

## **Prevent Hair loss, don't Regrow?**

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Editorials

One of the best reviews of hair loss options, causes, prevention, and psychology we've read. Many of you just starting to experience the first signs of hair loss tend to become gung-ho about dumping on the treatments. Many of your regimens are the same regimens men who have already lost a significant amount of hair are using to regrow entire sections of their scalp hair. However, preventing hair loss is nowhere near as difficult as regrowing lost hair, and its likely that you do not need so many treatments just to maintain what you have...Propecia, the current wonder drug, has an incredibly high success rate (83%) of maintaining men's hair counts. Propecia use alone has saved hundreds of thousands of men from a future of baldness, without the help of any other treatments at all. These men are fortunate, because they have an entire arsenal of treatments to add if or when Propecia ever stops working for them.

### **Pathology of male pattern hair loss**

Androgen-dependent skin conditions, such as male pattern hair loss (androgenetic alopecia, AGA) and acne, are among the dermatologic conditions most frequently encountered by the specialist and the general physician. AGA is the commonest form of human alopecia, affecting more than 50% of men by the age of 50 years, and a smaller but still significant proportion of women by the same age. Historically, the clinical management of AGA has been limited to the psychologic support of the client, and the use of cosmetics that thicken the remaining hair, or make the scalp less conspicuous. Hair systems (swatches, weaves, and wigs), and surgical procedures including punch grafts, follicular unit transplantation, and flap surgery are also widely used. In recent years however, drug therapy has increasingly become a realistic management option, as our understanding of the mechanisms of normal and pathologic hair growth has pointed the way to improved treatments.

The changes that occur in the distribution of scalp hair as AGA progresses follow a course that has been well documented in both sexes, as have the changes in the scalp and scalp hair that are commonly found to occur in male pattern hair loss. The most important recent development in our understanding is the recognition that androgens play a central role in the development of AGA. It has been observed that castrated men do not exhibit AGA; however, if they are given exogenous androgens, they will reversibly show signs of hair loss. Several recent lines of evidence implicated DHT, a metabolite of testosterone, as the active metabolite in AGA. The enzyme responsible for the conversion of testosterone to DHT is 5 $\alpha$ -reductase.

### **Psychology of hair loss, prevention, and regrowth**

Hair forms a vital element of an individual's physical appearance, and changes in the hair, including its loss, can have correspondingly profound effects on interpersonal reactions and on self image. Studies that have specifically addressed the psychosocial impact of hair loss in men have shown that men with visible hair loss are perceived as older, weaker, and less physically attractive than their nonbalding counterparts. Not surprisingly, such adverse social stereotyping of individuals with hair loss has a considerable impact on the self image, and therefore on the quality of life, of men with AGA. Studies confirm that the negative self-perception of hair loss by others is reflected in the psychologic responses of balding men to their own condition. Using

standard psychologic tests, men with AGA report experiencing distress about their hair loss, feeling less physically attractive, and having greater body image dissatisfaction than their nonbalding peers.

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Given that many men are strongly motivated to seek help with their AGA, the treatment objectives may variously include the prevention of further hair loss, the maintenance of existing hair, the regrowth and retention of lost hair, or any combination of the three.' In most cases, however, prevention and maintenance are the most realistic therapeutic options. In this context, it must be recognized that there is frequently a disparity between what the physician assumes are the patient's needs or requirements, and what the patient actually expects. Although there is a lack of rigorous scientific studies of men's attitudes towards regrowth of their lost hair as compared to the prevention of further hair loss, some indications are available in the literature. For example, in a study in which men with AGA completed the Hair Loss Effects Questionnaire (HLEQ), a high proportion gave responses that were directed towards a future rather than a present state: 93% worried about how much hair they would lose, 87% reported trying to estimate if they were losing more hair, and 80% tried to imagine how they would look with more hair loss. Cash" has also reported that balding men who anticipated more hair loss in the future experienced significantly greater negative events and cognitive preoccupation, and were also less satisfied with their hair and overall appearance than men who anticipated minimal future hair loss.

Some anecdotal evidence, based on market research among 2200 men with at least some degree of hair loss, strongly supports the importance of prevention rather than regrowth to the patient.

Thus, when asked directly whether they were more concerned about the amount of hair they currently had (i.e. regrowth) or the rate at which they were losing it (i.e. prevention), most respondents (61%) were equally concerned about the two; of those expressing a greater concern for one or the other, two-thirds were more concerned with prevention and one-third with regrowth. Although the ideal for most of the men involved in this research would clearly be a hair treatment that produced both regrowth and prevention, slightly more respondents thought that prevention (43%) rather than regrowth (34%) was essential in a hair loss treatment.

Therefore, it seems that many men are more anxious to prevent further hair loss in the future than they are to regrow the hair they have already lost. Nonetheless, physicians may incorrectly believe that the patient will only be satisfied with overt regrowth, when in fact he would be content with retaining his remaining hair. This is an important point because secondary prevention, that is the prevention of further loss, is currently a more realistic treatment goal for the physician to offer. This is demonstrated by the drug treatments that have been or are now available.

### **Drug treatments: Minoxidil**

The antihypertensive drug minoxidil was shown in the early 1980's to stimulate new hair growth, and was eventually approved as a topical treatment for AGA in men and women. Minoxidil is known to act as an opener of potassium channels, but the mechanism by which it exerts its effect on hair is unclear, as it is a vasodilator with no known antiandrogenic activity. It appears to convert vellus to terminal hairs, to normalize the hair follicular morphology, and to increase the number of follicles in mid to late anagen, the growth phase of the hair cycle. Multicenter clinical

trials have demonstrated the efficacy of minoxidil in AGA: in most patients treated with topical minoxidil 2% or 3% for 12 months, mean hair counts increased, and in some patients hair counts continued to increase for some time afterwards. 19-3

Topical minoxidil 2% nevertheless has only limited success and the individual response is highly variable. Recent clinical trials with topical minoxidil 5% have shown promising results: in one study, 54% of treated patients showed an increase in hair counts, compared to 29 % of patients on placebo.

Minoxidil has not been approved for systemic use because of potentially serious side-effects, notably cardiovascular, due to its antihypertensive action, and because extraneous hair growth has occasionally been seen even with topically applied minoxidil thought to be due to absorption and systemic action.

Furthermore, as discussed earlier, the majority of men appear to be more concerned with prevention of further hair loss than with regrowth: Minoxidil has not shown any preventive activity, and its ability in the long term to retain new growth against a background of genetically associated hair loss has not been demonstrated.

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### **Drug treatments: manipulating androgen metabolism to retard male pattern hair loss**

The most promising treatments modulate the metabolism of androgens in the scalp. Currently, only one pharmaceutical is available to the physician for the treatment of men with AGA. Finasteride (Propecia) is a potent, specific inhibitor of the type 2 5 $\alpha$ -reductase that is responsible for the conversion of testosterone to DHT. Given orally, Finasteride reduces DHT levels systemically and in the target tissues (i.e. scalp). In an animal model of AGA, the stump-tailed macaque, daily oral Finasteride given over a period of 6 months significantly reduced circulating DHT levels and increased scalp hair weight. 8 Finasteride at a dosage of 1 mg/day has recently been approved by the Food and Drug Administration (FDA) for the treatment of male pattern hair loss in men. Its efficacy has been demonstrated in three double-blind, placebo-controlled, randomized studies. Men with AGA, aged between 18 and 41 years, were given either oral Finasteride 1 mg/day or a placebo. Assessed by scalp hair counts, self-assessment by patients using a validated questionnaire, investigator assessment using a standardized seven-point rating scale of hair growth from baseline, and an independent expert review of photographs taken every 6 months, Finasteride treatment was evaluated as resulting in improvement. Finasteride produced a progressive increase in hair counts at 6, 12 and 24 months, while placebo treatment resulted in significant hair loss. By 24 months, 72% of patients on placebo had lost hair compared to baseline, while 83% of patients on Finasteride had experienced no further hair loss. Similarly, at 14 months, the expert panel considered 66% of Finasteride-treated patients greatly, moderately, or slightly improved vs. only 7% of those on placebo. There was little difference in the incidence of side-effects reported by men on Finasteride (4.2%) vs. placebo (2.2%) which resolved after discontinuation and in many of the men who remained on drug treatment.

These results are in line with our current understanding of the effect of DHT on hair physiology. Although, as mentioned previously, the molecular details of the mechanism by which androgens affect hair growth are not known, it is apparent that, in the androgen-sensitive scalp of genetically susceptible individuals, they cause a gradual miniaturization of the follicles and conversion of long, thick pigmented terminal hair to short, fine, unpigmented vellus hair.

Prevention of the androgen-mediated miniaturization will inhibit or retard the process leading to hair loss, and in some cases result in new hair growth. Furthermore, there is demonstrable heterogeneity in 5 $\alpha$ -reductase activity in scalp hair roots from patients with AGA, which may account for some of the variation in response to Finasteride.

### **Conclusions**

The likelihood is that the modulation of androgen metabolism will prevent further hair loss in the majority of patients, and induce hair growth in a smaller proportion, depending on the extent of their condition and their genetic background. It is vital therefore for the prescribing physician to bear in mind that the patient may suffer anxiety over the possible progression of hair loss in the future, while being able to tolerate his present condition. For many patients, prevention of further hair loss alone will constitute acceptable management. For the physician, the important message is that the best therapeutic prospects lie in drug modalities that utilize our increased understanding of normal and pathologic hair growth. Although topical minoxidil was the first effective drug to benefit some of these patients, targeting of type 2 5 $\alpha$ -reductase in the scalp hair follicle using oral Finasteride is now a realistic option for the prevention of further hair loss in the patient with male pattern baldness.

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