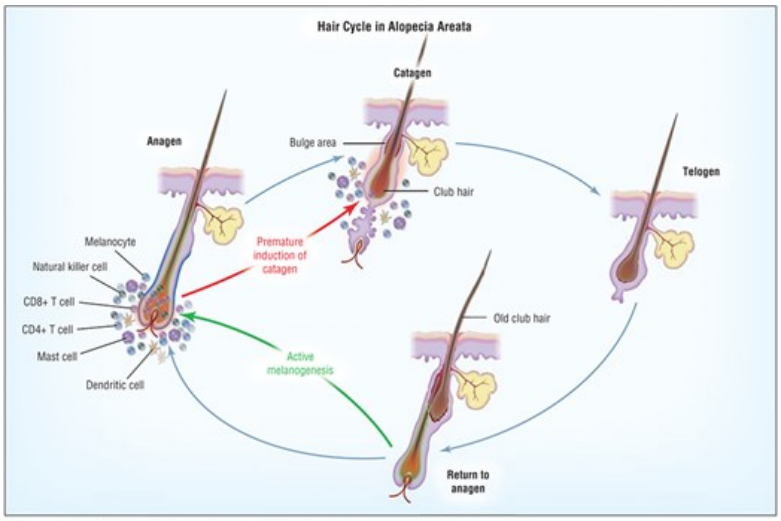
Types	Descriptions
Patchy AA	The most common type; localized hair loss; patchy; most commonly on scalp, sometimes involving beard area
AA totalis	Total hair loss on the scalp
AA universalis	Complete hair loss in all hair-bearing areas
Acute diffuse and total alopecia	Short clinical course ranging from a little hair loss to total baldness; favorable prognosis; rapid disease resolution, sometimes without treatment
Diffuse AA	Diffuse hair loss; can mimic telogen effluvium
Ophiasis	Hair loss only on the sides of the scalp (occipital areas) and the nape
Sisapho	A rare condition in which hair loss spares the sides of the scalp (occipital areas) and the nape and usually affects the central scalphis
Reticular patches	Several patches of AA coalescing to form a reticular pattern

Data from References 4,34.

AA involves abnormality in the hair cycle (shortened and disordered) due to the activity of inflammatory mediators released by a mixed inflammatory cell infiltrate (Fig. 120-4).[4]

FIGURE 120-4

The hair cycle in alopecia areata. *(Reprinted with permission from Gilhar A, Etzioni A, Paus R. Alopecia areata. N Engl J Med. 2012;366(16):1515–1525.)*



Alopecia in Children

Hair loss in the pediatric population is more common than expected—about 7.5% of pediatric patients in dermatology practices.[38] Although sharing many features with alopecia in adults, children may present with unique associations that require further examination.

A 5-year study in Jordan[38] showed that the three most common causes of alopecia in children are tinea capitis (40.5%), AA (17.6%), and telogen effluvium (17%). Tinea capitis is often straightforward with additional findings, such as itchy erythema and scaly border. However, in some communities, parents use unknown topical/herbal creams, some of which contain corticosteroids, and these can mask the presentation of tinea capitis. Therefore, potassium hydroxide (KOH) testing plays an important role in etiologic diagnosis.

Autoimmune diseases were found in 13.5% of the pediatric AA cases, including diabetes, hypothyroidism, and vitiligo. In pediatric AA, the male:female ratio is 3:2,[38] compared to 1:2.3 in adults.[39]

Telogen effluvium in children is commonly caused by a prior low-grade fever.[38] All of these cases presented with a healthy scalp, normal hair texture, and regular bulb of telogen hair. This condition was seen more in female children, usually within 4 to 6 months before coming to the clinic.

Approximately 20% of the examined cases had some elements of traction alopecia,[38] with female predominance and occurring at the hairline. Moreover, some cases showed follicular pustules and perifollicular inflammation. This type of hair loss may be more common than the 20% seen, as traction alopecia is easily noticed by parents and reversed by wearing a loosened hair style, perhaps making it underrepresented in the clinic.

Trichotillomania is an impulse-control disorder where patients consciously or unconsciously pull, twist, or twirl their hair. It is a relatively common disorder in children. The mean age of onset is at about age 13 years, and it affects an estimated 4% of the population. Patients usually present with frontoparietal patches of alopecia that progress posteriorly and bare patches are typical. Trichoscopy shows broken hair shafts of various lengths typically with frayed “split ends.” The condition is associated with problems of self-esteem and social avoidance. Complications include infection, skin damage, and scarring.[1,40]

The above and other causes of hair loss in children are listed in Table 120-8.

TABLE 120-8

Common Causes of Hair Loss in Children

Tinea capitis
Alopecia areata
Telogen effluvium
Traction alopecia
Diffuse hair loss with abnormal texture
Trichotillomania
Hair abnormalities with atopic eczema
Folliculitis decalvans

COMPLICATIONS

Like other medical conditions, alopecia can be distressing, affecting the quality of life and causing psychological problems.[41] Loss of normal scalp hair increases the risk of sunburn and injury. Moreover, studies have shown that hair loss can be associated with depression, low self-esteem, and

feelings of unattractiveness. Some studies show that men with hair loss are perceived, based solely on appearance, to be not as attractive and successful as men without hair loss. This is further discussed below in the "Hair Stigma" section.

DIAGNOSIS

Diagnosis of alopecia usually can be made clinically: by a meticulous patient history plus skin and hair examination. In cases of less certainty, further workup may be warranted.

Regarding patient history, the essential points to obtain include time of onset, course of hair loss, past medical history (autoimmune disease, medications, procedures, or surgery), and family history of alopecia. In children, physical and mental development should also be obtained. Then, an extensive physical evaluation can be performed to assess whether the patient has hypotrichosis or alopecia, the type of alopecia, hair shaft anomalies, hair quality, and other conditions of the scalp, including erythema, edema, pustules, scaling, atrophy, or scarring.

For hair examination, the hair tug and pull test is clinically popular since it is quick and easy to use, and it can also be done at multiple locations on the scalp for a more thorough assessment. This test distinguishes between loss from follicles and loss due to hair shaft fragility. First, the patient's hairs are separated into a 4- to 6-mm diameter bundle (approximately 50-60 hairs). The tug portion of the test involves gentle holding of hairs between the thumb and index finger near their root, then tugging with the other hand on the same strand at its distal part. The tug test is positive if more than 10% of the hairs fracture, suggesting hair shaft fragility. The pull test involves holding a hair close to the root between the thumb and index finger, then use a slight force to pull the hair out, causing mild discomfort but not pain. In general, telogen hairs are more likely to be extracted than anagen hairs. Furthermore, microscopic observation of the hair root can help distinguish anagen hairs (long sheath shaped) and telogen hairs (club shaped).[42]

In the case of suspected fungal infection, the wood lamp examination is an efficient test. For the test to be accurate, the hairs should be free of all hair applications such as deodorants or moisturizers. After the surroundings are darkened, the wood lamp is turned on and held about 5 to 10 in. (~12-25 cm) away from the skin. Some common fluorescent colors are listed in Table 120-9.

TABLE 120-9

Common Colors Shown on Wood Lamp Examination

Conditions/Organisms	Fluorescent color
Pityriasis versicolor by *Malassezia*	Yellowish or orange
Malassezia folliculitis	Bluish-white
Tinea capitis by *Microsporum* species	Blue-green
Tinea capitis by *Trichophyton schoenleinii*	Dull blue

Bacterial or viral infection usually can be further diagnosed with swabs for stain or culture.

In suspected cases of iron deficiency, complete blood count, ferritin, total iron-binding capacity, and transferrin saturation should be tested. If a female patient presents with alopecia along with virilization, clinicians should order dehydroepiandrosterone (DHEA) sulfate and testosterone analysis. Other systemic conditions such as lupus or hypothyroidism/hyperthyroidism can be assessed using their specific laboratory findings.

Alopecia in general does not need a biopsy for diagnosis, but this is sometimes performed for research purposes. Hairs can be biopsied transversely and may show miniaturization, especially in cases of AGA or telogen effluvium.

Genetic Testing in Androgenetic Alopecia

As mentioned in the pathophysiology section, many genetic factors may contribute to alopecia. However, more research is still needed before

clinicians can reach a consensus in the screening test for AGA. Therefore, no genetic testing is officially recommended.

TREATMENT

7 There are a myriad of distinct and diverse causes and types of alopecia as discussed above; thus, treatment or management strategies should be as cause-specific as possible. Identified causes should be treated and/or eliminated as soon as practically feasible. Cause-specific management/treatment strategies include several considerations—infections, chemotherapy, iron deficiency, other nutritional deficiencies, physiological or emotional trauma, trichotillomania, and autoimmune diseases.

Infectious causes should be treated with the appropriate anti-infective agent(s) and treatment regimen (whether systemic or topical therapy as appropriate). Tinea capitis, which commonly manifests as patchy alopecia and usually caused by a *Trichophyton* species, requires a systemic antifungal with oral terbinafine or itraconazole and not a topical agent (it does not penetrate hair follicles sufficiently). See Chapter 143, "Superficial Fungal Infections," for further discussion of the treatment of mycotic infections of the scalp.

Chemotherapy-induced alopecia is generally a reversible and temporary condition. However, for the patient undergoing chemotherapy, having their hair fall out—seeing clumps of hair on pillows and brushes and bald areas on their head—may be emotionally distressing. Cold caps and scalp cooling systems reduce the amount of chemotherapeutic agents reaching the hair follicles and have been shown to significantly reduce the amount of hair loss[43] without increasing the risk of scalp skin metastases.[44] Other nondrug strategies include wigs, scarves/hats or other head coverings, and counseling/psychological support. Limited studies of topical or systemic drug therapies for prevention and treatment (using alopecia treatments discussed below) have not been that promising especially in preventing hair loss,[24] and the risk for affecting chemotherapy efficacy or toxicity must be kept in mind, even with nutraceuticals.[24] Reassuring the patients that hair regrowth will happen may be comforting and letting them know that occasionally the hair grows back differently (eg, may be fuller or curlier) can provide a positive outlook.

Iron deficiency is a known and reversible cause of alopecia. In this case, appropriate treatment is iron replacement therapy followed by iron supplementation once iron stores are replenished. Iron-deficiency anemia is further discussed in Chapter 122, "Anemias."

Other *nutritional deficiencies* including specific trace element deficiencies should be corrected if found, as these may possibly play a role in alopecia. For example, there may be an association between copper deficiency and AGA; decreased copper level in the frontal zones of scalp hair and serum were found in both men and women with AGA when compared with their respective matched controls and the differences were statistically significant.[45] There may also be an association between defective copper metabolism and trichorrhexis nodosa, although there are many other possible causes, including hypothyroidism and Menkes disease.[1]

Any physiologic or emotional *trauma or stressors* that preceded the alopecia could be the inciting cause. If the traumatic events or stressors are still present and ongoing, management strategies to ameliorate them would be helpful (eg, mindfulness techniques, relaxation clinics, counseling, or psychotherapy).

Trichotillomania may be treated via nonpharmacologic and/or pharmacotherapy—the optimal treatment is unknown, and psychiatric referral may be indicated. Cognitive behavior therapy and selective serotonin reuptake inhibitors (SSRIs) may be effective, and using both together may be more effective than either treatment used alone. Olanzapine and clomipramine may also be effective.[46]

Alopecia that is thought to be associated with *autoimmune diseases* as discussed above (eg, SLE, hypothyroidism) sometimes improves with treatment of the specific autoimmune disorder. Antibodies (eg, thyroid-antimicrosomal antibodies) may be involved in the pilar follicles, as antifollicular antibodies have been reported in alopecia.[47]

Pattern Baldness: Androgenetic Alopecia

8 There are recent reviews[1,48,49] and evidence-based guidelines[50,51] on the treatment of AGA in women and in men. Treatments include topical minoxidil, oral 5α-reductase inhibitors (finasteride, dutasteride) for men, hormonal therapies for women, and miscellaneous therapies including nutritional supplements and laser light therapy, with variable efficacy.

Male Baldness

Topical Therapy: Minoxidil

Minoxidil (2% or 5%) topical solution is the most common treatment for male baldness. It can prevent the progression of baldness and improve hair density and thickness, with hair regrowth being more robust at the vertex than in the frontal area of the head.[52] Its exact mechanism of action on hair follicles remains unclear. However, the main benefits seen may be prolongation of the anagen phase and hair shaft diameter.[51]

The 5% concentration has been recommended for greater efficacy; a randomized controlled trial (RCT) comparing 5% versus 2% minoxidil in men aged 18 to 49 years found 45% higher hair counts in those given 5% versus those given 2%.[53] There is insufficient evidence to recommend the 5% foam over the 5% solution.[50] The response to treatment should be assessed at 6 months.[50] If successful, treatment needs to continue indefinitely as hair loss recurs when treatment is interrupted or discontinued.[1,50]

Side effects of minoxidil lotion include transient telogen hair shedding—an indication that minoxidil is stimulating telogen follicles to re-enter anagen[50]—this usually normalizes within a few weeks to months and therapy should be continued and not stopped.[50] Hypertrichosis is more common with the 5% concentration and may reflect incorrect application. To minimize drug contamination of the pillow and inadvertent contact with the face during sleep, patients should be advised to use the medication at least 2 hours before going to bed.[50] Irritant and contact dermatitis sometimes occur. Minoxidil is an antihypertensive agent when used systemically, and uncommon to rare side effects of topical administration are related to its systemic effects on blood pressure: dizziness, headache, hypotension, tachycardia, or chest pain.

Systemic Therapy: Finasteride, Dutasteride

The 5α-reductase enzyme converts testosterone to DHT, the main androgen causing AGA. There are two types of 5α-reductases in humans: type I is primarily found in liver, skin, and scalp; and type II is found in the prostate, genitourinary tract, and hair follicle.[50] 5α-Reductase inhibitors were originally marketed for treatment of benign prostatic hyperplasia (BPH), and their efficacy for AGA was an incidental finding based on a “side effect” of BPH treatment.

Finasteride is a selective type II 5α-reductase inhibitor that reduces scalp production of DHT. Multiple RCTs have shown significant increases in total hair counts and/or other hair growth benefits in men at 6 months,[54,55] 12 months,[56,57] and 24 months.[58] A dose-ranging study found benefits at all doses greater than 0.2 mg/day but no greater difference between 5 mg/day versus 1 mg/day.[54] Thus, the recommended dose for male pattern baldness is finasteride 1 mg/day (the dose for BPH is 5 mg/day). A 4-year study (2-year observation, 2-year finasteride) found that hair follicles that can still produce a thick hair fiber responded to finasteride 1 mg/day by reducing the hair cycle lag phase by 40% (thus initiating active growth more rapidly) and increasing the duration of the anagen phase by 23%.[58] However, miniaturized hair follicles (ie, those that were producing thinner hair, defined as <40 µm thick) did not respond to finasteride.[58] This may be useful in future for patient selection and may be an explanation for nonresponders. In 2019, a follow-up study by the same investigators assessing finasteride pharmacodynamics in responders found finasteride-dependency and a rebound effect when finasteride was discontinued: after 12 months off-treatment, viable drug-responsive hair follicles began to rapidly miniaturize; and by 30 months off-treatment, 94% had miniaturized, which worsened the alopecia.[59] The authors concluded that drug dependency and a rebound phenomenon are new findings for finasteride use in alopecia.[59]

Side effects of finasteride include orthostatic hypotension, dizziness, decreased libido, impotence, and ejaculatory disorder. Two recent systematic reviews identified growing concerns about sexual dysfunctions[8,60] and patient counseling should be provided prior to starting treatment.[8] Finasteride is extensively metabolized; monitoring parameters include liver function tests (LFTs) prior to starting therapy and repeated every 6 months.[61] Finasteride is teratogenic (risk category X), and crushed or broken tablets should not be touched by pregnant women or women seeking to become pregnant (including pharmacists, other health professionals, and caregivers), as exposure to the active ingredient can occur.

Dutasteride is a double inhibitor of both type I and type II 5α-reductase. It is only approved for BPH in men (and not for AGA) in the United States and Canada, although it is approved in other countries (eg, Korea) for AGA. RCTs have shown that dutasteride 0.5 mg/day has efficacy in 6 months without significant side effects[62] and that in comparison with finasteride 1 mg/day or placebo, it is significantly more efficacious.[55] Total hair counts (2.54 and 1.13 cm diameter [1 and 0.44 in. diameter]) and hair width but not terminal hair counts (2.54 cm diameter [1 in. diameter]) were significantly greater at 24 weeks with dutasteride compared with finasteride or placebo.[55] Incidences of sexual dysfunction and breast disorders were similar between

dutasteride and finasteride but lower in the placebo group.

Also similar to finasteride, dutasteride is teratogenic (risk category X), and skin contact with the active ingredient (if tablet is broken or crushed) should be avoided. Tablets should be swallowed whole and not chewed or crushed. There is a potential association with high-grade prostate cancer, but the risk is low. Dutasteride is also extensively metabolized; its already-long half-life (5 weeks) increases with age. Its concentration/pharmacodynamic effects may be increased during concomitant therapy with strong CYP3A4 inhibitors.

The most concerning side effect for 5α-reductase inhibitors (finasteride, dutasteride) appears to be sexual dysfunction. A 2019 systematic review and meta-analysis of adverse sexual effects of finasteride or dutasteride as treatment for male AGA evaluated 15 RCTs (4,495 participants).[60] This study found an overall 1.57-fold risk of any adverse sexual effects associated with the use of either finasteride 1 mg/day or dutasteride 0.5 mg/day; when analyzed separately, finasteride had a 1.66-fold risk and dutasteride had an increased risk that was not statistically significant (RR 1.37, 95% CI 0.81-2.32).[60] But there were many fewer dutasteride RCTs, which may account for the wide confidence interval.

Miscellaneous Therapies

Many other cosmetic, pharmaceutical, nutraceutical, and food products are marketed as alternative therapies for alopecia. But most of these have little to no clinical evidence of efficacy, especially robust RCTs. However, health practitioners should be somewhat knowledgeable about alternative therapies, as patients may be using them and/or have questions—for instance, if they have heard of or are considering these options.[50]

Mesotherapy is the microinjection of medications, vitamins, or other substances into the mesoderm (the middle layer of skin). Medications have included dutasteride, minoxidil, or other active ingredients. An RCT comparing mesotherapy to topical 5% minoxidil found little difference in the two types of treatments, the only difference being a variation of hair shaft diameter at 1 month that was not present at 4 months (the end of the study).[63] The mesohair solution contained 56 ingredients, including 24 amino acids, 13 vitamins, 4 coenzymes, 4 nucleic acids, 5 minerals, and 2 reducing agents, and the active ingredients decapeptide 4, acetyl decapeptide, and copper tripeptide.[63] A study of mesotherapy using 1 mL of dutasteride 0.01% demonstrated significant improvement after 9 months, but only 6 patients (5 males, 1 female) participated in the trial.[64]

Low-level laser (light) therapy (LLLT) can stimulate hair growth by scalp vasodilatation, but the exact mechanism is unclear.[65] LLLT devices are available commercially for home or clinic use in the United States and Canada.[66]

Platelet-rich plasma (PRP) therapy involves intradermal injections of autologous PRP into the scalp. A 2017 systematic review found that 7 of 14 studies reported a significant increase in hair density, ranging from 12.3 to 45.9 hairs/cm^2 (80-300 hairs/in.^{2}) with variable hair thickness and hair loss results.[67] The beneficial effects seem to begin with the first treatment and peak after 3 to 5 treatments, then attenuates and treatments must be continued to maintain benefits. Side effects include local irritation and pain.[66,67]

PRP is concentrated autologous platelets in plasma, and contains more than 20 growth factors, including platelet-derived growth factors. In AGA, PRP is thought to induce stem cell differentiation, prolong dermal papilla cell survival, prolong the anagen phase, and other mechanisms.[68] PRP has been compared to topical minoxidil and at 6 months, the PRP group scored higher in both global photography and patient satisfaction with a hair growth questionnaire.[69]

Ketoconazole inhibits the DHT pathway, and ketoconazole shampoo has been considered for use in combination with oral finasteride.[70]

Prostaglandin F2 analogues latanoprost and bimatoprost topical therapy are being studied for use in AGA. Early results seem promising.[70]

Topical valproic acid 8.3% spray was found to increase hair count in a recent RCT.[71] Alopecia is a fairly common adverse effect of systemic valproic acid.

Hair restoration surgery involves hair transplantation, scalp reduction surgery, or a combination of both.

Natural health products—including biotin, melatonin, saw palmetto, black cohosh, dong quai, false unicorn, chaste berry, and red clover—have been used in treatment of alopecia. Some of these may have anti-androgenic or estrogen-promoting activities.[65] However, there is scant evidence of efficacy as hair growth promoters in men, as shown in these summaries:

1. A small 2017 RCT of a combination traditional Chinese medicine (TCM) containing six herbal ingredients (*Ginseng Radix*, *Astragali Radix*, *Angelicae Sinensis Radix*, *Ligustri Fructus*, *Rehmannia glutinosa*, and *Eclipta prostrata* Linn.) versus placebo showed that 9 of 17 patients receiving TCM had increased hair growth versus 2 of 17 in the placebo group, a statistically significant difference. However, of the 9 responders in the TCM group, 1 minimally improved, 5 moderately improved, and only 3 showed significant improvement.[72]

2. Biotin is popularly used for AGA; although it is known that genetic biotinidase deficiency results in hair loss and biotin was found to reverse valproic acid–induced alopecia in a few patients, robust evidence is lacking.[73]

3. In contrast, a well-designed 2017 RCT of a commercially available product called Lambdapil (1,000 mg L-Cysteine, 100 mg *Serenoa repens*, 7.14 mg *Equisetum arvense L*, 0.5 mg silicon, 10 mg zinc, 16 mg vitamin B3, 6 mg vitamin B5, 1.4 mg vitamin B6, 50 µg D-biotin, 40 mg taurine), which enrolled both men and women in a 6 month placebo-controlled RCT using high-level methodology, found that Lambdapil increased the anagen/telogen ratio in men, with a 3.7% increase in anagen hair and an increase in hair volume. Quality of life was also improved.[74] (Results of the use of this product in women are discussed in the next section.)

Female Hair Loss

The majority of female hair loss is FPHL or female pattern AGA; however, women with PCOS also can develop male pattern baldness. A 2016 Cochrane review of interventions for FPHL reported moderate- to low-quality evidence of efficacy for minoxidil, low-quality evidence of efficacy for finasteride, and moderate- to low-quality evidence of efficacy for.[49] Hormonal therapy, nutraceuticals, and mesotherapy were not included in the review, although there are promising RCTs of these approaches. Other possibilities such as prostaglandin analogs are too early in development for review. Recently published management strategies include other hormone-modulating treatments (dutasteride, spironolactone, cyproterone acetate, flutamide), ketoconazole shampoo, platelet-rich plasma, microneedling, as well as updated comments on prostaglandin analogues (latanoprost, bimatoprost), light therapy, topical hormonal treatments, and hair transplant.[75]

Topical *minoxidil* 2% has been approved for use in females with AGA, but not the 5% concentration. Many RCTs using 2% minoxidil in women have shown efficacy, and pooled data from six studies (5 using 2%, 1 using 1%) confirmed the observation, with 157 of 593 patients demonstrating a moderate-to-marked increase in hair growth when compared with placebo (RR 1.93, 95% CI 1.51-2.47).[49] In 8 pooled studies (1,242 participants), there was a significant increase in total hair count (13.2/cm^2 [85/$in.^2$]) compared with placebo.[49] Four studies (1,006 participants) comparing minoxidil 2% versus 5% did not show a difference, although the quality of the evidence was moderate to low.[49] If successful, it should be continued indefinitely.[75] Women should be informed about transient telogen hair loss within the first few months of treatment and possible hypertrichosis as a side effect of treatment.[75] Minoxidil, including topical use, is contraindicated in pregnancy and lactation.

Oral *minoxidil* at low doses of 0.25 to 2.5 mg/day may be an option if unresponsive or intolerant to topical minoxidil treatment.[75] However, significant drops in blood pressure may occur, especially if other anti-hypertensive medications are used concomitantly.

Topical and oral prostaglandin analog treatments may be promising. Latanoprost, travoprost, and bimatoprost are prostaglandin analogs that are used for glaucoma, which caused eyelashes to grow as a side effect; they promote hair growth by prolonging the anagen phase. Blocking the prostaglandin D2 receptor (GPR44) may help to increase hair growth.[75] Setipiprant (KITH-105) is an oral GPR44 receptor inhibitor. Studies are ongoing but still too early to provide general guidance.

5α-Reductase inhibitors are not approved for use in females. One RCT showed efficacy with *finasteride* 1 mg/day in women with AGA while two others did not.[49] Higher doses (2.5-5 mg/day) have shown efficacy consistently[75-78] and are used in practice.[75] Patient selection and dose used may be key—at 1 mg/day four women with hyperandrogenism showed improvement with finasteride[79] but not postmenopausal women without hyperandrogenism.[48,80] However, at a dose of 5 mg/day, 86 mostly postmenopausal Asian women without hyperandrogenism showed significant increases in mean hair density and mean hair thickness after 12 months of treatment.[77] Studies in premenopausal women have shown conflicting results.[80] *Dutasteride* is a more potent 5α-reductase inhibitor that can lower serum DHT levels by more than 90%[80] and effectiveness has been reported in a 46-year-old woman.[81] Precautions and concerns with handling broken tablets are even more of an issue if used by a woman, as the drug is contraindicated in pregnancy and in women of childbearing age.

Hormonal therapy with antiandrogens with or without estrogens has shown some efficacy. In particular, *cyproterone acetate* was compared with topical minoxidil; results showed greater efficacy for minoxidil in women without hyperandrogenism and greater efficacy for cyproterone acetate in women with multiple symptoms of hyperandrogenism.[82] Cyproterone acetate may be more effective in a birth control formulation (eg, Diane or Diane-35, which is available in Canada and Europe but not in the United States). Suggested regimens for use in premenstrual women are either 100 mg/day on days 5 to 15 alongside ethinyl estradiol 50 µg on days 5 to 25, or 50 mg/day on days 1 to 10 with ethinyl estradiol 35 µg on days 1 to 21.[75] For postmenopausal women, a suggested regimen is cyproterone acetate 50 mg/day.[75]

Spironolactone has antiandrogenic activities and has been considered the most commonly used, off-label antiandrogen for the treatment of FPHL and hirsutism[48]; however, published studies are limited. An open intervention study found spironolactone to be equally effective when compared with cyproterone acetate.[83]

Flutamide has potent antiandrogenic effects and has shown efficacy for FPHL in clinical trials. In a 4-year prospective cohort study in which flutamide was used in annually reduced doses of 250 mg/day, 125 mg/day, and 62.5 mg/day, flutamide was used either alone or with an oral contraceptive reduced alopecia scores. The maximum drug effect occurred after 2 years and was maintained for the duration of the 4-year study.[84] The regimen of annually reduced doses was a dose-ranging attempt to minimize side effects; the study showed that the dose of 62.5 mg/day maintained efficacy with complete hepatic tolerability and high adherence. At the dose of 250 mg/day, the dropout rate was 4% due to drug-related hepatic changes.[84] Monitor serum transaminases at baseline, monthly for the first 4 months and periodically thereafter.[75,85]

Natural health products and nutritional supplements may be beneficial. RCTs showing efficacy are as follows[81]:

1. A 2015 RCT of a nutritional supplement combination (460-mg fish oil [exact amounts of EPA and DHA unspecified], 460-mg black currant seed oil, antioxidants [1-mg lycopene, 30-mg vitamin C, 5-mg vitamin E])[86,87] versus placebo in 120 women found that 62% of the supplement group had increased hair density compared with 28% in the placebo group. Anagen hair increased significantly and telogen hair decreased significantly in the supplement group.[86,87]

2. The well-designed 2017 RCT of Lambdapil as discussed in an earlier section enrolled both women with acute Telogen effluvium (aTE) and men with AGA in a 6-month, placebo-controlled design using high-level methodology. Results in women showed an increase in hair volume (slight to moderate) and an improved quality of life.[74]

3. A topical botanical lotion that acts by increasing Bcl-2, perifollicular Langerhans and mast cells, and perifollicular collagen was found in a 2018 single-blinded RCT to increase hair density, improve Dermatology Life Quality Index, and increase the anagen:telogen ratio at 24 weeks.[88]

LLLT increased the total hair count in women with FPHL in several studies.[49,89] A 2019 meta-analysis of 8 papers comprising a total of 11 RCTs found that LLLT device used (comb vs helmet) and the duration of treatment (short vs long) did not appear to matter. Thus, LLLT appears promising and is a potentially effective treatment for AGA.[89] Majority of studies to date have shown an overall improvement in hair regrowth, thickness, and patient satisfaction.[75] To this end, the FDA has approved various LLLT devices for use in AGA and these are available commercially. LLLT is usually well tolerated, with side effects that include scalp dryness, itching, tenderness, and a warm sensation.[75]

Platelet-Rich Plasma may be a promising option for female AGA[75,90]; however, current European Guidelines for AGA in women and men concluded that there is insufficient evidence to support its use.[75,91]

Mesotherapy containing nutritional supplements has been compared with topical minoxidil 5% lotion. No significant differences were found with regard to hair density or hair loss, but the mesotherapy group had a greater increase in the number of hair follicles.[92]

Hair transplantation is a viable option if other medical therapies are unsuccessful.[75] Cosmetic methods such as wigs, scarves, and hats are other alternatives.

Ketoconazole shampoo has been recommended for female AGA if seborrheic dermatitis or sebopsoriasis is present.[75]

Androgenetic Alopecia in Children

Familial predisposition may be present. Nonetheless, if AGA is seen in a prepubertal child, an endocrine evaluation is strongly recommended.[93] AGA in an adolescent is not uncommon and topical minoxidil may be effectively used.[42,94] One case report of AGA seen in a 15-year-old girl was successfully treated with topical minoxidil and oral contraceptives.[95]

Alopecia Areata

Alopecia areata (AA) can be emotionally devastating to a person and can cause a significant impact on the patient's quality of life and self-esteem.[4] It can cause stigmatization[34] (see the "Hair Stigma and Hair Discordance" section). It may lead to clinical depression, anxiety, and/or social phobia. Management and treatment of the psychological impact of AA must not be overlooked.

9 Curative therapy for AA does not yet exist; however, there is a high rate of spontaneous remission even with no pharmacotherapy.[4] Alopecia totalis and alopecia universalis are more resistant to treatment. Due to the autoimmune and inflammatory nature of AA, effective pharmacotherapy primarily involves immunosuppressive agents used systemically, intralesionally, and/or topically. Treatments that may be effective include high-dose oral corticosteroids, intralesional corticosteroids, topical corticosteroids, topical minoxidil, topical immunotherapy, systemic and topical biologic agents (in particular the Janus kinase inhibitors discussed later in this section), azathioprine and other immunosuppressive agents, and a few miscellaneous agents. Robust RCTs are lacking or limited for some of these therapies; some treatments may not be suitable for children with AA.

Intralesional corticosteroids are the treatment of choice in adults.[34] The best-tested immunosuppressive treatment is intradermal (intralesional) triamcinolone acetonide (5-10 mg/mL) every 2 weeks[4] or every 4 to 6 weeks.[34] Monthly intervals would be more convenient for the patient. An effective method is to inject 0.1 mL of solution into multiple sites at 1 cm (0.4 in.) apart, into the deep dermis, with a maximum volume of 20 mL injected at each clinic visit.[34] This treatment stimulates regrowth in more than 60% of patients.[4] If there is no improvement at 6 months or if significant atrophy is noted, treatment should be discontinued.

Hydrocortisone acetate (25 mg/mL) is an alternative. Side effects include pain at injection sites, localized skin atrophy, and hypopigmentation. Dermal atrophy usually recovers over 3 to 6 months.[34] Relapses are common with treatment discontinuation.[4]

Topical corticosteroids (TCS) are commonly used, especially in children (since scalp injections are painful) and in those adults with less than 50% scalp involvement.[4] High-potency TCS such as clobetasol propionate used under occlusion is more effective since this may further increase potency. (As an aside, although keloid is an entirely different disease entity, a recent RCT found that clobetasol propionate 0.05% cream under silicone occlusion dressing was equally efficacious and had fewer adverse effects compared with intralesional triamcinolone.[96]) Treatment for AA may need to be continued for 3 months before regrowth is seen.[34] Monitor for topical and potentially systemic side effects since potent TCS are being used.[97] Folliculitis is a common side effect. Refer to Chapter 118, "Psoriasis/Psoriatic Arthrtis," for a corticosteroid potency comparison chart and for a detailed discussion of TCS side effects. A recent article about rational and ethical use of TCS also provides a summary.[97]

Systemic corticosteroids are efficacious in patients with AA. However, their side effects profile limits their use to short treatment periods of 2 to 3 months. Pulse dosing (eg, once weekly) is used to minimize systemic side effects. Regimens include prednisolone 0.5 mg/kg/day (usually of 40-50 mg/day) daily for 3 months,[34] prednisolone 200 mg once weekly for 3 months,[4] or dexamethasone 0.1 mg/kg/day (mean dose about 8 mg) on 2 consecutive days once weekly for at least 4 months and then slowly tapered or discontinued (with some patients on treatment for 2 years).[98] This dexamethasone regimen was used in 31 patients with alopecia totalis or alopecia universalis, and complete response was seen in 22 patients (71%) and partial response in 3 patients (10%). The mean time to response was 1.55 months, and the mean duration of therapy was 12.9 months (range 4-24 months). Adverse effects were seen in 10 of 31 patients (32%), including weight gain in 9 patients and Cushing syndrome, striae, and irritability in 1 patient each.

Relapses are seen after treatment is discontinued and sometimes during treatment.[98] Pulse therapy with high-dose systemic steroids has been used in other studies and may be an option for severe, extensive, or recalcitrant AA.

Biologic agents have exploded on the treatment scene for many dermatologic inflammatory disorders such as psoriasis, atopic dermatitis (AD), and AA,

including the subtypes alopecia totalis (AT) and alopecia universalis (AU). Some biologic agents may be used topically for AA, and some have been successfully used in children and adolescents.

Janus kinase (JAK) inhibitors (tofacitinib, ruxolitinib, baricitinib) are a promising new class of biologic treatment for AA.[99,100] A JAK-STAT (signal transducer and activator of transcription) signaling pathway is important in the hair growth cycle, with key genes being highly expressed in the catagen and telogen phases but suppressed in the anagen phase.[99] JAK inhibitors inhibit the JAK-STAT pathway, resulting in various immunologic changes that result in prolonging the anagen phase, angiogenesis, stimulating/activating the proliferation of hair stem cells, and other changes, which all manifest in hair regrowth, as shown in these studies[99]:

1. Studies and case reports of oral and topical *tofacitinib* demonstrate efficacy in adults and children with AA, including AA subtypes AT and AU.[100] Patients with AA may have greater response than patients with AA subtypes. Systemic treatments may be more effective than the topical route. Using the Severity of Alopecia Tool (SALT), a cohort study of oral tofacitinib 5 to 10 mg twice daily in 90 adults with AA and subtypes, found that 58% improved their SALT score by 50% or more over 4 to 18 months of treatment. Patients with AA showed a greater degree of change in SALT than those with alopecia totalis or universalis (82% vs 59%).[100] A retrospective review of 13 adolescents with AA treated with tofacitinib 5 mg twice daily found a 90% median improvement in SALT score (1%-100%), and there are many other recent studies.[100] A retrospective review of children under 12 years with AA, AT, or AU treated with tofacitinib identified three children aged 5 years or younger who failed previous treatment before tofacitinib and who responded to tofacitinib 2.5 mg daily for 4 days then 5 mg daily for 3 days each week (one child with >90% hair regrowth after 12 months of treatment and the other two children with >50% improvement by 6 months and 21 months, respectively).[101] Results with topical JAK inhibitors are poorer than with oral agents. Topical tofacitinib or ruxolitinib were applied to eyebrow regions/upper eyelids/scalp in 6 pediatric patients aged 3 to 17 years with AA, and responses were only seen in 3 patients.[102] Additional clinical studies are under way.
2. Fewer reports and studies have examined the use of *ruxolitinib;* however, there are reports of efficacy in hair regrowth in a few patients with AT who had failed therapy with tofacitinib.[103] Encouraging results and additional studies are under way.
3. There is one case report of oral *baricitinib* being effective in AA as an incidental finding, and other JAK inhibitors are on the horizon, including filgotinib and decernotinib, which are being tested for rheumatoid arthritis.

Dupilumab is a new class of biologic agents (an IL-4 receptor-α-antagonist) marketed for AD. It was found to trigger hair regrowth in two case reports of AD patients using dupilumab for AD: one case was a patient with long-standing AT[104] and the other case was a patient with long-standing AU.[105]

Methotrexate is a systemic immunosuppressive agent which may be an option for AA with extensive hair loss where other treatments have been ineffective. If efficacious, regrowth may be seen in 3 months with full regrowth in 6 to 12 months. Methotrexate is more efficacious when used with prednisone or prednisolone (various regimens). A regimen starting with IV methylprednisolone (500 mg/d × 3 days, then monthly × 3 cycles) prior to starting oral methotrexate has also shown efficacy in several studies.[106] Various dosing regimens of methotrexate have been used, most with starting doses of 2.5-10 mg/week and increasing to 15-25 mg/week.[106] In adults and children with severe AA, response to methotrexate was better in adults than in children, confirming that combination treatment with a corticosteroid results in higher complete response rates than methotrexate used alone.[106] Tapering often resulted in recurrence.[106]

Azathioprine has also been successfully used to treat AU including recalcitrant cases in adults (nonresponders to oral corticosteroids and topical immunotherapy with diphencyprone). A case study of 14 adult patients showed a complete response in 6 of 14 patients (43%). No identifiable prognostic factors were found, and adverse effects included elevated liver enzymes (1 patient), pancreatitis (1 patient), bone marrow suppression (1 patient), and diarrhea (2 patients); treatment had to be discontinued in 4 patients.[107]

Other agents have been tried for treating AA over the years with varying levels of success, including topical anthralin,[108,109] topical diphenylcyclopropenone,[109] topical calcineurin inhibitors, and oral cyclosporine. None of these is commonly used today because of inconsistent efficacy and/or side effects.

Loss of Eyelashes and Eyebrows

Bimatoprost (Latisse) 0.03% drops is FDA approved for treatment of hypotrichosis of the eyelashes, discovered due to increased eyelash growth

observed through usual use for elevated intraocular pressure in glaucoma. One drop is applied along the skin of the upper eyelid at the base of eyelashes once daily at bedtime. Beneficial effects may take months to be seen.[110,111] Bimatoprost 0.03% solution has also shown efficacy in hypotrichosis of the eyebrows.[112]

HAIR CARE IN THE PATIENT WITH ALOPECIA

Patients suffering from alopecia may attempt to manipulate their hair to hide their hair loss and to make their head of hair appear fuller; however, most methods may actually further damage the hair and are not recommended. Chemical processing such as hair weaving or hair straightening can further damage the hair and cause hair breakage.

All hair dyes can damage the hair with the exception of temporary hair dyes. Temporary hair dyes have particle sizes that are too large to penetrate through the cuticle, which minimizes hair damage and accounts for their temporary nature (they are removed by a single shampooing).

Heat denatures the keratin protein structure of the hair shaft and turns the water in the hair shaft into steam. This can physically remove the cuticular scale as the steam escapes from the hair shaft. Without the structural protection afforded by the cuticular scale, the hair breaks easily. Heat-damaged hair is known as bubble hair and cannot be repaired. Frequent hair combing or brushing may also damage the hair by encouraging cuticle removal.[113]

Hair should be combed or brushed only when dry, and excessive combing or brushing should be avoided. Brushing the hair 100 strokes a day and massaging the scalp vigorously with the brush are not appropriate for the patient with alopecia.[113]

Hair conditioners coat the hair shaft and smooth the cuticle, and they should be routinely used. Instant conditioners that are applied after shampooing and rinsed out coat the hair shaft with a thin dimethicone or quaternary ammonium compound to temporarily “glue down” loosened cuticular scales. Supplementing these with a leave-in conditioner can provide a thicker coating to further protect the hair until the next shampoo. Hair conditioners reduce combing friction, improve hair shine, increase hair softness, minimize static electricity, and reduce frizziness.[113]

HAIR STIGMA AND HAIR DISCORDANCE

“Beauty standards of hair are a form of bias.”[114] Men, women, adolescents, and children are often distressed when there is hair loss, or when their hair is perceived as “different” from the societal norm—such as in minoritized people of color. Adolescents and children in particular may be subject to bullying by their peers, sometimes just for having a head of hair that looks different.[115] In 2019, an anti-bullying song/video was released and a cosmetic manufacturer partnered in an anti-bullying campaign.[114,115]

Imagine the potential stigmatization/bullying situation if the person had patchy AA or AA totalis? This is involuntary hair loss which is quite different from people who have chosen to shave their heads such as monks. Stigmatization affects adults as well. Healthcare professionals should be cognizant of the psychosocial impact on their patient’s quality of life. A 2015 review of the burden of disease for patients with AA reported rates for depression (8.8%) and generalized anxiety disorder (18.2%), both significantly higher than in the general population (about 1%-2%).[41] This review also found that the rate of psychiatric comorbidity was influenced by the age of onset of AA, with an increased risk of depression in patients aged <20 years and increased risks of anxiety and obsessive-compulsive disorder in patients aged 40 to 59 years.[41]

Similarly, in patients with AGA or other forms of alopecia, the psychosocial impact must not be overlooked. Even with temporary anagen hair loss (such as chemotherapy-induced alopecia), the onset is usually sudden and may be absolutely traumatizing to the patient.

In addition, hair discordance may be present between a healthcare professional and an alopecia patient of color seeking care. There may be patient discomfort and/or a negative perception of the ability of the healthcare professional to meet their care needs. A survey of Black women with alopecia reported that some physicians did not touch their hair, and some were unfamiliar with their usual hair care routine.[116] Another recent study noted that alopecia is one of the most common conditions for patients of African descent being seen by a dermatologist.[117]

Thus, healthcare professionals should be cognizant that hair stigma and hair discordance may be potential issues. Being aware of common cultural hair care practices and being empathetic in interactions with the patient with alopecia are important components of care.

An approach to examining tightly coiled hair for patients with hair loss in race-discordant patient-physician interactions is available, describing appropriate actions, tips for hair examination, and sample language appropriate for the interaction.[118]

CONCLUSION

Alopecia is the visible result of many diverse causes, some of which may be temporary and easily reversible and others refractory to therapy. Identifying the cause is key. Management/treatment of alopecia should be as cause-specific as possible. In addition, psychosocial support should always be considered.

ABBREVIATIONS

ACTH	adrenocorticotropic hormone
AA	alopecia areata
AD	atopic dermatitis
AGA	androgenetic alopecia
AT	alopecia totalis (or alopecia areata totalis)
aTE	acute telogen effluvium
AU	alopecia universalis (or alopecia areata universalis)
BMPs	bone morphogenetic proteins
BPH	benign prostatic hyperplasia
CI	confidence interval
DHEA	dehydroepiandrosterone
DHT	dihydrotestosterone
F	female
FGF	fibroblast growth factor
FPHL	female pattern hair loss
HGF	hepatic growth factor
IGF	insulin-like growth factor
IL	interleukin
JAK-STAT	Janus Kinase-signal transducer and activator of transcription
KOH	potassium hydroxide

LFTs	liver function tests
LLLL	low-level laser light
M	male
NT	neurotrophins
PCOS	polycystic ovarian syndrome
PRP	platelet-rich plasma
QoL	quality of life
RCT	randomized controlled trial
RR	risk ratio
SALT	severity of Alopecia Tool
SLE	systemic lupus erythematosus
SSRI	selective serotonin reuptake inhibitor
TCM	traditional Chinese medicine
TCS	topical corticosteroids
TGF	transforming growth factor
TNF	tumor necrosis factor
WNT	aportmanteau created from the name Wingless and the name Int-1
VEGF	vascular endothelial growth factor

REFERENCES

1. Phillips TG, Slomiany WP, Allison R. Hair loss: Common causes and treatment. *Am Fam Physician*. 2017;96(6):371–378. [PubMed: 28925637]

2. Buffoli B, Rinaldi F, Labanca M, et al. The human hair: From anatomy to physiology. *Int J Dermatol.* 2014;53(3):331–341. doi: 0.1111/ijd.12362.

3. Mandt N, Troilius A, Drosner M. Epilation today: Physiology of the hair follicle and clinical photo-epilation. *J Investig Dermatol Symp Proc.* 2005;10(3):271–274. [PubMed: 16382679]

4. Gilhar A, Etzioni A, Paus R. Alopecia areata. *N Engl J Med.* 2012;366(16):1515–1525. doi: 10.1056/NEJMra1103442.

5. Yang CC, Cotsarelis G. Review of hair follicle dermal cells. *J Dermatol Sci.* 2010;57(1):2–11. doi: 10.1016/j.jdermsci.2009.11.005.

6. Erdoğan B. (2017, May 03). Anatomy and physiology of hair. Retrieved May 22, 2019, from https://www.intechopen.com/books/hair-and-scalp-disorders/anatomy-and-physiology-of-hair.

7. Schneider MR, Schmidt-Ullrich R, Paus R. The hair follicle as a dynamic miniorgan. *Curr Biol.* 2009;19(3):R132–R142. doi: 10.1016/j.cub.2008.12.005.

8. Mysore V, Shashikumar BM. Guidelines on the use of finasteride in androgenetic alopecia. *Indian J Dermatol Venereol Leprol.* 2016;82(2):128–134. doi: 10.4103/0378-6323.177432.

9. Juárez-Rendón KJ, Rivera Sánchez G, Reyes-López MÁ, et al. Alopecia Areata. Current situation and perspectives. *Arch Argent Pediatr.* 2017;115(6):e404–e411. doi: 10.5546/aap.2017.eng.e404.

10. Ellis JA, Stebbing M, Harrap SB. Insulin gene polymorphism and premature male pattern baldness in the general population. *Clin Sci (Lond).* 1999;96(6):659–662. [PubMed: 10334972]

11. Ellis JA, Stebbing M, Harrap SB. Genetic analysis of male pattern baldness and the 5alpha-reductase genes. *J Invest Dermatol.* 1998;110(6):849–853. [PubMed: 9620288]

12. Hillmer AM, Kruse R, Macciardi F, et al. The hairless gene in androgenetic alopecia: Results of a systematic mutation screening and a family-based association approach. *Br J Dermatol.* 2002;146(4):601–608. [PubMed: 11966690]

13. Hillmer AM, Hanneken S, Ritzmann S, et al. Genetic variation in the human androgen receptor gene is the major determinant of common early-onset androgenetic alopecia. *Am J Hum Genet.* 2005;77(1):140–148. doi: 10.1086/431425.

14. Petukhova L, Duvic M, Hordinsky M, et al. Genome-wide association study in alopecia areata implicates both innate and adaptive immunity. *Nature*. 2010;466(7302):113–117. doi: 10.1038/nature09114.

15. Jagielska D, Redler S, Brockschmidt FF, et al. Follow-up study of the first genome-wide association scan in alopecia areata: IL13 and KIAA0350 as susceptibility loci supported with genome-wide significance. *J Invest Dermatol.* 2012;132(9):2192–2197. doi: 10.1038/jid.2012.129.

16. Courtois M, Loussouarn G, Hourseau C, Grollier JF. Hair cycle and alopecia. *Skin Pharmacol.* 1994;7(1-2):84–89. [PubMed: 8003330]

17. Guarrera M, Rebora A. Anagen hairs may fail to replace telogen hairs in early androgenic female alopecia. *Dermatology*. 1996;192(1):28–31. [PubMed: 8832948]

18. Kibar M, Aktan S, Bilgin M. Scalp dermatoscopic findings in androgenetic alopecia and their relations with disease severity. *Ann Dermatol.* 2014;26(4):478–484. doi: 10.5021/ad.2014.26.4.478.

19. Cranwell W, Sinclair R, et al. Male androgenetic alopecia. [Updated 2016 Feb 29]. In: Feingold KR, Anawalt B, Boyce A, et al., eds. *Endotext [Internet].* South Dartmouth (MA): MDText.com, Inc; 2000. Available at: https://www.ncbi.nlm.nih.gov/books/NBK278957/

20. Zhao Y, Zhang B, Caulloo S, Chen X, Li Y, Zhang X. Diffuse alopecia areata is associated with intense inflammatory infiltration and CD8+ T cells in hair loss regions and an increase in serum IgE level. *Indian J Dermatol Venereol Leprol.* 2012;78(6):709–714. [PubMed: 23075639]

21. Filbrandt R, Rufaut N, Jones L, Sinclair R. Primary cicatricial alopecia: Diagnosis and treatment. *CMAJ.* 2013;185(18):1579–1585. doi: 10.1503/cmaj.111570.

22. Harries MJ, Sinclair RD, Macdonald-Hull S, Whiting DA, Griffiths CE, Paus R. Management of primary cicatricial alopecias: Options for treatment. *Br J Dermatol.* 2008;159(1):1–22. doi: 10.1111/j.1365-2133.2008.08591.x.

23. Piraccini BM, Alessandrini A. Androgenetic alopecia. *G Ital Dermatol Venereol.* 2014;149(1):15–24. [PubMed: 24566563]

24. Rubio-Gonzalez B, Juhász M, Fortman J, Mesinkovska NA. Pathogenesis and treatment options for chemotherapy-induced alopecia: A systematic review. *Int J Dermatol.* 2018;57(12):1417–1424. doi: 10.1111/ijd.13906.

25. Dhurat RP, Deshpande DJ. Loose anagen hair syndrome. *Int J Trichology*. 2010;2(2):96–100. doi: 10.4103/0974-7753.77513.

26. Loh SH, Lew BL, Sim WY. Localized telogen effluvium following hair transplantation. *Ann Dermatol.* 2018;30(2):214–217. doi: 10.5021/ad.2018.30.2.214.

27. Harvard Health Publishing. Harvard Medical School. Treating female pattern hair loss. https://www.health.harvard.edu/staying-healthy/treating-female-pattern-hair-loss. November 14, 2018; August 24, 2019.

28. Hay RJ. Tinea capitis: Current status. *Mycopathologia.* 2017;182(1-2):87–93. doi: 10.1007/s11046-016-0058-8.

29. Almeida MC, Romiti R, Doche I, Valente NY, Donati A. Psoriatic scarring alopecia. *An Bras Dermatol.* 2013;88(6 suppl 1):29–31. doi: 10.1590/abd1806-4841.20132241.

30. Borda LJ, Wikramanayake TC. Seborrheic dermatitis and dandruff: A comprehensive review. *J Clin Investig Dermatol.* 2015;3(2). doi: 10.13188/2373-1044.1000019.

31. Tosti A, Piraccini BM, van Neste DJ. Telogen effluvium after allergic contact dermatitis of the scalp. *Arch Dermatol.* 2001;137(2):187–190. [PubMed: 11176691]

32. Brown F, Badri T. Pityriasis Rubra Pilaris. [Updated 2019 February 22]. In: *StatPearls [Internet]*. Treasure Island (FL): StatPearls Publishing; 2019. Available at: https://www.ncbi.nlm.nih.gov/books/NBK482436/.

33. Rothe MJ, Bialy TL, Grant-Kels JM. Erythroderma. *Dermatol Clin.* 2000 Jul;18(3):405–415. [PubMed: 10943536]

34. Perera E, Yip L, Sinclair R. Alopecia areata. In: Ioannides D, Tosti A, eds. *Alopecias—Practical Evaluation and Management. Curr Probl Dermatol.* Basel: Karger, 2015;47:67–75. doi: 10.1159/000369406.

35. Kyriakis KP, Paltatzidou K, Kosma E, Sofouri E, Tadros A, Rachioti E. Alopecia areata prevalence by gender and age. *J Eur Acad Dermatol Venereol.* 2009;23(5):572–573. doi: 10.1111/j.1468-3083.2008.02956.x.

36. Amin SS, Sachdeva S. (n.d.). Alopecia areata: An update. Retrieved May 22, 2019, from http://jpad.com.pk/index.php/jpad/article/view/346.

37. Seetharam KA. Alopecia areata: An update. *Indian J Dermatol Venereol Leprol.* 2013;79(5):563–575. doi: 10.4103/0378-6323.116725.

38. Al-Refu K. Hair loss in children: Common and uncommon causes; clinical and epidemiological study in Jordan. *Int J Trichology*. 2013;5(4):185–189. doi: 10.4103/0974-7753.130393.

39. Lundin M, Chawa S, Sachdev A, Bhanusali D, Seiffert-Sinha K, Sinha AA. Gender differences in alopecia areata. *J Drugs Dermatol.* 2014;13(4):409–413. [PubMed: 24719059]

40. Lacarrubba F, Micali G, Tosti A. Scalp dermoscopy or trichoscopy. *Curr Probl Dermatol.* 2015;47:21–32. doi: 10.1159/000369402.

41. Villasante Fricke AC, Miteva M. Epidemiology and burden of alopecia areata: A systematic review. *Clin Cosmet Investig Dermatol.* 2015;8:397–403. doi: 10.2147/CCID.S53985.

42. Xu L, Liu KX, Senna MM. A practical approach to the diagnosis and management of hair loss in children and adolescents. *Front Med (Lausanne)*. 2017;4:112. doi: 10.3389/fmed.2017.00112.

43. Torborg L. Mayo Clinic Q & A: Cold cap therapy can reduce hair loss caused by chemotherapy. January 30, 2018. Mayo Clinic. Available at: https://newsnetwork.mayoclinic.org/discussion/mayo-clinic-q-and-a-cold-cap-therapy-can-reduce-hair-loss-caused-by-chemotherapy/. Accessed May 19, 2019.

44. Cold caps and scalp cooling systems. March 11, 2019. BreastCancer.org. Available at: https://www.breastcancer.org/tips/hair_skin_nails/cold-caps. Accessed May 19, 2019.

45. Skalnaya MG. Chapter 17: Copper deficiency a new reason of androgenetic alopecia? Pharmacology and Nutritional Intervention in the Treatment of Disease. Available at: http://dx.doi.org/10.5772/58416. Accessed April 30, 2019.

46. Ninan PT, Rothbaum BO, Marsteller FA, et al. A placebo-controlled trial of cognitive-behavioural therapy and clomipramine in trichotillomania. *J Clin Psychiatry*. 2000;61(1):47–50. [PubMed: 10695646]

47. Likhitkar M, Shakur AA, Bansal KK, Pande M. Alopecia—Reason and possible treatments. *MOJ Drug Design Development & Therapy*. 2018;2(5):198–208.

48. Fabbrocini G, Cantelli M, Masarà A, Annunziata MC, Marasca C, Cacciapuoti S. Female pattern hair loss: A clinical, pathophysiologic, and therapeutic review. *Int J Womens Dermatol.* 2018;4(4):203–211. doi: 10.1016/j.ijwd.2018.05.001.

49. van Zuuren EJ, Fedorowicz Z, Schoones J. Interventions for female pattern hair loss. *Cochrane Database Syst Rev.* 2016;2016(5):CD007628. doi: 10.1002/14651858.CD007628.pub4.

50. Blumeyer A, Tosti A, Messenger A, et al.; European Dermatology Forum (EDF). Evidence-based (S3) guideline for the treatment of androgenetic alopecia in women and in men. *J Dtsch Dermatol Ges.* 2011;9(suppl 6):S1–S57. doi: 10.1111/j.1610-0379.2011.07802.x.

51. Lee WS, Lee HJ, Choi GS, et al. Guidelines for management of androgenetic alopecia based on BASP classification—The Asian Consensus Committee guideline. *J Eur Acad Dermatol Venereol.* 2013;27(8):1026–1034. doi: 10.1111/jdv.12034.

52. Torres F. Androgenetic, diffuse and senescent alopecia in men: Practical evaluation and management. In: Ioannides D, Tosti A, eds. *Alopecia—Practical Evaluation and Management. Curr Probl Dermatol.* Basel: Karger; 2015;47:33–44. doi: 10.1159/000369403.

53. Olsen EA, Dunlap FE, Funicella T, et al. A randomized clinical trial of 5% topical minoxidil versus 2% topical minoxidil and placebo in the treatment of androgenetic alopecia in men. *J Am Acad Dermatol.* 2002;47(3):377–385. [PubMed: 12196747]

54. Roberts JL, Fiedler V, Imperato-McGinley J, et al. Clinical dose ranging studies with finasteride, a type 2 5alpha-reductase inhibitor, in men with male pattern hair loss. *J Am Acad Dermatol.* 1999;41(4):555–563. [PubMed: 10495375]

55. Gubelin Harcha W, Barboza Martínez J, Tsai TF, et al. A randomized, active- and placebo-controlled study of the efficacy and safety of different doses of dutasteride versus placebo and finasteride in the treatment of male subjects with androgenetic alopecia. *J Am Acad Dermatol.* 2014;70(3):489–498 e3. doi: 10.1016/j.jaad.2013.10.049.

56. Stough DB, Rao NA, Kaufman KD, Mitchell C. Finasteride improves male pattern hair loss in a randomized study in identical twins. *Eur J Dermatol.* 2002;12(1):32–37. [PubMed: 11809593]

57. Van Neste D, Fuh V, Sanchez-Pedreno P, et al. Finasteride increases anagen hair in men with androgenetic alopecia. *Br J Dermatol.* 2000;143(4):804–810. [PubMed: 11069460]

58. Van Neste D. Natural scalp hair regression in preclinical stages of male androgenetic alopecia and its reversal by finasteride. *Skin Pharmacol Physiol.* 2006;19(3):168–176. [PubMed: 16679818]

59. Neste DV. (2019, May 12). Maintenance of optimised hair growth from viable terminal scalp hair follicles at baseline with oral finasteride in male

pattern hair loss and first evidence of a “drug dependency” and a post-finasteride “rebound effect”. Retrieved May 22, 2019. Available at: https://onlinelibrary.wiley.com/doi/abs/10.1111/srt.12707.

60. Lee S, Lee YB, Choe SJ, Lee WS. Adverse sexual effects of treatment with finasteride or dutasteride for male androgenetic alopecia: A systematic review and meta-analysis. *Acta Derm Venereol.* 2019;99(1):12–17. doi: 10.2340/00015555-3035.

61. Torres F. Androgenetic, and senescent alopecia in men: Practical evaluation and management. In: Ioannides D, Tosti A, eds. *Alopecia—Practical Evaluation and Management. Curr Probl Dermatol.* Basel: Karger; 2015:47:33–44. doi: 10.1159/000369403.

62. Eun HC, Kwon OS, Yeon JH, et al. Efficacy, safety, and tolerability of dutasteride 0.5 mg once daily in male patients with male pattern hair loss: A randomized, double-blind, placebo-controlled, phase III study. *J Am Acad Dermatol.* 2010;63(2):252–258. doi: 10.1016/j.jaad.2009.09.018.

63. Gajjar PC, Mehta HH, Barvaliya M, Sonagra B. Comparative study between mesotherapy and topical 5% minoxidil by dermoscopic evaluation for androgenic alopecia in male: A randomized controlled trial. *Int J Trichology*. 2019;11(2):58–67. doi: 10.4103/ijt.ijt_89_18.

64. Saceda-Corralo D, Rodrigues-Barata AR, Vañó-Galván S, Jaén-Olasolo P. Mesotherapy with dutasteride in the treatment of androgenetic alopecia. *Int J Trichology*. 2017;9(3):143–145. doi: 10.4103/ijt.ijt_73_16.

65. McElwee KJ, Shapiro JS. Promising therapies for treating and/or preventing androgenic alopecia. *Skin Therapy Lett.* 2012;17(6):1–4. [PubMed: 22735503]

66. Jones MC. (2018, August 17). Treatment Options for Androgenetic Alopecia. Retrieved May 22, 2019. Available at: https://www.uspharmacist.com/article/treatment-options-for-androgenetic-alopecia.

67. Picard F, Hersant B, Niddam J, Meningaud JP. Injections of platelet-rich plasma for androgenic alopecia: A systematic review. *J Stomatol Oral Maxillofac Surg.* 2017;118(5):291–297. doi: 10.1016/j.jormas.2017.06.011.

68. Cervelli V, Garcovich S, Bielli A, et al. The effect of autologous activated platelet rich plasma (AA-PRP) injection on pattern hair loss: Clinical and histomorphometric evaluation. *Biomed Res Int.* 2014;2014. doi: 10.1155/2014/760709.

69. Verma K, Tegta GR, Verma G, Gupta M, Negi A, Sharma R. A study to compare the efficacy of platelet-rich plasma and minoxidil therapy for the treatment of androgenetic alopecia. *Int J Trichology*. 2019;11(2):68–79. doi: 10.4103/ijt.ijt_64_18.

70. Kelly Y, Blanco A, Tosti A. Androgenetic alopecia: An update of treatment options. *Drugs*. 2016;76(14):1349–1364. doi: 10.1007/s40265-016-0629-5.

71. Jo SJ, Shin H, Park YW, et al. Topical valproic acid increases the hair count in male patients with androgenetic alopecia: A randomized, comparative, clinical feasibility study using phototrichogram analysis. *J Dermatol.* 2014;41(4):285–291. [PubMed: 24533507]

72. Lee CY, Wei CC, Yu MC, et al. Hair growth effect of traditional Chinese medicine BeauTop on androgenetic alopecia patients: A randomized double-blind placebo-controlled clinical trial. *Exp Ther Med.* 2017;13(1):194–202. doi: 10.3892/etm.2016.3935.

73. Sonthalia S, Daulatabad D, Tosti A. (2016, January 23). Hair Restoration in Androgenetic Alopecia: Looking Beyond Minoxidil, Finasteride and Hair Transplantation. Retrieved May 22, 2019. Available at: https://www.omicsonline.org/open-access/hair-restoration-in-androgenetic-alopecia-looking-beyond-minoxidil-finasteride-and-hair-transplantation-jctt1000105.php?aid=68395.

74. Narda M, Aladren S, Cestone E, Nobile V. (2017, November 30). Efficacy and Safety of a Food Supplement Containing L-cystine, Serenoa repens Extract and Biotin for Hair Loss in Healthy Males and Females. A Prospective, Randomized, Double-blinded, Controlled Clinical Trial. Available at: https://www.omicsonline.org/open-access/efficacy-and-safety-of-a-food-supplement-containing-lcystine-serenoa-repens-extract-and-biotin-for-hair-loss-in-healthy-males-and-2471-9323-1000127-96167.html.

75. Starace M, Orlando G, Alessandrini A, Piraccini BM. Female androgenic alopecia: An update on diagnosis and management. *Am J Clin Dermatol.*

2020;21(1):69–84. [PubMed: 31677111]

76. Won YY, Lew BL, Sim WY. Clinical efficacy of oral administration of finasteride at a dose of 2.5 mg/day in women with female pattern hair loss. *Dermatol Ther.* 2018;31(2):e12588. [PubMed: 29464847]

77. Yeon JH, Jung JY, Choi JW, et al. 5 mg/day finasteride treatment for normoandrogenic Asian women with female pattern hair loss. *J Eur Acad Dermatol Venereol.* 2011;25:211–214. [PubMed: 20569283]

78. Oliveira-Soares R, E Silva JM, Correia MP, Andre MC. Finasteride 5 mg/day treatment of patterned hair loss in normo-androgenetic postmenopausal women. *Int J Trichol.* 2013;5:22–25.

79. Shum KW, Cullen DR, Messenger AG. Hair loss in women with hyperandrogenism: Four cases responding to finasteride. *J Am Acad Dermatol.* 2002;47(5):733–739. [PubMed: 12399766]

80. Ioannides D, Lazaridou E. Female pattern hair loss. *Curr Probl Dermatol.* 2015:47:45–54. doi: 10.1159/000369404.

81. Olszewska M, Rudnicka L. Effective treatment of female androgenic alopecia with dutasteride. *J Drugs Dermatol.* 2005;4(5):637–640. [PubMed: 16167423]

82. Vexiau P, Chaspoux C, Boudou P, et al. Effects of minoxidil 2% vs. cyproterone acetate treatment on female androgenetic alopecia: A controlled, 12-month randomized trial. *Br J Dermatol.* 2002;146(6):992–999. [PubMed: 12072067]

83. Sinclair R, Wewerinke M, Jolley D. Treatment of female pattern hair loss with oral antiandrogens. *Br J Dermatol.* 2005;152(3):466–473. [PubMed: 15787815]

84. Paradisi R, Porcu E, Fabbri R, Seracchioli R, Battaglia C, Venturoli S. Prospective cohort study on the effects and tolerability of flutamide in patients with female pattern hair loss. *Ann Pharmacother.* 2011;45(4):469–475. doi: 10.1345/aph.1P600.

85. Azarchi S, Bienenfeld A, Lo Sicco K et al. Androgens in women: Hormone modulating therapies for skin disease (part II). *J Am Acad Dermatol.* 2019;80(6):1509–1521. doi: 10.1016/j.jaad.2018.08.061.

86. Le Floc'h C, Cheniti A, Connétable S, Piccardi N, Vincenzi C, Tosti A. Effect of a nutritional supplement on hair loss in women. *J Cosmet Dermatol.* 2015;14(1):76–82. doi: 10.1111/jocd.12127.

87. Torkos S, Gazella K. (2015, April). Essential Fatty Acids and Antioxidants Benefit Women With Female Pattern Hair Loss. Retrieved May 22, 2019. Available at: https://www.naturalmedicinejournal.com/journal/2015-04/essential-fatty-acids-and-antioxidants-benefit-women-female-pattern-hair-loss.

88. Katoulis AC, Liakou AI, Alevizou A, et al. Efficacy and safety of a topical botanical in female androgenetic alopecia: A randomized, single-blinded, vehicle-controlled study. *Skin Appendage Disord.* 2018;4(3):160–165. doi: 10.1159/000480024.

89. Liu KH, Liu D, Chen YT, Chin SY. Comparative effectiveness of low-level laser therapy for adult androgenic alopecia: A system review and meta-analysis of randomized controlled trials. *Lasers Med Sci.* 2019;34(6):1063–1069. [PubMed: 30706177]

90. Starace M, Alessandrini A, D'Acunto C, et al. Platelet-rich plasma on female androgenetic alopecia: Tested on 10 patients. *J Cosmet Dermatol.* 2019;18(1):59–64. [PubMed: 29707872]

91. Kanti V, Messenger A, Dobos G, et al. Evidence-based (S3) guideline for the treatment of androgenetic alopecia in women and men. *Eur Acad Dermatol.* 2018;32(1):11–22.

92. Hunter N, Sayed K, Hay RA, Allam R, Hussein N. Comparing the efficacy of mesotherapy to topical minoxidil in the treatment of female pattern hair

loss using ultrasound biomicroscopy: A randomized controlled trial. *Acta Dermatovenerol Croat.* 2019;27(1):1–7. [PubMed: 31032783]

93. Tosti A, Iorizzo M, Piraccini BM. Androgenetic alopecia in children: Report of 20 cases. *Br J Dermatol.* 2005;152(3):556–559. [PubMed: 15787828]

94. Price VH. Androgenetic alopecia in adolescents. *Cutis*. 2003;71(2):115–121. [PubMed: 12635889]

95. Rodrigues M, Antunes I, Magalhães S, et al. Androgenic alopecia: An entity to consider in adolescence. *Case Reports*. 2017; 2017:bcr-2017-220679.

96. Nor NM, Ismail R, Jamil A, Shah SA, Imran FH. A randomized, single-blind trial of clobetasol propionate 0.05% cream under silicone dressing occlusion versus intra-lesional triamcinolone for treatment of keloid. *Clin Drug Investig*. 2017;37(3):295–301. doi: 10.1007/s40261-016-0484-x.

97. Rathi SK, D'Souza P. Rational and ethical use of topical corticosteroids based on safety and efficacy. *Indian J Dermatol.* 2012;57(4):251–259. doi: 10.4103/0019-5154.97655.

98. Vañó-Galván S, Hermosa-Gelbard Á, Sánchez-Neila N, et al. Pulse corticosteroid therapy with oral dexamethasone for the treatment of adult alopecia totalis and universalis. *J Am Acad Dermatol.* 2016;74(5):1005–1007. [PubMed: 27085229]

99. Triyangkulsri K, Suchonwanit P. Role of janus kinase inhibitors in the treatment of alopecia areata. *Drug Des Devel Ther.* 2018;12:2323–2335. doi: 10.2147/DDDT.S172638.

100. Liu LY, Craiglow BG, Dai F, King BA. Tofacitinib for the treatment of severe alopecia areata and variants: A study of 90 patients. *J Am Acad Dermatol.* 2017;76(1):22–28. doi: 10.1016/j.jaad.2016.09.007.

101. Dai YX, Chen CC. Tofacitinib therapy for children with severe alopecia areata. *J Am Acad Dermatol.* 2019;80(4):1164–1166. doi: 10.1016/j.jaad.2018.12.041.

102. Bayart CB, DeNiro KL, Brichta L, Craiglow BG, Sidbury R. Topical Janus kinase inhibitors for the treatment of pediatric alopecia areata. *J Am Acad Dermatol.* 2017;77(1):167–170. doi: 10.1016/j.jaad.2017.03.024.

103. Liu LY, King BA. Ruxolitinib for the treatment of severe alopecia areata. *J Am Acad Dermatol.* 2019;80(2):566–568. doi: 10.1016/j.jaad.2018.08.040.

104. Penzi LR, Yasuda M, Manatis-Lornell A, Hagigeorges D, Senna MM. Hair regrowth in a patient with long-standing alopecia totalis and atopic dermatitis treated with dupilumab. *JAMA Dermatol.* 2018;154(11):1358–1360. doi: 10.1001/jamadermatol.2018.2976.

105. Smogorzewski J, Sierro T, Compoginis G, Kim G. Remission of alopecia universalis in a patient with atopic dermatitis treated with dupilumab. *JAAD Case Rep.* 2019;5(2):116–117. doi: 10.1016/j.jdcr.2018.11.007.

106. Phan K, Ramachandran V, Sebaratnam DF. Methotrexate for alopecia areata: A systematic review and meta-analysis. *J Am Acad Dermatol.* 2019;80(1):120–127.e2. [PubMed: 30003990]

107. Vañó-Galván S, Hermosa-Gelbard Á, Sánchez-Neila N, et al. Treatment of recalcitrant adult alopecia areata universalis with oral azathioprine. *J Am Acad Dermatol.* 2016;74(5):1007–1008. doi: 10.1016/j.

108. Fiedler-Weiss VC, Buys CM. Evaluation of anthralin in the treatment of alopecia areata. *Arch Dermatol.* 1987;123(11):1491–1493. [PubMed: 3314718]

109. Spano F, Donovan JC. Alopecia areata: Part 2: Treatment. *Can Fam Physician*. 2015;61(9):757–761. [PubMed: 26371098]

110. Jha AK, Sarkar R, Udavan UK et al. Bimatoprost in dermatology. *Ind Dermatol Online J.* 2018;9(3):224–228.

111. Barron-Hernandez YL, Tosti A. Bimatoprost for the treatment of eyelash, eyebrow, and scalp alopecia. *Expert Opin Invest Drugs*. 2017;26(4):515–

522. doi: 10.1080/13543784.2017.1303480.

112. Riahi RR, Cohen PH. Topical treatment of eyebrow hypotrichosis with bimatoprost 0.03% solution: Case report and literature review. *Cureus*. 2018;10(5):e2666. doi: 10.7759/cureus.2666.

113. Draelos ZD. Hair care and dyeing. *Curr Probl Dermatol.* 2015;47:121–127. doi: 10.1159/000368412.

114. Dove US (a skin care product company). YouTube. Beauty standards of hair are a form of bias. Available at: https://www.youtube.com/watch?v=agptI1_1C40. August 25, 2019.

115. Rowland K. YouTube. Crown. Available at: https://www.youtube.com/watch?v=LUkqY-pR5EU. August 25, 2019.

116. Gorbatenko-Roth K, Prose N, Kundu RV, Patterson S. Assessment of Black patients' perception of their dermatology care. *JAMA Dermatol.* 2019;155(10):1129–1134. doi: 10.1001/jamadermatol.2019.2063.

117. Gaulding JV, Gutierrez D, Bhatia BK et al. Epidemiology of skin diseases in a diverse patient population. *J Drugs Dermatol.* 2018;17(10):1032–1036. [PubMed: 30365582]

118. Grayson C, Heath C. An approach to examining tightly coiled hair among patients with hair loss in race-discordant patient-physician interactions. *JAMA Dermatol.* 2021;157(5):505–506. [PubMed: 33787820]

SELF-ASSESSMENT QUESTIONS

1. Which of the following statements about the hair shaft is incorrect?
   A. The cuticle is responsible for elasticity and resiliency.
   B. The cortex contains melanin and determines hair color.
   C. The medulla contains keratin and determines whether the hair is straight or curly.
   D. There are three layers of the hair shaft namely the cuticle, the cortex, and the medulla.
2. The infundibulum is:
   A. A reservoir for the sebaceous gland
   B. A funnel shaped cavity
   C. Usually filled with sebum
   D. In the lower segment of the hair follicle
3. The phases of the hair cycle, beginning with the growth phase, are:
   A. Anagen, Telogen, Catagen, Exogen
   B. Anagen, Catagen, Telogen, Exogen
   C. Catagen, Telogen, Exogen, Anagen
   D. Anagen, Catagen, Telogen, Exogen
4. Which of the following growth factors is not part of the anagen phase?

A. Transforming growth factor β1 (TGF-β1)

B. Insulin-like growth factor-1 (IGF-1)

C. Fibroblast growth factor-7 (FGF-7)

D. Hepatic growth factor (HGF)

5. The hormone most responsible for pattern hair loss is:

A. Testosterone

B. Adrenocorticotropic hormone

C. Dihydrotestosterone (DHT)

D. Thyroid hormone

6. The most common cause of inflammation-induced alopecia is:

A. Alopecia areata

B. Androgenetic alopecia

C. Psoriatic alopecia

D. Isotretinoin

7. Tinea capitis presents with all of the following EXCEPT:

A. Scaling

B. Patchy hair loss

C. Black dots

D. Honey-colored crusts

8. Scarring hair loss may be caused by:

A. Frontal fibrosing alopecia

B. Chronic cutaneous lupus erythematosus

C. Burns

D. All of the above

9. “Exclamation mark” hairs are associated with:

A. Androgenetic alopecia

B. Alopecia areata

C. Cicatricial alopecia

D. Allergic contact dermatitis of the scalp

10. Treatment of trichotillomania includes all of the following EXCEPT:

    A. Cognitive behavior therapy

    B. Selective serotonin reuptake inhibitors

    C. Mesotherapy

    D. Olanzapine

11. Which of the following statements is true about topical minoxidil?

    A. It is a treatment for alopecia areata.

    B. The 5% lotion is recommended for use in women with alopecia.

    C. Hair shedding/hair loss may occur for a few weeks to months when it is first used.

    D. Topical use avoids systemic side effects totally.

12. Which of the following statements is true about finasteride?

    A. It reduces scalp production of DHT.

    B. It can increase total hair counts after 6 months of use.

    C. Miniaturized hair follicles do not respond to finasteride.

    D. All of the above are true statements.

13. The most concerning side effect for finasteride and dutasteride is:

    A. Nephrotoxicity

    B. Sexual dysfunction

    C. GI intolerance

    D. Muscle cramps

14. The treatment of choice for alopecia areata in adults is:

    A. Intralesional corticosteroids such as triamcinolone acetonide

    B. Systemic corticosteroids such as prednisone

    C. Dupilumab

    D. Azathioprine

15. Appropriate hair care for patients with alopecia include all of the following EXCEPT:

    A. Hair conditioners after each shampoo

    B. Supplementing with a leave-in hair conditioner

    C. Combing/brushing hair only when dry

    D. Brushing the hair 100 strokes a day

SELF-ASSESSMENT QUESTION-ANSWERS

1. **C.** It's the cortex that contains keratin and determines whether the hair is straight or curly.
2. **D.** It is in the upper segment of the hair follicle.
3. **D.** Response D shows the correct order of the hair cycle, beginning with the growth phase.
4. **A.** The transforming growth factor is part of the catagen phase.
5. **C.** DHT has greater affinity to androgen receptors than testosterone and is responsible for shortening the telogen phase, leading to more rapid hair loss.
6. **A.** Alopecia areata is the most common cause of inflammation-induced alopecia, although inflammation also plays a role in androgenetic alopecia and psoriatic alopecia.
7. **D.** Honey-colored crusts are associated with seborrheic dermatitis.
8. **D.** All are potentials causes of scarring hair loss.
9. **B.** "Exclamation mark" hairs are hairs where the distal hair shaft is broader than the proximal end, and this is associated with alopecia areata.
10. **C.** Mesotherapy is a treatment possibly useful for androgenetic alopecia.
11. **C.** Transient hair loss may initially occur, which indicates that minoxidil is stimulating telogen follicles to re-enter anagen.
12. **D.** All of the listed statements are correct with regard to finasteride.
13. **B.** Sexual dysfunction is the most concerning adverse effect of these agents.
14. **A.** Although benefits have been shown for B, C, and D, these are not the treatment of choice. Systemic corticosteroids should only be used for short treatment periods of 23 months due to their side-effects profile. Dupilumab is marketed for atopic dermatitis, and benefits in alopecia areata has been an incidental finding. Azathioprine may be an alternative treatment in recalcitrant cases in adults.
15. **D.** It is inappropriate to brush the hair 100 strokes a day or massage the scalp vigorously with the hair brush.