# Hair: What is New in Diagnosis and Management?

## Female Pattern Hair Loss Update: Diagnosis and Treatment

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**KEYWORDS**

• Alopecia • Pattern hair loss • New • Update • Treatment • Androgenetic

**KEY POINTS**

- Female pattern hair loss (FPHL) is the most common cause of alopecia in women, and it is characterized by follicular miniaturization.
- Androgens and estrogens are the main hormonal regulators implicated in FPHL.
- Realistic expectations need to be set when treating patients with FPHL.
- All treatments seem to work best when initiated early and when used in combinations.

### DEFINITION

Female pattern hair loss (FPHL) is the most common cause of alopecia in women. It affects 6% to 12% of women between the ages of 20 and 30 years, and more than 55% of women older than 70 years.[1] FPHL clinically presents with diffuse nonscarring loss of hair, with prominent thinning over the frontal, central, and parietal scalp. The frontal hairline is characteristically retained. A similar pattern of hair loss with follicular miniaturization is seen in male androgenetic alopecia (AGA). Because the role of androgens on alopecia in women remains uncertain, FPHL has emerged as the preferred term rather than AGA in women.[2]

### DIAGNOSIS

The diagnosis of FPHL is made clinically based on the appearance of the scalp. Biopsies are reserved only for situations when the diagnosis is uncertain. A 4-mm cylindrical punch from the central area of hair loss is preferred. It is recommended to avoid biopsies from the temporal area, because miniaturized hair follicles can be found there even in the absence of FPHL.[3] Preferably vertical and horizontal tissue sections should be processed, and reviewed by a dermatopathologist experienced in interpreting alopecia biopsies.

FPHL is characterized histologically with increased numbers of miniaturized, velluslike hair follicles. In FPHL, the ratio of terminal to velluslike hairs is usually less than 3:1.[4] There is a reduction in follicle size, depth, and hair shaft diameter, with an increased telogen/anagen ratio.[5] Low levels of inflammation can be found as lymphocytic microfolliculitis targeting the hair bulge, with IgM and complement deposits on the basement membrane.[6]

Although most patients with FPHL have normal levels of testosterone, this type of alopecia can be a marker of hyperandrogenism in women.[7] Evaluation of patients with FPHL should include

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clinical assessment for hirsutism, menstrual abnormalities, and acne. Hormonal studies should include serum levels of androgens, to evaluate for presence of polycystic ovary syndrome (PCOS), androgen-producing tumors, or congenital adrenal hyperplasia. A referral to an endocrinologist may be helpful in complicated cases. Additional useful laboratory tests include thyroid, iron studies with ferritin, prolactin, and zinc levels.

## PATHOGENESIS

Androgens and estrogens are the main hormonal regulators implicated in FPHL. The hair follicle is sensitive to alterations in circulating estrogen and androgen levels; these hormones are also synthesized and metabolized locally.[8] Most of the evidence about the role of androgens comes from studies of male AGA. Androgens have a clearly established role via binding of dihydrotestosterone (DHT) to hair follicle androgen receptors (AR) in male pattern hair loss. In scalp hair follicles, testosterone is converted to DHT by the enzyme 5-$\alpha$ reductase type II. DHT has a 5-fold higher affinity for the AR and is believed to be the more important player in AGA.[9] The 5a reductase inhibitors, finasteride and dutasteride, can be used to block DHT synthesis and arrest hair loss in men. Functional polymorphisms of AR can be a marker for premature AGA in men and can predict treatment response to 5a reductase inhibitors.[10]

In contrast, the role of androgens in FPHL has not been clearly established and it does not seem to be as essential as in AGA. Pattern hair loss has been described in cases with complete androgen insensitivity syndromes, suggesting that mechanisms other than androgens may be involved.[11] Although FPHL can be associated with hyperandrogenic states, the circulating testosterone levels do not differ between patients with FPHL and normal controls.[7] Many women with FPHL have low levels of circulating sex hormone binding globulin (SHBG), which may increase the available free testosterone at the level of the hair follicle.[11] Although it has been postulated that there is an increased peripheral sensitivity to androgens in FPHL, the response to treatment with 5a reductase inhibitors is unpredictable. Also, AR polymorphisms have not been uniformly confirmed and cannot completely explain the mechanism of FPHL.[12]

The observed differences between androgen regulation in FPHL and male AGA may lie in the presence of estrogens. Estrogen signaling can modify androgen metabolism at the hair follicle, by unclear mechanisms. Estrogens may positively affect hair loss through inhibition of 5a reductase.[13] High systemic estrogen levels in pregnancy are implicated in the prolongation of anagen. The sudden loss of estrogen postpartum is believed to lead to shedding, known as telogen gravidarum.[14] Conversely, lower systemic estrogen levels have been implicated in the increase of FPHL after menopause.[15] FPHL has been correlated with low systemic estrogen levels when aromatase inhibitors are used in cancer therapy. Topical estrogen preparations are used to treat FPHL in some countries, but their efficacy is questionable.[16]

Outside the sex hormonal milieu, FPHL may be influenced by insulin resistance, microvascular insufficiency, and inflammatory abnormalities. Insulin resistance has been associated with low circulating levels of SHBG and early onset of AGA in male patients.[17] Patients with FPHL show higher prevalence of carotid atheromatosis, with higher levels of inflammatory markers, such as C-reactive protein, fibrinogen, and D-dimer.[18] Increased systolic blood pressures are found in patients with FPHL in comparison to control individuals.

### *Genetic Studies*

Studies on the genetic base of FPHL show increased frequency of alopecia in both male (54%) and female (21%) first-degree relatives.[19] Based on the experience from AGA, the speculated FPHL genetic link may lie in variations of the AR gene.[20] The AR gene is a nuclear transcription factor located on the X-chromosome. The amino-terminal domain of the AR gene contains a region of CAG repeats, which affects its transcriptional activity.[20] The number of CAG repeats inversely correlates with androgen function. Particular CAG variants in the AR gene are implicated with a risk of developing AGA in men.[10] Variations in the CAG length have been associated with PCOS, hirsutism, and acne in women.[21] These findings led to the development of a screening test for FPHL and AGA, the Hair Genetic Test (http://hairdx.com), which differs for men and women. In women, the Hair Genetic Test measures the length of CAG and GGC repeats within the AR gene. Shorter CAG and GGC repeats are associated with a significant risk of developing FPHL. Short repeat lengths (15 or less) correlate with types of FPHL in 97.3% of patients.[22]

## TREATMENT

The goal of treatment of FPHL is to arrest hair loss progression and stimulate hair regrowth. Realistic expectations need to be set, because the efforts to treat FPHL have mixed success and do not accomplish complete regrowth. All treatments seem to work best when initiated early. Combinations of treatments tend to be more efficacious than single products (**Fig. 1**). The treatments for