Management of Male Pattern Hair Loss

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The management of androgenetic alopecia (AGA) has been materially altered by the availability of the 5α-reductase type 2 inhibitor, finasteride. Nevertheless, this agent is only one component of successful management, and an understanding of the role of camouflage agents, surgical options, and other medical treatments is important. Because no treatment completely reverses baldness, it is important to communicate the limitations of each modality to the patient so that he has appropriate expectations of the outcome of any intervention. Patient counseling and support are also often relevant.

Androgenetic alopecia (AGA), or male pattern hair loss, is characterized by progressive hair loss from the vertex and frontal regions of the scalp. It occurs in genetically predisposed men when they are exposed to the physiologic levels of androgens that accompany and follow normal puberty. The inheritance is polygenic. At least one of the susceptibility genes resides on the X chromosome, indicating maternal spread to affected men.[1] AGA is sufficiently common to be considered a normal physiologic variation; however, the age of onset differs from person to person. Approximately 20% of Caucasian men will have detectable AGA by the age of 20 years, 30% by age 30, 40% by age 40, 50% by age 50, and 80% by age 80.[2] Although many men regard AGA as a normal result of aging, a substantial number of men find progressive hair loss distressing.[3]

AGA is distinguished from other forms of hair loss by its pattern, as shown in a modified Hamilton-Norwood grading scale (Figure 1). AGA starts with recession of the frontal hairline and is followed initially by diffuse thinning over the vertex of the scalp.[4,5] Gradually, a bald spot emerges on the vertex that enlarges and ultimately merges with the frontal recession until only the marginal parietal and occipital hair remains.

The key histologic features of AGA are progressive miniaturization of the hair follicle and alteration of the hair cycle dynamics. The normal hair growth cycle is shown in Figure 2. The duration of the growth phase (anagen) of the hair cycle is progressively shortened, whereas the duration of the resting phase (telogen) remains constant, leading to a decrease in the ratio of anagen hairs to telogen resting hairs.[6] This results in the gradual replacement of long terminal hairs by finer, hypopigmented vellus hairs with a growth phase so short that the hairs may not even reach the skin surface before entering catagen and subsequently telogen (Figure 3).

Both the age of onset and the speed of progression of AGA are variable and influenced by factors that are still poorly understood. Although one study has shown an average rate of hair loss at 5% per year,[5] the rate of hair loss is variable. Some men take 15 to 25 years to reach the advanced stages of AGA, while others progress within 5 years. Both hair loss and hair growth show seasonal and environmental fluctuations.[7] The key hormone regulating AGA is dihydrotestosterone (DHT). DHT is produced by catalytic conversion of testosterone by 5α-reductase. Both testosterone and DHT bind to the common androgen receptor, however, DHT binds 5 times more avidly. Factors that regulate the levels of DHT and androgen receptors are not known. Although serum levels of DHT in balding men do not appear to be materially different from levels in nonbalding men, inhibition of 5α-reductase has become a key target for evolving treatments of AGA.

Available Management

Because AGA progresses slowly and hair loss is often episodic, patients may link spontaneous temporary reductions in hair shedding with coincidental treatments or changes in behavior. This has resulted in the proliferation of over-the-counter treatments such as vitamin-containing creams and lotions, none of which have been proven effective.[8,9] Men distressed by their hair loss have only 5 options: do nothing, camouflage the hair loss, have surgery, use topical minoxidil, or take oral finasteride.

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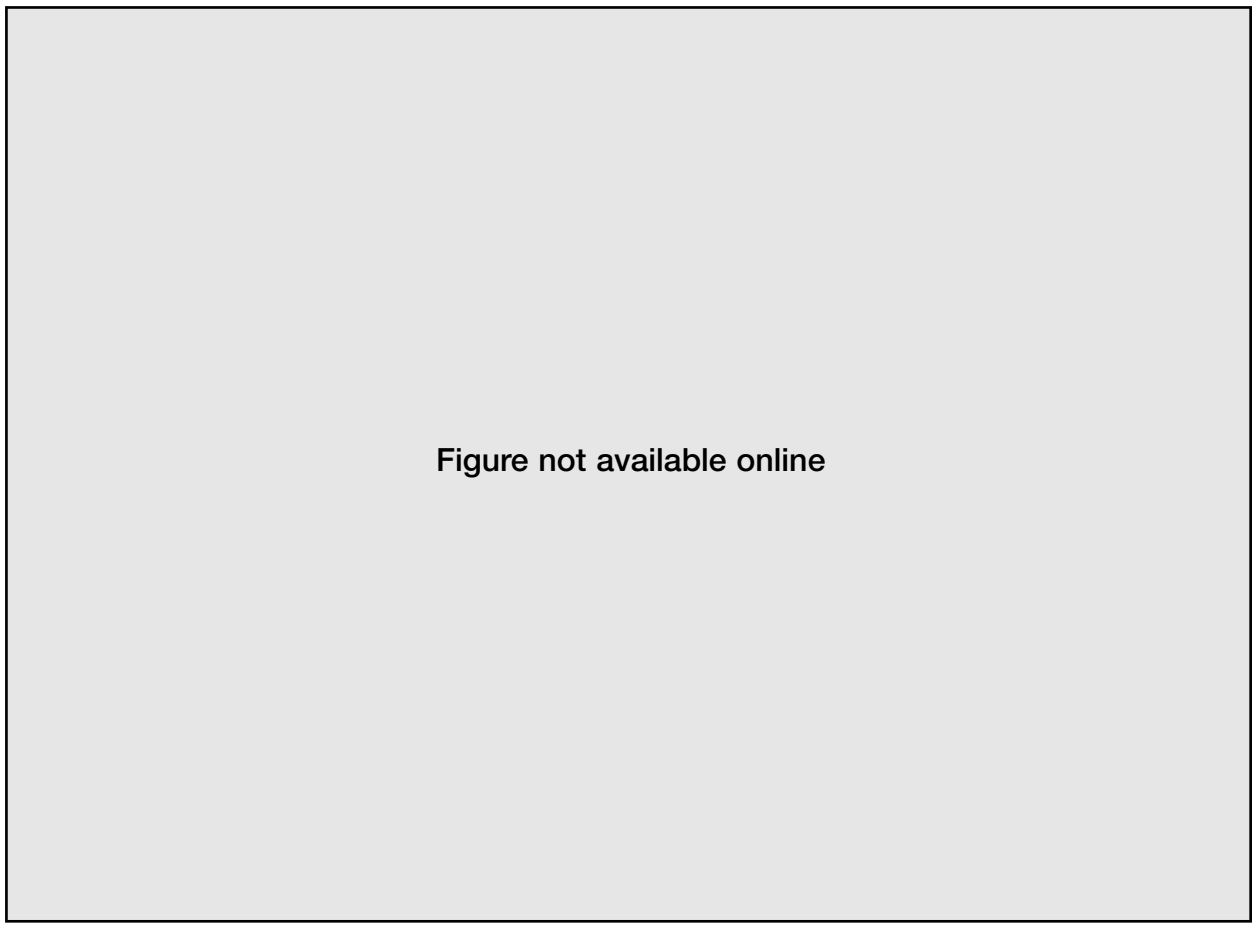

Figure 1. Modified Hamilton-Norwood grading scale for androgenetic alopecia. Reprinted with permission.

Do Nothing

Many patients do not require active treatment and, particularly in the early stages of hair loss, will be satisfied by simple reassurance and an explanation of the pathogenesis and natural history of AGA. Men distressed by their hair loss may require psychological support. After a detailed explanation of the natural history of AGA and available options, many patients will decline active treatment.[10] Baldness suits many men, and it is currently fashionable for affected men to shave their existing hair.

Camouflage

The simplest way to disguise hair loss is the comb-over. A central part line displays AGA at it fullest. Careful hairstyling can very effectively hide early hair loss. Spray on camouflage treatments decrease visibility of the scalp through thinning hair by dyeing the scalp the same color as the hair. Numerous brands are on the market, and some are combined with hairspray and sunscreen. Sprays or shampoos containing thickening agents act by increasing the electrostatic repulsive forces between hairs, causing them to separate and thereby give the appearance of thicker hair. These simple methods are relatively inexpensive and useful during the early stages of AGA. However, these methods have several disadvantages that may discourage patients from long-term use. Patients generally wash the dye out each night and need to reapply it the following morning. Dyes may contaminate and discolor the hands, bed linens, or other surfaces. Because these treatments are not waterproof, reapplication is necessary after swimming or if the hair gets wet in the rain. Ultimately, hair loss will progress beyond the point at which these methods provide a satisfactory appearance.

Many men with AGA (or other forms of alopecia whose hair loss has progressed beyond camouflage with cosmetics or skillful hairstyling) choose a wig or toupee instead of scalp surgery. Despite its popularity, this method of management has a poor reputation because, usually, only bad hairpieces are noticed. By definition, good hairpieces should blend with a person's natural hair.

Modern hairpieces made of human hair can be highly effective because they look natural. However, they are less robust than synthetic ones and are prone to fading. Synthetic materials have generally

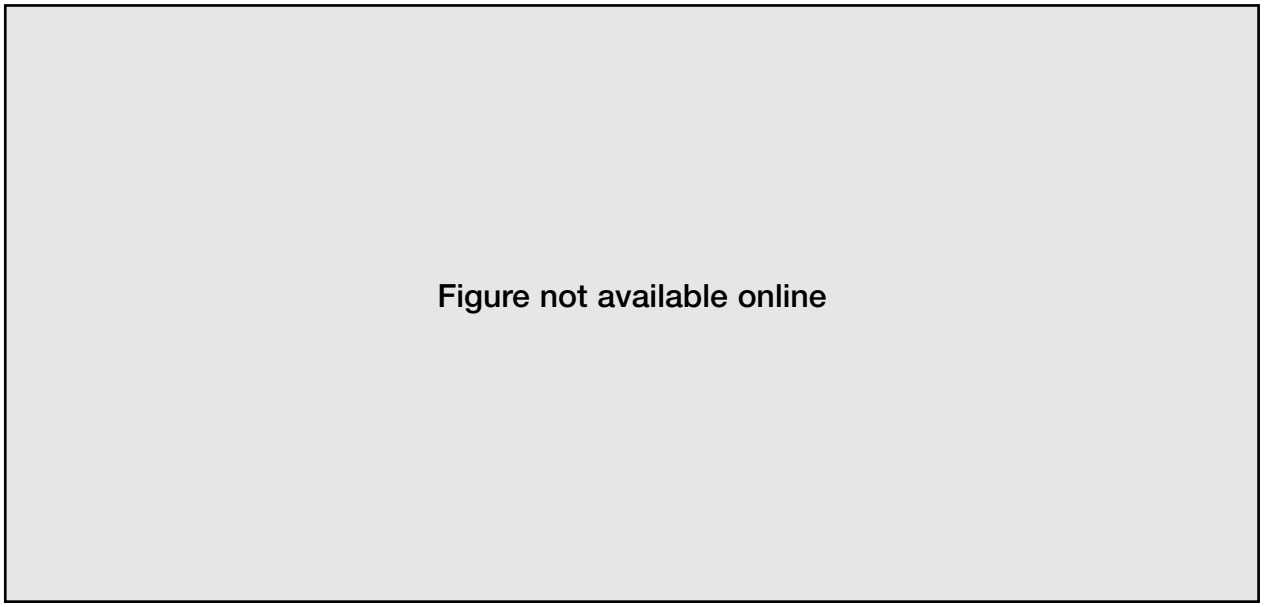

Figure 2. Normal hair growth cycle. Copyright 2001, The Anatomical Chart Company, Lippincott Williams & Wilkins.

been less aesthetically pleasing, but there are encouraging developments due to modern technologies that may lead to an increase in their popularity. Hairpieces can be attached using tape, clips, or weaves. Bonding (long-term attachment with medical adhesive) is becoming more popular, particularly among younger men who do not wish to be reminded of their hair loss.

Despite these improvements, there are still substantial disadvantages to hair systems. A good wig, whether of natural or synthetic fiber, is expensive and must be replaced at regular intervals. With long-term bonding, regular maintenance to tighten the hair system is required. Some patients also find the discomfort caused by heat and irritation of the scalp intolerable, particularly in hotter climates.

Surgery

Surgical procedures rely on donor dominance (the fact that transplanted hair retains the characteristics of the donor site), using parietal and occipital hairs that are relatively unresponsive to androgens to cover areas with hair loss.[11] Transplants are the most common and most popular surgical procedure to treat hair loss. Many surgeons are now experienced in the procedure, an important consideration for patients because the aesthetic success of the technique depends largely on a combination of technical skill and artistic flair. Scalp reduction (removal of tissue that shows hair loss) and rotation flaps also have been used for many years and can provide good results in experienced hands.[12-14.] Other techniques include punch grafting, follicular unit grafts, and single-follicle transplantation.[15]

Excellent results can be achieved with surgical procedures; however, potential complications such as unsightly scarring, postoperative hypoaesthesia, and infection have been reported.[16] Surgery is also expensive and difficult to reverse if the cosmetic result is unsatisfactory. One of the greatest disadvantages of surgery is that it only treats bald spots and does nothing to protect vulnerable areas. As the AGA progresses, the persisting tufts of transplanted hair may produce an unnatural appearance. This may lead to the need for repeated surgery, with a diminishing donor population of hairs to draw from.[17]

Topical Minoxidil

Minoxidil is a vasodilator antihypertensive that was fortuitously found to stimulate hair growth in patients being treated for hypertension. It has been shown to normalize the morphology of the hair follicle, increase the number of follicles in anagen, and convert vellus hairs to terminal hairs normally found on the scalp. The efficacy of topical minoxidil (2%, 3%, and 5%) has been demonstrated in many clinical trials.[18-21] When results were assessed by hair weight, 5% minoxidil was significantly better than 2% minoxidil. Maximum increase was seen at 18 weeks for the 5% minoxidil and at 24 weeks for the 2% minoxidil. The increase was maintained for the duration of the study (96 weeks). Follow-up during the subsequent 24 weeks noted resumption of hair loss; however, the patients still had more hair than they did at baseline.[22]

Although minoxidil has been able to regrow some hair in men with AGA, use of this drug has a number of disadvantages. The individual response

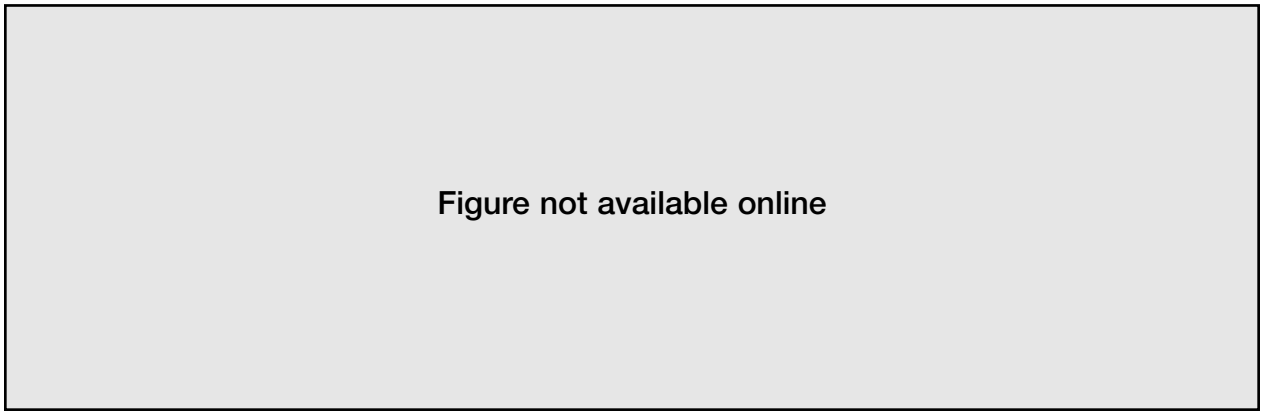

Figure 3. Miniaturization of hair follicles in baldness. Copyright 2001, The Anatomical Chart Company, Lippincott Williams & Wilkins.

to minoxidil varies, with some patients showing a rapid marked response and others showing no noticeable change. Long-term patient compliance is often poor because twice daily application is required, which can be time-consuming and leaves the hair with a sticky texture. In one 30-month trial of minoxidil, compliance fell to less than 50%.[19] The treatment must be continued indefinitely to maintain its effects. Patients may notice a resumption of hair shedding within months of stopping treatment. Although it stimulates hair regrowth, minoxidil does not arrest progression of AGA, and over time the initial increase in hair density may be eroded by progressive hair loss.

Minoxidil is not recommended for systemic use because of the possibility of cardiovascular disturbances and cerebrovascular complications. Systemic use of minoxidil is no more effective than topical minoxidil in treating AGA, and it may induce hypertrichosis on the face and other sites.

Oral Finasteride

The realization that DHT is the pivotal androgen in the development and progression of AGA has enabled specific treatment targets to be identified.[23-25] In general, drugs that inhibit conversion of testosterone into DHT are more suitable for men than drugs that inhibit testosterone production or antagonise, the common androgen receptor for testosterone and DHT, as men tolerate feminization and impotence poorly.

The most promising strategy is targeted modulation of androgen metabolism to reduce DHT production without concomitant general antiandrogen effects. Conversion of testosterone to DHT is catalyzed by the enzyme 5α-reductase, which has 2 isoenzymes, type 1 and type 2. A natural model of type 2 5α-reductase deficiency is present in the pseudohermaphrodite. These men are born with ambiguous genitalia but become clearly male at puberty. They do not develop prostate hypertrophy or AGA but are apparently normal otherwise.[26,27] This natural model of resistance to AGA-established type 2 5α-reductase is the most likely target for the treatment of AGA in postpubertal men.

Both the type 1 and type 2 isoenzymes of 5α-reductase are present on the scalp, with type 2 strongly expressed in the scalp hair root sheath, where it may potentially affect hair morphology and development.[28-30] In corroboration, the male balding scalp exhibits increased conversion of testosterone to DHT.[31]

Finasteride is a synthetic, steroidal derivative that specifically inhibits the type 2 isoenzyme of 5α-reductase.[32,33] Studies show that 1 mg daily of oral finasteride effectively reduces DHT levels in human subjects and in the stump-tailed macaque, a primate model of AGA.[34,35] In addition, placebo-controlled clinical trials in which 1 mg of daily finasteride was used to treat men with frontal or vertex hair loss have demonstrated that the drug effectively prevents further hair loss in most patients and, in a significant percentage, promotes overt hair growth.[36] Finasteride was approved by the US Food and Drug Administration in December 1997 for the treatment of men with AGA, and it has since been approved in a number of other countries, including Australia and New Zealand.

Patients generally need to take finasteride for approximately 6 to 12 months before any effect is seen and must continue to take it indefinitely to maintain the benefit. A reduction in the number of hairs shed daily may be observed within 4 to 6 months. In one study, the patients were assessed photographically as either unchanged, minimally improved, moderately improved, or markedly improved (Figure 4). After 2 years of continuous use, approximately one third of patients appeared

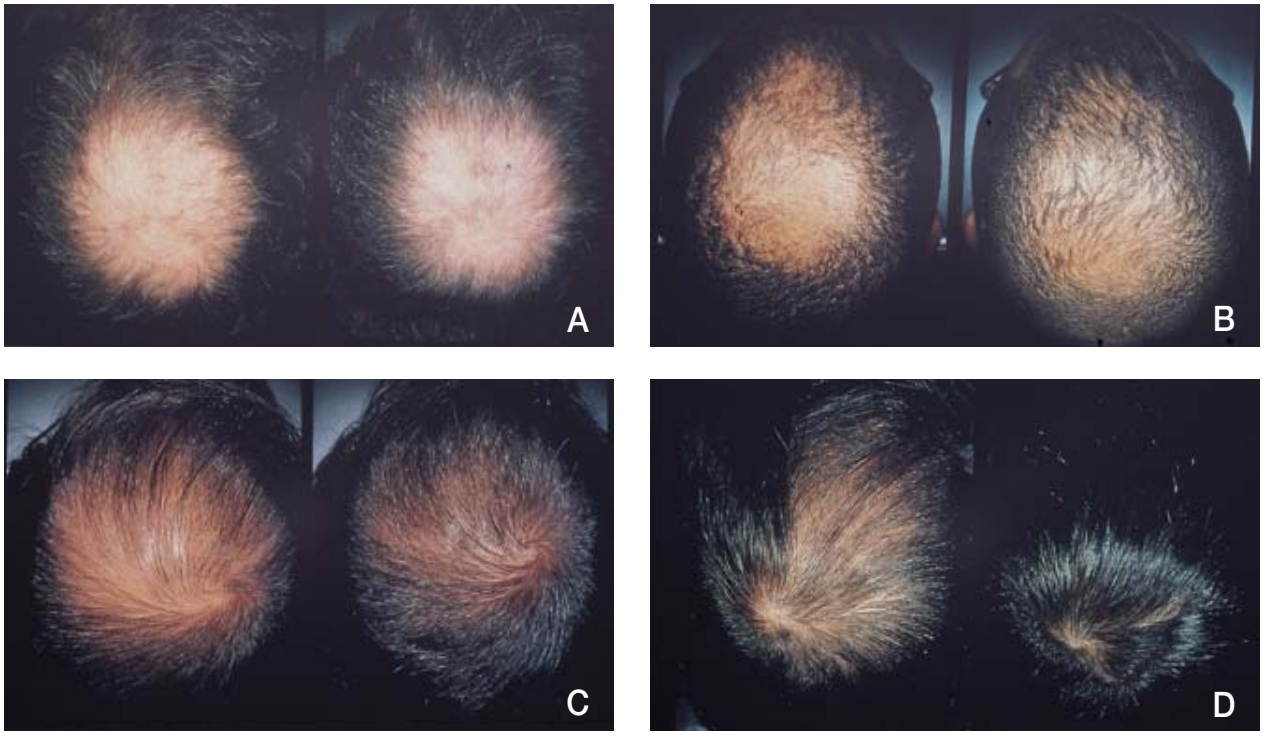

Figure 4. Grading scale for assessment of patients receiving finasteride in clinical trials: no change (A), slight improvement (B), moderate improvement (C), marked improvement (D).

unchanged, one third had minimal regrowth sufficient to be detected by high-quality standardized photography, and one third had moderate or marked regrowth. Only 1% of patients had progression of their AGA. In contrast, 64% of the placebo group appeared unchanged, and 33% obviously progressed.[36]

Although two thirds of the patients taking finasteride achieved regrowth after 2 years, only half of these men were clearly aware of the regrowth. Management of patient expectations and reassurance that the AGA has not progressed is crucial to ensure long-term compliance and full benefit of treatment.

Five year data on the use of finasteride has recently become available. Although most of the regrowth is achieved in the first 2 years of continuous usage, the regrowth is retained, and the progression of the AGA is arrested over the ensuing 3 years. In contrast, the differences between treated and untreated groups continues to expand as those in the placebo category continue to lose their hair.[37]

Conclusion

Until minoxidil became available, AGA was generally believed to be irreversible. Although not universally successful in the treatment of AGA, minoxidil has proven that drugs that induce scalp hair growth can be developed. This caused an enormous interest and injection of resources into the science of AGA, which culminated in the discovery and development of finasteride. Clinical trials have subsequently confirmed the efficacy and safety of finasteride, and the product is now available in the United States and many other countries.

Hair replacement research is continuing, and more than 20 new inhibitors of both the type 1 and type 2 5α-reductase isoenzymes have been patented in the United States,[38] a number of which are already in the clinical trial phase. Phase 2 studies with dutasteride (GI198745), a combined type 1 and type 2 antagonist, has shown it to be superior to both placebo and finasteride for hair regrowth at 12 months. Sexual side effects such as reduction in libido were more common and affected around 4% of participants. In vitro production of hair follicles from stem cells for implantation is also an area of intense interest.[39] Although many men will still choose to go bald naturally, the development of finasteride represents a significant advance for those men sufficiently disturbed by hair loss who choose long-term medication.

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