Hair Biology
Growth and Pigmentation

Andrea M. Park, MD[a,*,1], Sajjad Khan, MD[b], Jeffrey Rawnsley, MD[a]

KEYWORDS

• Hair growth cycle • Hair pigmentation • Gray hair • Hair biology • Minoxidil • Finasteride • Dutasteride • PRP

KEY POINTS

- The 3 phases of the hair growth cycle are anagen, catagen, and telogen.
- Topical minoxidil opens potassium channels and increases the diameter of existing hairs.
- Oral finasteride is a Food and Drug Administration–approved type 2 5α-reductase inhibitor that affects the follicle, size, and amount of hair.
- Dutasteride is a type 1 and type 2 5α-reductase inhibitor used off-label to treat hair loss.

INTRODUCTION

For both men and women, having healthy hair denotes health, youth, and vitality. In mammals, hair serves a protective and evolutionary function. Although hair in humans may not be important for skin barrier protection from a biologic perspective, hair and pigment, or lack thereof, can have a significant impact on perceived social relevance as well emotional and psychological health. According to the American Hair Loss Association, more than $3.5 billion are spent each year by both men and women in the United States to treat hair loss. The practice of hair coloring has been documented since 1500 BC, and interest in hair restoration has not waned. The development of synthetic dyes for hair can be traced to the 1860s with the discovery of reactivity of paraphenylenediamine with air. Today, even with the advent of follicular unit extraction and various synthetic hair pigmentation regimens available to rejuvenate scalp hair, there remains a great demand for a product that could potentially halt, slow, or even reverse hair senescence. This article reviews the anatomy and physiology of hair growth and pigmentation as well as briefly reviewing the various biologic modifiers most commonly used.

ANATOMY OF THE HAIR FOLLICLE

Hair can grow individually, in groups of 2 to 3, or even at times in groups of 4 to 5. These groups are known as *follicular units*. Each individual hair shaft in the growth phase is composed of 3 main concentric regions: the medulla, cortex, and cuticle. The medulla comprises the innermost layer and is formed from transparent cells and air spaces that vary among different hair types. It is often difficult to identify on light microscopy and at times may be entirely absent. The cells comprising the medulla contain glycogen-rich vacuoles and medullary granules, which contain citrulline. The middle layer is called the cortex and is the business center of the hair shaft. The cortex is what comprises the bulk and lends the mechanical strength to the hair shaft; it is comprised of a highly structured protein, keratin, which is organized filaments made up of long,

Disclosure: None.
[a] Department of Otolaryngology Head and Neck Surgery, Division of Facial Plastic and Reconstructive Surgery, UCLA, 200 UCLA Medical Plaza, Suite 550, Los Angeles, CA 90095, USA; [b] Medcare Hospital, Dubai, United Arab Emirates
[1] Present address: 2038 Butler Avenue, Los Angeles, CA 90025.
* Corresponding author. 221 West Pueblo Street, Santa Barbara, CA 93105.
E-mail address: ampark@mednet.ucla.edu

Facial Plast Surg Clin N Am ■ (2018) ■–■
https://doi.org/10.1016/j.fsc.2018.06.003

helical strands. The cells keratinize without forming granules through a process known as *trichilemmal keratinization*, as they move gradually upward from the hair matrix. The filamentous structure allows a single hair shaft to resist strain of up to 100 g, whereas the helical structure lends it elasticity. Therefore, the average full head of hair can hold more than 10 tons of weight. The groups of filaments form the cortex and are held together with disulfide, hydrogen, and salt bonds. This layer also has many important roles, such as storing the majority of the hair's moisture and housing the cells that lend pigment to the hair shaft. The number, distribution, and types of melanin granules contained in the cortex are what gives the hair fiber its pigment. Finally, the outer layer is known as the cuticle. This layer is composed of overlapping layers of 8 to 10 flat cells pointed outward and upward that interlock with the inner root sheath (IRS). When viewed under light electron microscopy, it has the appearance of roof shingles and is approximately 3 μm to 4 μm in thickness. When this layer is intact, it can last up to 6 years; it also reflects light and gives hair its shine and the appearance of good health.[1,2]

The hair follicle can be divided into 3 segments: lower, middle, and upper (**Figs. 1** and **2**). The lower segment is the area from the base of the follicle to the insertion of the arrector pili muscle and consists of the bulb and suprabulb regions. The bulb

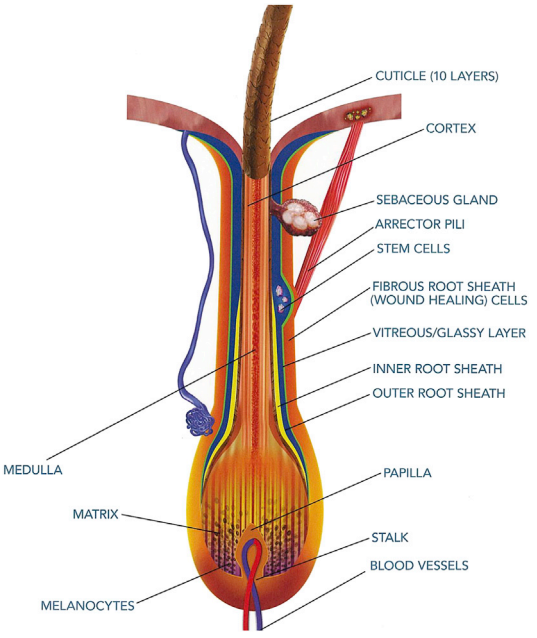

Fig. 1. Anatomy of a hair follicle. This is an illustration of the anatomy of a hair follicle and its associated adnexal structures. (*Courtesy of* Sajjad Khan, MD, Dubai, United Arab Emirates.)

is comprised of the dermal papilla and the surrounding matrix. The papilla protrudes into the hair bulb and consists of an accumulation of egg-shaped mesenchymal cells, which direct hair growth. An abundance of melanin can be found within the melanophages that reside within the dermal papilla. The lower aspect of the papilla merges with the fibrous root sheath (FRS), which surrounds the hair follicle. It is the size of the papilla and the bulb that determines a hair's diameter. The matrix contains the hair's germination cells; this collection of peridermal cells divides rapidly and migrates upward to give rise to the hair shaft and internal root sheath. Melanin is transferred from the melanocytes found between the basal cells of the hair matrix to the cells, which make up the hair shaft. Hair pigmentation is determined by the quantity of melanin deposited to the growing hair shaft. The hair matrix cells give rise to 6 different types of cells that make up the different layers of the hair shaft and the IRS.[1,2]

The suprabulb region is the area between the hair bulb and the isthmus. It consists of the hair shaft, the IRS, the outer root sheath (ORS), vitreous layer (VR), and the FRS (see **Fig. 2**). The IRS serves to coat and support the hair shaft until it reaches the level of the isthmus, at which point it degenerates and exfoliates in the infundibular space. The IRS is composed of 3 concentric cell layers, which keratinize by forming trichohyalin granules (soft keratin): outer, middle, and inner. The outermost layer, also known as the Henle layer, keratinizes first. The middle layer, also referred to as the Huxley layer, keratinizes last. The cells of the innermost layer, also known as the IRS cuticle layer, keratinizes after the Henle layer. The cells of this innermost layer point downward and inward to interdigitate with the cells of the hair cuticle. Although these 3 layers are distinct, they keratinize relatively low in the hair follicle and become indistinguishable at higher levels, thereby enabling it to function as a single unit to cover the hair shaft. The ORS covers the IRS as it extends up from the matrix cells at the lower end of the hair bulb to the meatus of the sebaceous gland duct. It is thinnest at the bulb and thickest in the middle portion of the hair follicle. Only once the IRS disintegrates at the level of the isthmus does the ORS keratinize without forming granules. The ORS cells have a clear, vacuolated appearance due to the large amounts of glycogen. When the ORS reaches the level of the infundibulum, the keratinization changes to normal epidermal keratinization with formation of the granular cell layer and the stratum corneum. The vitreous (glossy) layer is an acellular, eosinophilic zone the surrounds the ORS. It is continuous

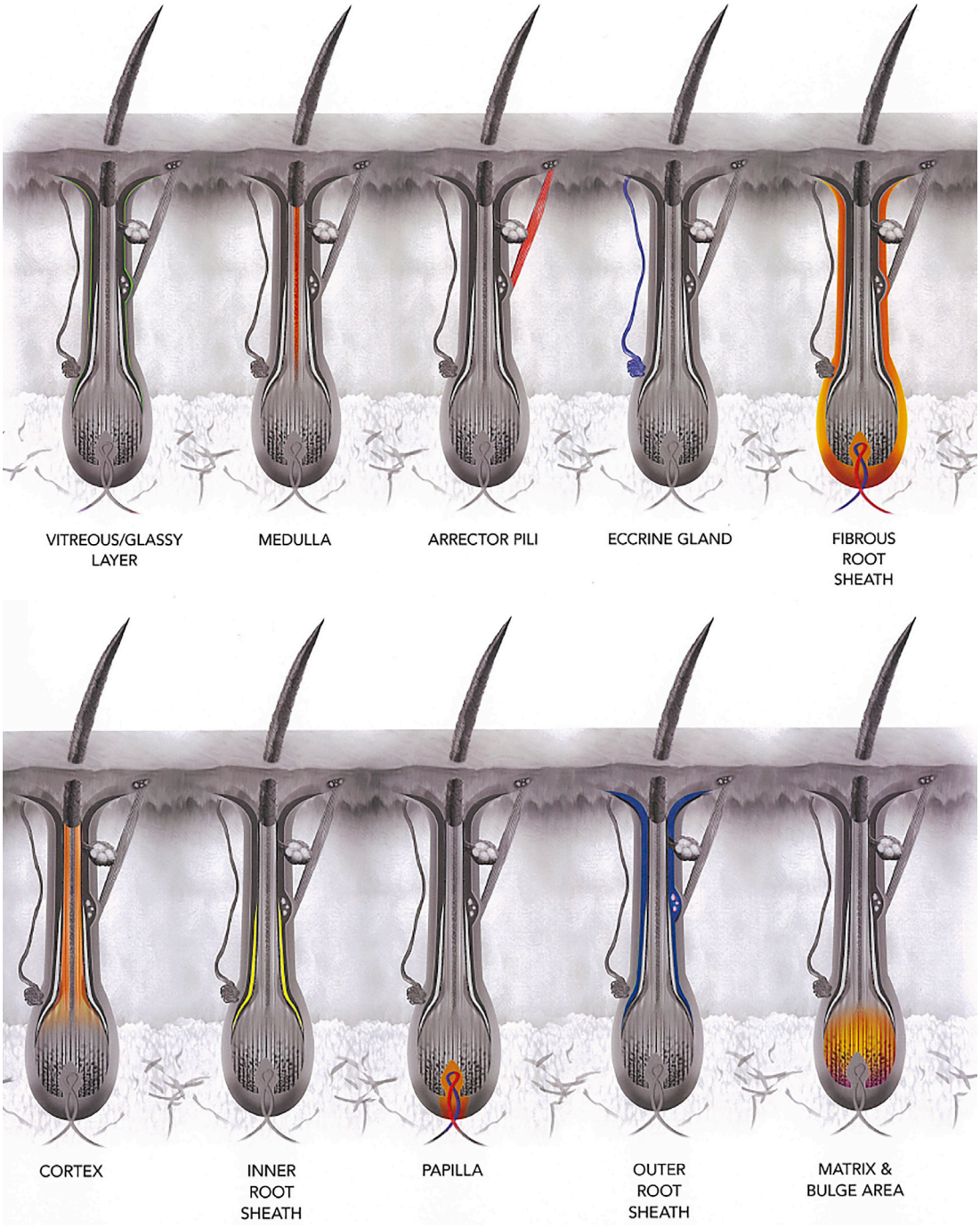

Fig. 2. Components of a hair follicle. This is an illustration of the unique components of a human hair follicle. (*Courtesy of* Sajjad Khan, MD, Dubai, United Arab Emirates.)

with the epidermal basement membrane. A distinguishing feature of catagen phase hairs is that the VR thickens and takes on a corrugated appearance. The FRS comprises the outermost layer of hair follicle and surrounds the VR. It consists of thickened collagen bundles that coat the entire hair follicle. The FRS is continuous with the dermal papilla and the papillary dermis above it.[1,2]

The middle segment (isthmus) is short and spans from the insertion of the arrector pili muscle to the meatus of the sebaceous gland duct (see **Fig. 2**). The IRS fragments and exfoliates at this

level, and at this point the ORS is fully keratinized via trichilemmal keratinization. The bulge region is difficult to appreciate on routine histology and is made up of densely packed cells with pluripotent capabilities encircled by the arrector pili muscle. Some believe that these stem cells that are residing in the bulge region are responsible for generating new hairs. Lastly, the upper segment of the hair follicle (infundibulum) extends from the meatus of the sebaceous gland duct to the follicular orifice. The epidermal surface lines the infundibulum and contains active pigmented melanocytes. The basal layer contains the inactive melanocytes, which are held in reserve and can become melanin-producing cells after injury to the skin. These cells then proliferate and migrate toward the regenerating upper portion of the ORS and the epidermis.[1,2]

When the hair transitions into the catagen phase (discussed later), the hair bulb keratinizes and turns into the club hair. This is then pushed upward to the surface by a column of thick and corrugated epithelial cells, which progressively shorten until it is reduced to a small saclike configuration, the secondary follicular germ. The dermal papilla also migrates upward, following the epithelial sac. During telogen, the secondary follicular germ and the dermal papilla form the telogen germinal unit, which gives rise to developing hair during anagen. The primary prenatal follicular germ unit regenerates the adnexal structures (ie, sebaceous and apocrine glands), whereas the telogen germinal unit does not.[1,2]

HAIR GROWTH CYCLE CHRONOLOGY

The average human has approximately 100,000+ scalp hair shafts, each in varying degrees of the hair growth cycle. The average life cycle of a human hair shaft is approximately 3.5 years, and it grows approximately 0.05 in per month. There are 3 major phases of the hair growth cycle: anagen (growth), catagen (involution), and telogen (resting phase prior to being shed). The anagen phase lasts an average of 2 years to 7 years, the catagen phase approximately 2 weeks to 4 weeks, and the telogen phase approximately 3 months. Approximately 84% of scalp hairs are in the anagen phase, 1% to 2% in the catagen phase, and 10% to 15% in the telogen phase. Hair can be thick, long terminal hair or fine, short villous hair. In contrast, the eyelash hair follicles are shorter, lack an arrector pili muscle, and have a shorter hair cycle.[3]

Anagen refers to the active growth phase of hair, when the pigmented hair shafts are generated and the follicle reaches its maximal length and volume. Approximately 85% to 90.6% of hair follicles are in this phase, which can last from 2 years to 6 years.[4,5] Catagen refers to the period of involution. During this phase, the epithelium of the lower follicle disintegrates and rises upwards with the papilla until it rests below the bulge zone, thereby forming the club hair. A streamer remains, which consists of the collapsed outermost layer (FRS). The hair follicle then enters a phase of relative quiescence, also known as telogen. This resting or dormant stage of the hair growth cycle is characterized by a marked decrease in proliferative and biochemical activity of the hair follicle. Although there is active hair growth or involution occurring, the existence of some baseline activity is believed important in intrinsic regulation of the hair cycle. During this phase, estrogen receptors are maximally expressed.[6] Exogen, also known as anagen stage IV, refers to the shedding of the hair shafts. These hairs are passively retained within the hair follicle but are distinguished from telogen clubs by the lack the cellular elements of the ORSs.[7]

HAIR PIGMENTATION

Unique hair color is a result of variations in the amount and type of melanin pigment production by cutaneous and follicular melanocytes. The biosynthesis of melanin occurs in intracellular lysosome-related organelles, known as melanosomes. The melanin produced by these melanosomes is then transferred from the melanocytes to the keratinocytes of skin and hair.

Two enzymes coded by the TYRP1 and DCT genes have been shown to biochemically alter the quality of melanin produced. Genes that have been shown to affect hair color include KITLG, IRF4, SLC24A4, and TPCN2.[8] The various stimulators and inhibitor of melanogenesis are listed in **Table 1**. Both melanocyte-stimulating hormone (MSH) and corticotropin are derived from proopiomelanocortin, which is synthesized by the pituitary gland and keratinocytes. MSH is believed to cause dispersion of the melanosomes and increase their melanogenic activity; α-MSH aids in the repairing of melanocytic DNA damage caused by exposure to UV radiation via reduction in UV-induced hydrogen peroxide formation, thereby maintaining melanosomal pH.

The loss of skin pigmentation from the skin epidermis can be indicative of the loss of pigment from hair follicles that have reached their terminal stage. During embryogenesis, the neural crest cells develop into hair follicle melanocytes. Hair follicles and sweat glands serve as reservoirs of melanocyte stem cells (MSCs). These melanocytes are

Table 1
Stimulators and inhibitors of melanogenesis

Stimulators	Inhibitors
MSH (α-MSH repairs DNA damage and maintains melanosomal pH)	Sphingolipids
ACTH	Bone morphogenetic protein 4
Endothelin-1	Autoimmune processes (eg, vitiligo)
Steel factor	
Prostaglandins and leukotrienes (inflammatory mediators)	
Neutrophins	
Basic fibroblast growth factor	
Nitric oxide	
Catecholamines	

Data from Talwar GP, Hasnain SE, Sarin SK. Textbook of biochemistry, biotechnology, allied and molecular medicine. 4th edition. Delhi (India): PHI Learning Private Limited; 2016. p. 277; with permission.

unable to produce melanin. These cells then undergo a life cycle of variable activity states that range from quiescent stem cells (melanoblasts), to proliferating, differentiating, and senescing terminally differentiated melanocytes. It is these mature melanocytes that produce melanin, but these cells are much more prone to cellular damage and apoptosis. Several factors, including microphthalmia-associated transcription factor, SOX10, PAX3, fibroblast growth factor-2, and endothelin-3, among others, are involved in committing early neural crest cells to the melanocyte lineage. Once committed to the melanocyte lineage, these cells then differentiate further into different melanocyte populations; several follicular melanocyte subpopulations exist in the adult human scalp and there is active turnover of these cells in accordance with the hair growth cycle.[9]

Hair color changes can be attributed to various cutaneous and systemic diseases as well as from exogenous influences. Hair darkening has been associated with Addison disease, neurodermatitis, and ad porphyria cutanea tarda. In contrast, hair lightening has been attributed to hyperthyroidism, acute extensive alopecia areata, vitiligo, and other genetic disorders, such as Werner syndrome, ataxia-telangiectasia, and Waardenburg syndrome.[10] There are also several systemic drugs that have been known to induce hair color changes. Chloroquine, hydroxychloroquine, sunitinib, pazopanib, dasatinib, phenytoin, phenobarbital, tamoxifen, low-dose interferon, and mephenesin have all been reported to cause depigmentation of hair. Imatinib, valproate, cisplatin, acitretin, and etretinate have been reported to cause either hyperpigmentation/repigmentation of gray hair or depigmentation, depending on the individual. Hyperpigmentation has been reported with the use of cyclosporine, indinavir, zidovudine, verapamil, and P-aminobenzoic acid. Additionally, different drug combinations can also result in color change. Cyclophosphamide, bleomycin, plus CCNU can change red hair to black; vincristine, bleomycin, and doxorubicin or vincristine alone can change black hair to red; cyclophosphamide, Adriamycin, and fluorouracil can change hair from blonde to dark brown, and a single dose of propofol, 140 mg, has been reported to turn blonde hair green within 2 days. Many, but not all, of these hair color changes have been reported to be reversible after cessation of drug administration.[11]

Hair pigment can be temporarily altered with the use of natural (ie, henna, indigo, berries, and other herbs) or synthetic hair coloring. Coating the hair cuticle or adding to the hair cuticle with color molecules gives temporary or semipermanent changes in hair pigmentation, whereas adding the color molecules to the deeper cortex layer yields more permanent alterations in hair color. Hydrogen peroxide is a key ingredient in the developer as it penetrates into the cortex layer and oxidizes the melanin, thereby removing color. Agents with a high pH (alkaline), such as ammonia, opens the cuticle to allow dye to enter the cortex and bind the keratin. Agents that are more acidic in the pH range of 4 to 5.5 seals the cuticle, thereby helping to lock in the new, desired color.

AGE-RELATED HAIR CHANGES

Genetics plays a large role in hair loss. Testosterone typically enters the papilla, ORS, and sebaceous gland cells where it is converted by 5α-reductase to dihydrotestosterone (DHT). DHT then binds to the androgen receptors and enters the nucleus where it binds the DNA and activates the production of proteins harmful to the follicle, thereby leading to disruption of the normal hair growth cycle. The overall growth cycle is altered in that the anagen phase is shortened, resulting in premature regression of the hair during its catagen and telogen phases. As new hair grows, there is a gradual reduction in the diameter of the hair follicle and the developing hair shaft. With each growth cycle, the anagen phase further shortens, resulting in a progressive miniaturization of hair and, eventually, hair loss. Genetics also plays a role in graying hair. In general, whites start to gray in their mid-30s, Asians in their late-30s, and Africans in their mid-40s. Those who develop graying hair in their 20s (or 30s for African

Americans) are believed prematurely gray, likely due to a lack of pigment cell formation or to hydrogen buildup, which leads to hair bleaching. One of the byproducts of the hair growth process is the production of hydrogen peroxide, which is normally degraded by catalase. With aging, the decrement in catalase present in the cells allows for the accumulation of hydrogen peroxide and damage to the melanocytes.[1,12]

Additionally, the hair follicle is sensitive to cutaneous, systemic, and even environmental cues. These various inputs exert a modulatory effect on HF cycling, hair shaft growth, and hair pigmentation.[13] Age-related loss of hair pigmentation, also referred to as graying, has been linked to UV light and (genotoxic) reactive oxygen species (ROS)-induced cell damage. The hair follicle bulge harbors melanocyte stem cells, which then gives rise to mature melanocytes, which then synthesize and secrete hair pigment during Anagen. Several animal studies have demonstrated the effect of oxidant stress on hair coloring, and further studies have shown that graying human hair follicles contain melanocytes with accumulated oxidative stress and subsequent depletion of the stem cell population.[14] Melanotic bulbar melanocytes naturally express high levels of BCL-2, an antioxidant protein believed to help fight against melanogenesis and UV-A injury due to ROS formation. One animal study investigated the effect of BCL-2 in a mouse knockout model. Depilation-induced hair growth demonstrated a lack of visible melanin granules. It was hypothesized that increasing BCL-2 levels could enhance the antioxidant capacity of the hair follicle and thereby prevent hair graying. High levels of BCL-2, however, have been associated with the adverse effect of also increasing oncogenic potential.[15]

MODIFIERS OF HAIR GROWTH

There are many environmental and genetic factors that can affect the overall health of hair. The nutritional effects are summarized in **Table 2**. The various biologic modifiers are discussed later, and both the agent and its effects on hair are summarized in **Table 3**.

Minoxidil

The oral formulation of minoxidil was originally studied for its antihypertensive properties, but a notable side effect was that it caused generalized hypertrichosis. The topical application of minoxidil is often the first-line treatment for both men and women with hair loss. It is available over the counter as a solution (2% or 5%) or as foam (5%). The 2% solution is preferred for women because the 5% solution has been associated with an increased incidence of hypertrichosis outside of the treatment area.

Although minoxidil has been shown effective as a solo agent, multiple studies have demonstrated increased efficacy when used with other agents. The 5% topical minoxidil can be used in conjunction with oral finasteride, 1 mg, to enhance its overall antiandrogenetic alopecia effects. It can also be used once daily in combination with 0.01% tretinoin, which has been found more effective than the use of just 5% minoxidil twice daily; application of the 5% topical solution or foam resulted in an increase in hair regrowth in 45% of male subjects.

How minoxidil asserts its effects on the growth of the hair follicle is poorly understood. Initially it was suggested that minoxidil caused vasodilation of the follicle cell vasculature, but a recent study by Shorter and colleagues[16] suggested that it may affect the regulation of one of the 2 ATP-sensitive potassium channels present in human follicular dermal papillae, SUR2. Additional animal and human studies have demonstrated that there is an increase in hair weight with use of minoxidil, which suggests that the therapeutic effect may be due to increasing the diameter of hair or the hair follicle.[17]

Finasteride (Propeci/Proscara)

Another commonly prescribed agent for male and female hair loss is finasteride. This type 2 5α-reductase inhibitor is Food and Drug Administration (FDA) approved in 1997 for the treatment of male pattern hair loss and is orally administered at the optimal dose of 1 mg daily. Use of finasteride, 1 mg, resulted in a 64% decrease in median scalp DHT compared with placebo and a 71% decrease in median serum DHT levels.[18] After several months of therapy, patients report increased hair diameter, growth rate, and, to a lesser extent, increased hair counts.

Dutasteride (Avodart)

The agent dutasteride (Avodart) was approved by the FDA in 2002 for the treatment of benign prostatic hypertrophy, but due to its potent antiandrogenic effects has also been used off-label for the treatment of hair loss. It is both a type 1 and type 2 5α-reductase inhibitor. A study comparing the effects of dutasteride to finasteride and placebo demonstrated that a daily dose of dutasteride, 2.5 mg, was statistically superior to finasteride in increasing hair counts.[19]

Platelet-Rich Plasma

Platelet-rich plasma (PRP) is prepared by concentrating the red blood cells and separating it from

Table 2
Nutritional effects on hair growth and health. This chart summarizes the nutritious foods and their effect on hair. Biotin, also known as vitamin B_7, is not listed but is believed to play an important role in the health and growth of skin, hair, and nails. A deficiency in this vitamin is believed to contribute to hair loss

Nutritional Agent	Effect on Hair	Associated Food(s)
Water	Moisture	8 glasses/d
Iron	Carries oxygen to hair and promotes growth	Chicken Spinach Lentils Beef liver
Vitamin A	Antioxidant reduces free radicals and inflammation	Carrots Spinach Sweet potatoes Kale
B-complex vitamins (biotin, niacin, and cobalamine)	Restore shine and thickness to hair strands	Peanuts Sweet potatoes Almonds Eggs Chicken Sardines Tuna Whole grains
Vitamin D	Important for hair follicle cycling	Mushrooms Beef liver Salmon Low-fat diary Whole grains
Vitamin C	Helps grow and strengthen hair, also absorbs iron	Broccoli Bell peppers Strawberries Pineapple Oranges
Vitamin E	Strengthens hair, improves volume and circulation	Almonds Peanuts Spinach
Silica	Strengthens hair	Green beans Oats Cucumber Bell peppers
Copper	Essential for health of hair; needed to produce antioxidant superoxide dismutase	Sesame seeds Legumes Seaweed Cashews Animal liver
Selenium	Important for healthy scalp	Mushrooms Shrimp Whole grains Tuna fish Brazil nuts
Potassium	Helps maintain hair moisture and healthy pH	Sweet potatoes Bananas Yogurt Spinach Coconut water Swiss chard

(*continued on next page*)

Table 2
(*continued*)

Nutritional Agent	Effect on Hair	Associated Food(s)
Magnesium	Essential for proper hair growth and strengthens hair	Swiss chard Pumpkin seeds Spinach Dark chocolate Beet greens
Omega-3 fatty acids	Prevents inflammation and promotes hair growth	Salmon Chia Flax Sardine fish Walnuts Beef
Calcium	A key component of hair growth	Low-fat dairy Spinach Sardine fish

the platelets and plasma. When the concentrated platelets are activated, they release growth factors that have been shown beneficial in the treatment of hair loss. It is believed that the platelet growth factors may reverse the miniaturization process and result in restoration of the normal hair cycle. A recent review determined an average of 3 injection treatments are needed to achieve some benefit.[20] For more information, see Karam W. Badran and Jordan P. Sand's article, "Platelet Rich Plasma for Hair Loss: Review of Methods and Results," in this issue.

Latisse (Bimatoprost Ophthalmic Solution 0.03%)

Originally prescribed to treat open-angle glaucoma and ocular hypertension, the agent bimatoprost ophthalmic solution, 0.03% (Latisse) lowers the intraocular pressure by increasing the outflow of aqueous humor via the trabecular meshwork and the uveoscleral routes. It was incidentally noted that the patient using this medication also developed longer eyelashes. The exact mechanism of action by which eyelash growth is

Table 3
Biologics and effects on hair. This chart summarizes the various biologic agents that modify hair growth

Agent	Mechanism of Effect
Minoxidil	Vasodilation of follicle vasculature. May affect ATP-sensitive K^+ channels in human follicular dermal papillae (SUR2). May result in increased hair follicle diameter.
Finasteride	Type 2 5α-reductase inhibitor.
Dutasteride	Type 1 and type 2 5α-reductase inhibitor
PRP	Platelet growth factors may reverse the miniaturization process and results in restoration of normal hair cycle.
Latisse	A synthetic prostaglandin $F_{2\alpha}$ analog that prolongs anagen phase of eyelash hair follicles.
Aldactone/spironolactone	Blocks the receptor binding of DHT. Spironolactone slows adrenal gland and ovarian production of androgens.
PTHrP antagonist	Promotes hair follicle activation.
Cimetidine	Histamine blocker and also blocks DHT from binding the follicular receptor sites.
Cyproterone acetate	Blocks the binding of DHT to its receptors. Available in Europe only.
Oral contraceptives	Decreases ovarian androgen production, thus used to treat androgenetic alopecia in women.

stimulated is unknown, but it is believed to prolong the anagen phase of eyelash hair follicles. Bimatoprost is a synthetic prostaglandin $F_{2\alpha}$ analog.[21] An irreversible side effect noted in 1% to 2% of glaucoma patients using this medication is iris hyperpigmentation (increased brown pigmentation), in addition to possible reversible darkening of the eyelid skin.

ALTERNATIVE TREATMENT OPTIONS

Spironolactone (Aldactone)

Spironolactone (Aldactone) is a popular potassium-sparing diuretic used in the treatment of hypertension but is also an antiandrogen. Spironolactone slows down adrenal gland and ovarian production of androgens. Additionally, it also blocks the binding of DHT to its androgenetic receptor.

Parathyroid Hormone–Related Peptide Antagonists

Two key studies published in 1994 demonstrated in vitro and in vivo that parathyroid hormone–related peptide (PTHrP) antagonists promoted follicular activation whereas PTHrP agonists inhibited hair follicle formation. A subsequent study investigated 2 different antagonists and showed that these increased anagen hair follicles at 2 weeks.[22]

Cimetidine (Tagament)

Cimetidine (Tagament) is a well-known histamine blocker used to treat gastrointestinal ulcers. Cimetadine, however, also has a powerful antiandrogenic effect and has been shown to block DHT from binding the follicle receptor sites. This agent has been used to treat hirsutism in women, and its use in initial studies to treat androgenic alopecia has shown promise.

Cyproterone Acetate

The agent cyproterone acetate is not available in the United States but is available in Europe. It has been used to reduce sex drive in men and has also been used to treat severe hirsutism in women. Cyproterone acetate blocks the binding of DHT to its receptors but, due to its long-term side effects, is considered a last resort for treating female pattern hair loss. When combined with ethinylestradiol, it is sold under the brand names Diane-35 and Diane-50 in Europe as a contraceptive agent.

Estrogen/Progesterone

Estrogen/progesterone is prescribed to women in menopause as hormone replacement therapy in the form of pills or cream and is used as a systemic form of treatment of androgenetic alopecia in menopausal women or in those with low hormone levels.

Oral Contraceptives

Birth control pills exert their effects by decreasing the production of ovarian androgens; therefore, birth control pills may be used to treat androgenetic alopecia in women. Low androgen index birth control pills are used to treat hair loss. High androgen index birth control pills are avoided because use of these can trigger hair loss.

REFERENCES

1. Khan S. Guide to hair. Dr. Sajjad Khan Publisher; 2017.
2. Alaiti S, Meyers A, Talavera F, et al. Hair anatomy. Available at: https://emedicine.medscape.com/article/835470. Accessed December 13, 2017.
3. Paus R, Burgoa I, Platt CI, et al. Biology of the eyelash hair follicle: an enigma in plain sight. Br J Dermatol 2016;174:741–52.
4. Mulinari-Brenner F, Neto FJ, Ross FMB, et al. Morphometry of normal scalp hair follicles. An Bras Dermatol 2006;81(1):46–52.
5. Wosicka H, Cal K. Targeting to the hair follicles: current status and potential. J Dermatol Sci 2010;57:83–9.
6. Paus R, Foitzik K. In search of the "hair cycle clock": a guided tour. Differentiation 2004;72:489–511.
7. Van neste D, Leroy T, Conil S. Exogen hair characterization in human scalp. Skin Res Technol 2007;13(4):436–43.
8. Sturm R. Molecular genetics of human pigmentation diversity. Hum Mol Genet 2009;18(R1):R9–17.
9. Commo S, Bernard BA. Melanocyte subpopulation turnover during the human hair cycle: an immunohistochemial study. Pigment Cell Res 2000;13(4):253–9.
10. Francesco R, De Simone C, DelRegno L, et al. Drug-induced hair colour changes. Eur J Dermatol 2016;26(6):531–6.
11. Ricci F, De Simone C, Del Regno L, et al. Drug-induced hair colour changes. Eur J Dermatol 2016;26(6):531–6.
12. Westgate GE, Botchkareva NV, Tobin DJ. The biology of hair diversity. Int J Cosmet Sci 2013;35(4):329–36.
13. Paus R, Lagan EA, Vidali S, et al. Neuroendocrinology of the hair follicle: principles and clinical perspectives. Trends Mol Med 2014;20(10):559–70.
14. Geyfman M, Andersen B. Clock genes, hair growth and aging. Aging 2010;2(3):122–8.
15. Selberg M. Age-induced hair greying – the multiple effects of oxidative stress. Int J Cosmet Sci 2013;35:532–8.

16. Shorter K, Farjo NP, Picksley SM, et al. Human hair follicles contain two forms of ATP-sensitive potassium channels, only one of which is sensitive to minoxidil. FASEB J 2008;22(6):1725–36.
17. Nusbaum AG, Rose PT, Nusbaum BP. Nonsurgical therapy for hair loss. Facial Plast Surg Clin North Am 2013;21:335–42.
18. Drake L, Hordinsky M, Fiedler V. The effects of finasteride on scalp skin and serum androgen levels in men with androgenetic alopecia. J Am Acad Dermatol 1999;41:550–4.
19. Olsen EA, Hordinsky M, Whiting D, et al. The importance of dual 5alpha-reductase inhibition in the treatment of male pattern hair loss: results of a randomized placebo-controlled study of dutasteride versus finasteride. J Am Acad Dermatol 2006;55(6):1014–23.
20. Sand JP, Nabili V, Kochhar A, et al. Platelet-rich plasma for the aesthetic surgeon. Facial Plast Surg 2017;33:437–43.
21. Cohen J. Enhancing the growth of natural eyelashes: the mechanism of bimatoprost-induced eyelash growth. Dermatol Surg 2010;36:1361–71.
22. Robert C. Gensure. Parathyoid hormone-related peptide and the hair cycle – is it the agonists or the antagonists that cuase hair growth? Exp Dermatol 2014;23:865–7.