

CLINICAL REVIEWS

Evaluation and treatment of male and female pattern hair loss

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Twenty years ago, there were neither specific treatments available for pattern hair loss nor full understanding of the pathophysiology of this common disorder. Male pattern hair loss (MPHL) [or androgenetic alopecia (AGA), male pattern baldness (MPB)] had been clearly recognized as an androgen-dependent hereditary disorder since the 1940s.¹ The principle of donor dominance was first appreciated at that time and led to the development of hair transplantation as a form of

treatment.² However, it was not until recognition of the phenotype of individuals with the genetic deficiency of 5 α -reductase (5 α R),³ the isolation of the two isoforms of 5 α -reductase (5 α R-1 and 5 α R-2),^{4,5} along with the documented utility of 5 α -reductase inhibitors in male pattern baldness,⁶ that the essential role of dihydrotestosterone (DHT) in male pattern hair loss was clearly established.

Much less is known about female pattern hair loss (FPHL) than MPHL, partly because of less recognizable patterns of hair loss in women, but also because of the common presence of other confounding factors.

The purpose of this review is to provide current information on the potential pathophysiology, clinical presentation, and histology of pattern hair loss in men and women. We also present our consensus opinion of an approach to the evaluation and treatment of pattern hair loss.

PATHOPHYSIOLOGY

A. In men

- MPHL is a common age-dependent trait: the frequency and severity increase with age so that at least 80% of Caucasian men show at least some signs of MPHL by age 70.^{7,8} Whether the thinning that occurs after age 50 to 60 is all androgen-related or is secondary to some other factor related to aging is not entirely clear.
- Asian, Native American, and many

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Disclaimer: None of the treatments discussed, particularly those that are not FDA-approved for male pattern hair loss or female pattern hair loss, should be construed as endorsements or specific recommendations for individual patients. These suggestions and opinions are meant to supply an evidence-based record of information from which a physician can make informed judgments about diagnosis and treatment.

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men of African heritage have a decreased frequency of frontal hair loss and less extensive hair loss compared to Caucasians.⁹⁻¹²

- Male pattern hair loss is clearly androgen-dependent.
- In Hamilton's studies, MPHL was absent in men castrated before puberty. However, PHL developed in 4 of 12 male castrates treated with testosterone.¹
- MPHL has not been reported in Complete Androgen Insensitivity Syndrome in which there is failure of androgen receptor expression.¹³
- Although testosterone is the major circulating androgen in men, the testosterone metabolite, dihydrotestosterone, plays a dominant role in MPHL.
- The conversion of testosterone to dihydrotestosterone is catalyzed by 5 α R.
- There are two isoforms of 5 α R with different tissue distributions and encoded by different genes.⁵
- Type I 5 α R is widely expressed but its physiological function is uncertain.
- Type II 5 α R is expressed in androgen-dependent tissues such as the prostate and hair follicle.
- MPHL is absent in men with genetic deficiency of Type II 5 α R.^{3,4}
- Treatment with finasteride, a selective inhibitor of Type II 5 α R, slows the progression of MPHL and produces some regrowth of hair in about 2/3 of men.⁶
- The primary target of androgen action in the hair follicle is uncertain but there is some evidence that it is mesenchymally derived tissue (dermal papilla [DP] and dermal sheath [DS]).¹⁴⁻²⁰
- Genetic factors predispose to MPHL, but their nature and the mode of inheritance is uncertain.
- Inheritance of MPHL is most likely polygenic.²¹
- There is increased frequency of MPHL in sons of men with MPHL.^{8,22} The maternal influence on MPHL is less well defined.

- The early onset of MPHL may be a marker of the carrier status of a gene responsible for polycystic ovarian syndrome in some women.²³ This gene has not been identified.
- Polymorphism in the androgen receptor gene is associated with MPHL, particularly early onset.²⁴ However, this does not explain the paternal effect in men with MPHL since the androgen receptor gene is located on the X chromosome and, therefore, inherited only from the mother.

B. In women

- As in men, the frequency and severity of FPHL increase with age.²⁵
- The role of androgens in all cases of FPHL is less certain and the authors recommend the more general term 'female pattern hair loss' rather than the term androgenetic alopecia.²⁶
- FPHL undoubtedly, but not necessarily, occurs in women with hyperandrogenemia.²⁷
- These women with hyperandrogenemia may show a 'male' pattern of hair loss.
- These women typically have other signs of hyperandrogenism, eg, hirsutism and/or menstrual disturbance. Hyperandrogenism implies an increased expression of androgen-related conditions but does not require an absolute elevation of serum androgens.
- Women with pattern hair loss in the presence of signs of hyperandrogenism may respond to treatment with finasteride,²⁸ or cyproterone acetate.²⁹
- But:
- The pattern of hair loss in women with FPHL is usually different from that seen in men with MPHL (see clinical findings below).
- Most women with FPHL show no other clinical or biochemical evidence of androgen excess.²⁷
- The family histories of women with FPHL are not as straightforward as those of men with MPHL.³⁰
- There was no response in postmenopausal women to treatment with finasteride³¹ or in

women without signs of androgen excess to cyproterone acetate.²⁹

General

Whatever the etiology, the follicular changes in MPHL and FPHL appear identical, ie, there is a 'final common pathway' of follicular miniaturization. This includes:

- Progressive reduction in the duration of anagen.
- The prolongation of the latent period of the hair cycle³² (not yet confirmed in women). Normally, anagen reasserts itself after a fixed period of telogen towards the end of which the hair is shed. The latent period is a period of persistent suspension of growth of the follicle after the hair shaft has been shed.
- Follicular miniaturization.

CLINICAL FINDINGS

A. In men

- Onset:
 - May begin anytime post-puberty, usually by age 40.
 - 14% of healthy boys aged 15-17 years old show early signs of MPHL. (Trancik RJ, Spindler JR, Rose S et al: Incidence of andro-genetic alopecia in males 15-17 years of age. Poster presented at 3rd Intercontinental Meeting of the Hair Research Societies, June 13-15, 2001, Tokyo, Japan.)
- Distribution: Central scalp (this encompasses the frontal, mid, and vertex scalp).³³
- Pattern:
 - Most common: Varying degrees of hair loss in the bitemporal, frontal, mid scalp, and vertex regions that generally fall into one of the Hamilton-Norwood patterns of hair loss.³⁴
 - Uncommon: Diffuse scalp hair loss or female pattern of hair loss with diffuse central scalp hair thinning.
- Hair pull: May be positive in active early hair loss in the central scalp but generally negative in long-standing hair loss. If there

is concomitant eogen effluvium, the hair pull may be positive diffusely over scalp.

- Affected hairs: Miniaturization (finer, shorter hairs) and decreased hair density to the same degree in a given area of the scalp may lead to baldness (no hair) in that area.
- Scalp: Generally normal. Concomitant seborrheic dermatitis is common. If the patient has perifollicular erythema or hyperkeratoses, consider a cicatricial alopecia variant.³⁵ A scalp biopsy is recommended in the latter case.
- Associated findings: A higher incidence of coronary artery disease (CAD) has been reported in men with MPHL.^{36,37} In one study of 19,112 US male physicians,³⁶ the relative risk of CAD was 1.32 (95% CI, 1.10- 1.59) for moderate vertex baldness and, although independent of age, hypertension, or increased cholesterol, was stronger in men with hypertension or high cholesterol.
- Family history: Commonly positive for MPHL on either side of the family but 20% of patients do not have a family history of MPHL.

B. In women

- Onset:
 - May begin any time post menarche or adrenarche.
 - Many women also first complain of hair loss in the 40-50-year-old age group: Whether this is an exacerbation of long standing FPHL which has not been previously diagnosed or is truly late onset FPHL is not clear. That these women do not respond to a Type II 5 α R inhibitor raises questions about the androgen-dependence of this subset of FPHL.³¹
- Distribution: Central scalp +/- sides of scalp.
- Pattern:
 - Tends to be one of two patterns in most women: Diffuse central thinning³⁸ or frontal accentuation ("Christmas tree" pattern).^{26,39}

- Fronto-temporal recession/vertex loss, ie, "male pattern", is a third, but uncommon, pattern.
- Bitemporal thinning is commonly associated with, but not necessarily indicative of, FPHL.
- There is not usually any recession of the frontal hairline although the hairs on the frontal margin are commonly miniaturized, ie, finer and shorter.
- Hair pull: May be positive in active early loss in the central scalp but generally negative in long-standing hair loss. If there is a concomitant telo-gen effluvium, the hair pull may be positive diffusely over the scalp.
- Affected hairs: Miniaturization is generally not as uniform nor as profound in specific scalp areas as that in MPHL, and hence, there are no regions of absolute baldness as with MPHL.
- Scalp: Generally normal. Concomitant seborrheic dermatitis is common. If the patient has perifol-licular erythema or hyperkeratoses, consider a cic-atricial alopecia ariant.³⁵ A scalp biopsy is recommended in the latter case.
- Associated findings: Signs or symptoms of hyper-androgenism should be looked for, ie, hirsutism, moderate to severe or treatment-refractory acne, irregular menses, infertility, and/or galactorrhea. Acanthosis nigricans is a marker for insulin re-sistance which is commonly associated with hyperandrogenism.⁴⁰
- Family history: Women with FPHL are less likely than men with MPHL to have a history of first-degree relatives with MPHL.⁴¹

EVALUATION

A. General

- It is important to exclude other causes of hair loss that may mimic pattern hair loss (PHL) since some treatments for PHL are selective (eg, finas-teride in MPHL). It is also important to determine if there are other concomitant hair disorders whose untreated presence could ultimately affect the utility of

the treatments used for PHL (eg, iron deficiency in FPHL).⁴² The differential diagnosis of PHL should include acute and chronic telogen effluvium, diffuse or reverse ophiasis alopecia arcata, and early cicatricial alopecia.

B. In men

- Anabolic steroids or supplemental androgens may worsen PHL.
- Consider checking thyroid stimulating hormone (TSH) if the hair loss is diffuse and not localized exclusively to typical MPHL areas.
- Consider iron evaluation in men on a strictly vegetarian or otherwise deficient diet or where blood loss could be an issue.

C. In women

- Screening blood work is generally recommended in all women. In otherwise healthy women, check TSH and serum ferritin. Hypothyroidism may cause a telogen effluvium⁴³ and iron deficiency is speculated to both cause a telogen effluvium⁴⁴ and to interfere with the efficacy of treatment of FPHL.⁴² Iron deficiency may be screened by two methods: serum ferritin or serum iron and total iron binding capacity (TIBC). A low serum ferritin is diagnostic of iron deficiency. However, de-pleted iron stores in patients with chronic disease may not be detected by serum ferritin measurements since ferritin is an acute phase reactant, and active inflammatory disorders, malignancy, and infections increase its synthesis and may, by its elevation in these situations,⁴⁵ give a false sense of normal iron stores. Some physicians prefer to have a sedimentation rate drawn with the ferritin to rule out falsely high or normal levels of ferritin in those with underlying active medical problems. If physicians elect to check serum iron and total iron binding capacity instead of ferritin, patients should not be taking concomitant iron-containing preparations (ie, multivitamins with iron or oral

contraceptive pills [OCPs] containing iron) for at least 24 hours beforehand since exogenous iron can increase serum iron transiently but mask deficient marrow iron stores. Iron supplements taken for ≥ 3 weeks can falsely elevate ferritin levels in the face of iron deficiency. Iron deficiency is associated with low serum iron and relatively high total iron binding capacity and low percent saturation.

- Other screening tests may be indicated by history including a complete blood cell count (CBC) and/ or free thyroxine (T4).
- The majority of women with FPHL have no clinical or biochemical evidence of androgen excess.²⁷ However, a subset of women with FPHL does, and women with concomitant signs/symptoms of hirsutism, moderate to severe and/or treatment-refractory adult acne, acanthosis nigricans, irregular menses, and/or galactorrhea should be adequately screened for hyperandrogenemia. In these cases, blood tests should include:
 1. Free and/or total testosterone +/- dehydroepiandrosterone sulfate (DHEAS) at a minimum. Tests ideally should be done off of OCPs since OCP's will inhibit both ovarian and adrenal sources of androgens.⁴⁶ If these tests are normal on OCPs, but the suspicion is high for underlying hyperandrogenemia, they should be repeated at least one month after cessation of OCPs.
 2. If testosterone is greater than $2.5 \times$ normal or >200 ng/dL, or DHEAS is greater than $2 \times$ normal or >700 ug/dL in premenopausal or >400 ug/dL in postmenopausal women, a work-up for a tumor with radiographic tests should be undertaken.⁴⁷
 3. Consider checking serum prolactin if galactorrhea is present or if there is increased testosterone or free testosterone.
 4. Consider screening for congenital adrenal hyperplasia (CAH) if testosterone or DHEAS is elevated. An early morning serum 17-OH progesterone during the

follicular phase of the cycle (days 1-14) would be a reasonable screening test for the most common form of CAH, ie, 21-hydroxylase deficiency.⁴⁸ However, a serum 17-OH progesterone pre- and post-Cortrosyn (synthetic adrenocorticotrophic hormone [ACTH]) stimulation test is the most reliable way of screening for 21-hydroxylase deficiency. If either prolactin or 17-OH progesterone is increased, one may wish to refer the patient to an interested endocrinologist for further evaluation and treatment.

HISTOPATHOLOGY

A. Indications for biopsy

- Diagnosis:
 - Males: Usually not necessary unless a female pattern of hair loss, diffuse hair loss, or scalp changes suggestive of cicatricial alopecia confuse the diagnosis.
 - Females: Sometimes necessary to exclude chronic telogen effluvium, diffuse alopecia areata or cicatricial hair loss such as early central centrifugal cicatricial alopecia seen commonly in African American women.
- Site of biopsy: The preferred area for biopsy is the central scalp in an area representative of the hair loss process. Biopsy should not be from the bitemporal area as this region may have miniaturized hairs independent of MPHL or FPHL.
- Type of biopsy: A punch biopsy of not less than 4 mm in diameter that follows the direction of the hair shafts and is taken deep into the subcutaneous fat where anagen hair bulbs are located is standard. Many dermatopathologists favor horizontal sectioning of biopsies.⁴⁹
- Histologic diagnosis:⁴⁹⁻⁵¹
 1. The key change is miniaturization of terminal hairs into vellus-like hairs. This change is progressive over time. The same changes characterize both male and female pattern hair loss.
 2. The percentage of telogen hairs increases from a normal of 5%-10% to 15%-20% on average with a corresponding decrease in

the percent-age of anagen hairs. The percentage of telogen hairs is slightly less in female pattern hair loss than in male pattern hair loss.

3. Horizontal sections permit accurate follicular counts of terminal and vellus and vellus-like hairs and characterization of terminal hairs as anagen, catagen, or telogen. Terminal hairs have hair shafts that are >0.03 mm in diameter and thicker than the follicle's inner root sheath. Vellus or vellus-like (miniaturized) hairs have hair shafts that are ≤ 0.03 mm in diameter and thinner than the follicle's inner root sheath.
4. Vertical sections show a limited number of hair follicles but do allow one to estimate the proportion of anagen, catagen, and telogen hairs and terminal vs vellus or vellus-like hairs.
5. The ratio of terminal to vellus or vellus-like hair normally is 7:1. In PHL, the ratio decreases to 1.9:1 (both sexes combined) or 1.5:1 (males only), 2.2:1 (females only).⁵² The amount of vellus or vellus-like hairs is slightly less in FPHL than in MPHIL.
6. The total number of hairs per unit area is usually normal in PHL (normal being approximately 240-400 hairs/cm² or 30-50 hairs per 4 mm punch biopsy in normal adults),^{52,53} but may be reduced in severe baldness or in elderly patients.
7. A perifollicular infiltrate, predominantly lymphohistiocytic, may be present in pattern hair loss, around the upper or lower follicle. The prognostic implications of this finding are uncertain at this time.
8. Perifollicular fibrosis, usually comprising concentric layers of collagen deposition, may be present in pattern hair loss around the upper and lower follicle. This may have negative implications for potential regrowth⁴⁹ although further data are needed to corroborate this.

TREATMENT

A. General principles

- The diagnosis should be confirmed. Some

treatments are specific to the pathophysiology of PHL, and others are nonspecific hair growth promoters.

- Patients should avoid hair care products likely to damage scalp/hair. This is particularly important for African American women.
- Patients should maintain an adequate diet, especially one with adequate protein. The National Institutes of Health (NIH) recommended daily allowance for protein is 0.35 gm/lb or 0.8 gm/kg, which translates into 45 grams for a 150-lb. person.
- Topical medications work only where the medication is applied; therefore, the entire area at risk of hair loss (the top of the scalp) should be treated with a given topical agent.
- If possible, any drugs that could negatively affect hair growth should be stopped and alternative substitutes made. Although certain drugs are more commonly associated with hair loss than others, any drug can potentially cause a telogen effluvium. Medications for which hair loss is a common potential side effect include retinoids, cytotoxic agents, and anticoagulants.
- Treat any underlying scalp disorder such as seborrheic dermatitis or scalp psoriasis as these conditions can affect the ability to use topical treatments for hair loss without irritation.

B. Medical treatment for men

GENERAL

- Currently, only finasteride 1 mg and minoxidil topical solution (2% and 5%) are FDA-approved for the treatment of male pattern hair loss.
- Both drugs retard further thinning and increase scalp coverage. However, in many patients, the main perceived response may be maintenance of current hair density.
- Neither drug restores all the lost hair. Neither drug is able to reverse total baldness.
- Both drugs require chronic use to maintain effectiveness. If treatment is discontinued,

the effects of the drug are lost over several months, and the hair density will evolve into what it would have been without treatment.

- Treatment should be used for 12 months before making a decision about efficacy although benefit may be seen sooner.

FINASTERIDE (1 MG ORAL DAILY)

- FDA-approved for men ≥ 18 years old.
- Mode of action:
 - Competitive inhibitor of type II 5 α R that decreases the conversion of testosterone (T) to DHT. DHT in serum and scalp is decreased $\sim 2/3$ with treatment.⁵⁴
- Efficacy:
 - Target area hair counts (TAHC) are generally used to assess efficacy in clinical trials of MPHL. TAHCs are circular target areas 1 cm to 1 inch in diameter typically at the anterior leading edge of the vertex balding area where the terminal, non-vellus, or visible hairs are counted pre- and post-treatment.
 - Target area hair counts increase over the first year and peak by ~ 12 months: In men age 18-41, hair counts increased 16.9/cm² for those on 1 mg finasteride vs ~ 4.1 /cm² for those on placebo.⁶
 - By expert panel review of global photographs, hair growth continues to improve for at least the first 24 months of treatment as the hairs grow longer and thicker. In men aged 18-41, $\sim 50\%$ of men showed an increase in hair growth by 1 year, and 66% by 2 years on finasteride, compared to 7% and 7% at both 1 and 2 years respectively for placebo.⁶ In men aged 41-60, 39% on finasteride versus 3% on placebo showed increased hair growth at 2 years.⁵⁵
 - 5-year placebo-controlled trials using both hair counts and expert panel review of global photographs as endpoints confirm that continued use of finasteride helps to maintain this effect and to slow further hair loss.⁵⁶
 - If treatment with finasteride is discontinued, any positive effect on hair growth will be lost in 12 months.⁶

• Safety

- No known drug interactions.
- No effects on liver, kidney, bone marrow, or bone or serum lipids.
- No effect on spermatogenesis.
- Reversible sexually-related side effects (decreased libido, erectile dysfunction, decreased ejaculate volume) were seen in 1.8% of men aged 18-41 versus 1.1% of those on placebo.⁶ In older men aged 41-60, sexually-related side effects were seen in 8.7% on finasteride vs 5.1% on placebo.⁵⁴ These side effects often resolve during continued treatment or within days to weeks after treatment with finasteride is discontinued.
- The level of finasteride in semen of men taking finasteride is very low and semen from a man taking finasteride poses no risk to a pregnant woman or to her fetus.⁵⁷
- Reduction in prostate specific antigen (PSA) is physiologically based on the effect of decreased DHT on the prostate. Recommendation is that any PSA test value should be doubled for any man taking finasteride to compensate for the effect of the drug.^{58,59}
- Recent data from a long-term (7 year) trial of 18,882 men greater than or equal to 55 years old with normal digital rectal examination and less than or equal to 3.0 ng/mL serum PSA who took 5 mg finasteride (5 \times the standard dose recommended for MPHL) vs placebo revealed a 25% decrease in prostate cancer for those on finasteride (803 on finasteride vs 1147 on placebo).⁶⁰ However, 6.4% of men on finasteride developed histologically high grade cancer (defined as Gleason score 7-10) vs 5.1% of those on placebo. This study only monitored changes in the number of prostate cancers and histologic subtype but did not address the biological aggressiveness of the tumors or outcome. Potential hypotheses for the findings include that: (a) finasteride may selectively inhibit low grade prostate tumors, (b) low DHT may induce histologic changes that mimic high grade disease, or (c) low DHT may induce higher grade prostate cancers. Further research and long-term

observation of men taking finasteride 1 mg needs to be done on this issue.

MINOXIDIL TOPICAL SOLUTION 2% AND 5%

- FDA-approved for men ≥ 18 years old. Adolescents have been treated with topical minoxidil solution without any additional problems (Trancik RJ, Spindler JR, Cuddihy RV, et al.: Clinician survey evaluating minoxidil topical solution in the treatment of androgenetic alopecia in patients under 18 years of age. Poster presented at 3rd Intercontinental Meeting of the Hair Research Societies, June 13-15, 2001, Tokyo, Japan).
- Mode of action:
 - Increases duration of anagen and enlarges miniaturized follicles.
 - Potassium channel opener and vasodilator. The precise mechanism of action is unknown but appears independent of vasodilation.⁶¹
- Application: 1 mL twice daily to dry scalp, preferably using a dropper application. Topical minoxidil solution requires approximately 1 hour for absorption. If the patient shampoos or the scalp becomes wet, eg, from excessive sweating or rain, the medication should be re-applied. If gel or hair spray is used, the medication should be applied first so that absorption is not affected.
- Efficacy:
 - Target area hair counts and global photographs confirm a significant increase in hair density.⁶² The hair growth appears to peak at 16 weeks.⁶² Placebo-controlled trials of both target area hair counts and expert panel review of global photographs at 1 year⁶² and hair weight studies over 2 years⁶³ confirm that continued use of topical minoxidil solution helps to maintain this effect and to slow further loss.
 - 5% topical minoxidil solution is superior to 2% topical minoxidil solution by target hair counts, expert panel review of global photographs,⁶² and hair weight studies in men with MPHL.⁶³ Target area hair count increases are 18.6/cm² for 5% topical

minoxidil solution, 12.7/cm² for 2% topical minoxidil solution, and 3.9/cm² for placebo at 48 weeks. Expert panel review of global photographs show increased growth at 1 year in 57.9% on 5% topical minoxidil solution, 40.8% on 2% topical minoxidil solution, and 23.2% on placebo.⁶²

- If treatment is discontinued, any positive effect on hair growth will be lost in 4-6 months.⁶⁴
- Topical minoxidil solution may initially cause a telogen effluvium beginning 2-8 weeks after treatment initiation. This temporary shedding, resulting from the minoxidil initiated release of telogen hairs ("exogen") as anagen promotion begins, is self-limiting with continued treatment and should not be a cause for concern. Patients should, however, be forewarned so that treatment is not interrupted.
- Safety: Adverse effects are mainly dermatologic.⁶²
 - Scalp irritation, including dryness, scaling, itching, and/or redness, may occur; these are more common with the 5% topical minoxidil solution than the 2% topical minoxidil solution.
 - Allergic contact dermatitis is uncommon.⁵⁶ Patch test kits are available from Pfizer and may help to sort out whether a rash is an irritant or allergic contact dermatitis and whether it is related to minoxidil or propylene glycol.
- Combination treatment of finasteride and topical minoxidil
 - There have been no well-controlled studies in humans. A study in the stump-tailed macaque, an animal model for pattern hair loss in both sexes, showed an additive effect when both drugs were used concurrently.⁶⁵
 - Men who wish to switch from treatment with one of these agents to the other should continue using the original medication in addition to the new agent for at least 3 months before discontinuing it. This cross-over period is needed to provide time for the newer drug to reach a point of effectiveness to avoid excess shedding.

C. Medical treatment for women WOMEN WITH OR WITHOUT HYPER- ANDROGENISM:

- If women are on hormone replacement therapy or an OCP, the dose and type should be stabilized. Over-the-counter DHEA or testosterone in hormone replacement therapies should be avoided. In this way, women with FPHL will minimize external additions to any potential underlying androgen sensitivity.
- Minoxidil topical solution:

Efficacy:

-Currently, only 2% topical minoxidil solution is FDA-approved for the treatment of "women with thinning hair."⁶⁶

-5% topical minoxidil solution, although not currently FDA-approved for use in women, has been evaluated in women with FPHL and was found to be significantly more effective than placebo by both target area hair counts and subject assessment.⁶⁷ There was a trend towards superior efficacy of 5% topical minoxidil solution over 2% topical minoxidil solution but this was not consistently statistically significant. Target area hair counts at 48 weeks showed a change from baseline of 24.5/cm², 20.7/cm², and 9.4/cm² in the 5% topical minoxidil solution, 2% topical minoxidil solution, and placebo group respectively. The sensitivity of target area hair counts as a primary end-point in FPHL has been questioned.³³

-Treatment should be used for 12 months before making a decision about efficacy although benefit may be seen sooner.

-Topical minoxidil solution works in those women with FPHL both with and without hyperandrogenism and in young and old, pre- and postmenopausal women alike.

Safety:

-Either 2% or 5% topical minoxidil solution appears safe to use in women with FPHL, with the only additional risk of the 5% topical minoxidil solution over the 2% topical minoxidil solution being a higher incidence of facial hypertrichosis. The hypertrichosis tends to occur over the cheeks and forehead as vellus, not terminal, hair and

disappears within 4 months of stopping the drug. Although this may be related to inadvertent spreading to the face after local application to the scalp, this may also be a result of hypersensitivity to low levels of systemic absorption of minoxidil. Other local side effects are the same as in men.

WOMEN WITH HYPERANDROGENISM

- Hyperandrogenism is synonymous with excessive secretion of androgens,⁶⁸ the indirect evidence of which is the existence of hirsutism, severe or treatment refractory acne and/or irregular menses (the latter in a woman of childbearing potential off of OCPs), and/or the elevation of serum testosterone, free testosterone, or DHEAS. Less than 40% of women with FPHL have hyperandrogenism²⁷ but this population, with clear-cut evidence of androgen hypersensitivity or overproduction, may respond differently to drugs that block the production or effect of androgens than those women with FPHL and no hyperandrogenism.
- Antiandrogens and 5 α -reductase inhibitors
 - There are few studies evaluating the effect of antiandrogens or 5 α R inhibitors in FPHL and only one that is large and placebo-controlled. Most studies showing efficacy of these agents have been done in women with hyperandrogenism, particularly those with hirsutism. Studies of these agents in women with FPHL who do not have overt hyperandrogenism have not specifically shown proven efficacy. In the United States, all of these agents are used off-label for the treatment of hirsutism or female pattern hair loss.
 - Since all antiandrogens or 5 α R inhibitors may cause feminization of a male fetus, all women of childbearing potential should use effective means of contraception while taking any of these drugs. OCPs have the additional advantage of also lowering serum androgens. Women of childbearing potential who use an antiandrogen or 5 α -reductase inhibitor should be cautioned to stop the

medication and call their doctor if their menses are late.

-If of childbearing potential and on an OCP for at least 1 month with a negative pregnancy test, or if of non-childbearing potential, one may try either:

-Spironolactone 100-200 mg per day.

1. Only small, uncontrolled studies with spironolactone in FPHL have been published but they support efficacy in the subset of FPHL with hyperandrogenism.⁶⁹

2. For safety purposes, one should check serum potassium at baseline and 1 month after beginning treatment since hyperkalemia is a rare side effect. Patients should keep well hydrated.

- Finasteride 1-1.25 mg per day

1. In a well-controlled study, finasteride 1 mg per day, was not shown to be useful in postmenopausal women with FPHL.³¹ These subjects were not specifically stratified for hyper-androgenism.

2. Some positive reports in women with hyperandrogenism treated with 1.25 mg per day have emerged.²⁸

3. There are no anticipated side effects and no blood tests are necessary.

-Cyproterone acetate:

1. 100 mg days 5-15 combined with 50 ug ethinyl estradiol on days 5-25 of the menstrual cycle appears most useful.⁷⁰

2. Only one well-controlled study has been done with FPHL and this proves the value of cyproterone acetate in women with hyperandrogenism only.²⁹

3. Diane (2 mg cyproterone acetate days 5-15 and 50 ug ethinyl estradiol days 5-25 of the menstrual cycle) appears to be less effective in hair loss.⁷¹

4. No specific blood tests are necessary.

D. Cosmetic aids

- Nonmedical approaches can provide cosmetic relief to men and women with thinning hair if medical treatments are not indicated, not effective, or not desired by the patient. They can also be used as adjuvant therapy if medical or surgical treatments are used.

- Tinted powders, lotions, and hair sprays can all provide a cosmetic covering of the scalp in areas of scalp hair thinning and can be useful in camouflaging it.

- Wigs, hair pieces, and hair extensions can be used to cover a thinning scalp. Advances in the technology of these prostheses have made their use much more acceptable.

E. Surgical treatment⁷²⁻⁷⁴

HAIR TRANSPLANTS

- Criteria for assessing male candidates:

- Age:

- Patients over the age of 25 years are preferable. The predictive value of future hair loss is much lower for individuals between the ages of 15 and 25 years of age and surgery in this young group of men may result in misplaced hairlines or an unnatural appearance 20 or 30 years later. Young men with early hair loss (Hamilton-Norwood I and II patterns) already have enough hair for facial framing and will receive limited aesthetic benefit from surgery.

- Degree of frontal and vertex hair loss:

Vertex baldness is a progressive process and

therefore, hair transplantation of the vertex should be approached with extreme caution. Ideal candidates are those with just frontal and mid-frontal hair loss. When frontal baldness is corrected, this creates the most dramatic positive change in appearance.

- Density of donor area should be adequate:

Patients with <40 follicular units/cm² in the donor area are considered poor candidates.

- Hair caliber and color: Thicker hair shafts (>60 -70 microns) demonstrate better coverage compared to finer hair. Lighter colored hair in caucasians gives a more natural look compared to dark colored hair since the contrast between hair and skin is not as apparent.

- Criteria for assessing female candidates:

- Women with mild female pattern alopecia (early Ludwig I) are not optimal surgical candidates since differences in pre-transplanted scalp vs post-transplanted scalp

are difficult to appreciate.

- Those with diffuse unpatterned alopecia are poor surgical candidates for the obvious reason that the entire scalp is suffering hair loss, thus, the donor area is of limited value as it is also susceptible to loss.
- The ideal female patients for hair transplantation are those with high-density donor hair and extensive hair loss or thinning of the frontal scalp.
- Number of sessions:
Experienced surgical teams can create significant coverage in one to two sessions with dense packing of higher number of grafts (1000-2000) being performed per session. Final results are usually seen 5-6 months after the procedure, and thus, timing between sessions, if needed, is usually a minimum of 6 months.
- Complications:
 - Facial edema, scalp erythema, and recipient site crusts of the scalp are common but usually resolve within 3-7 days although crusting may persist a few additional days.
 - Other possible complications of hair transplants include nausea and vomiting, post operative bleeding (less than 0.5%), infection (less than 0.5%), excessive swelling (5%), temporary headache, temporary numbness of the scalp, abnormal scarring around the grafts (less than 1%), poor growth of grafts, fainting (less than 1%), folliculitis, keloid formation, neuroma, persistent scalp pain, telogen effluvium, and arterio-venous fistula formation.

SCALP REDUCTIONS

- Description:
 - Hair-bearing skin is brought closer together by removing the center scalp affected by the alopecia.

- Not commonly performed currently.
- Many different designs employed in excising the balding area.
- Reductions may be performed in conjunction with hair transplantation to the remaining bald scalp for a more optimum result.
- Potential complications:
 - The efficacy diminishes over time due to the unpredictable progression of hair loss in any given individual.
 - Excision scars become noticeable over time.
 - The scar may potentially widen secondary to stretching of adjacent scalp skin.
 - Usually more than one scalp reduction is necessary to effectively address a pe baldness.

Adjunctive medical therapy with surgery

The use of finasteride and/or topical minoxidil may stabilize underlying hair loss therefore necessitating less donor harvesting and less scalp reductions. This will also allow the patient to maintain a more natural appearance over time.

CONCLUSION

Although the clinical aspects of pattern hair loss are well-recognized in both men and women and the role of DHT in MPHL is well documented, much remains to be determined regarding the genetics and pathophysiology of these common conditions. There are effective treatments, either medical or surgical, available currently for some men and women with pattern hair loss, but clearly further treatment options are desired, particularly for women with FPHL.

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