

## My Pellet Patient is Complaining of Hair Loss... Now What?

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There is no evidence that T or T therapy is a cause of hair loss in either men or women. Although men do have higher T levels than women, men are more likely to have hair loss with age. Even though women with PCOS and insulin resistance have higher T levels and commonly hair loss, this does not prove causation. Dr. Rebecca Glaser treated 285 women for a minimum of 1 year with T pellets for symptoms of androgen deficiency and were asked to complete a survey that included questions on scalp and facial hair. Two-thirds of women treated with subcutaneous T implants had scalp hair re-growth on therapy. Women who did not regrow hair on T were more likely to be hypo- or hyperthyroid, iron deficient, or have elevated body mass index. None of the patients treated complained of hair loss, despite pharmacologic serum T levels on therapy. Moreover, in Dr. Glaser's clinical experience of treating more than 1,100 female patients with over 10,000 subcutaneous testosterone pellet insertions, hair thinning was rarely reported. The proposed benefit of T therapy is due to the anabolic effect of it on hair growth. <sup>1,2</sup>

Hair thinning and/or hair loss is a common complaint in a doctor's office. In the setting of a patient undergoing pellet therapy, the "knee jerk reflex" is to blame it on the pellets. Our job is to assess the patient and look for the root cause and identify any underlying disease. In the end, the main contributing factor for hair loss, regardless of pellet status, is genetics. However, stress, beauty treatments for the hair, thyroid issues, illness, medications, iron deficiency, hormone imbalance, and nutritional deficiencies are other common causes, to name a few. The first step when a patient complains of hair loss is to perform a thorough history and physical. The first question should be about the timing of the hair loss. Was it "fast and furious" or "slow and gradual?" This question often differentiates the two most common conditions of hair loss.

The fast pattern is most commonly known as telogen effluvium (TE) which is brisk shedding all over the scalp during times of stress. It often causes a high degree of concern in patients, as they can lose up to 3 times the normal amount of hair in a day. TE usually occurs several months after the inciting factor and resolves in 6-9 months after the stressor has been removed. A simple "pull test" during the physical exam can help diagnosis this condition. You can lightly grab about an inch of hair with your thumb and index finger and gently pull. If more than 3-6 telogen hairs come out, this is a positive test. A telogen hair characteristically has a white bulb on the end of it. It is not uncommon to have this type of shedding after the first round of pellets in a patient that was hormone depleted. The body sees that depleted state as a stressor and once the hormones are optimized, the hair enters the anagen growing phase again and pushes out the dormant telogen hair. Reassurance to the patient that time will resolve this type of hair loss, and that the hair will be healthier and stronger in the future is important.

The slow pattern is most commonly known as androgen alopecia (AGA) which features progressive miniaturization of the hair follicle in predisposed individuals without scarring. The incidence of AGA depends on age, sex, and ethnicity with 50 percent of white men by the age 50. In addition, 40-50% of white women will develop AGA during their lifetime. People with Asian or African ethnicity have a lower prevalence of AGA.<sup>3</sup> The most common (pathognomonic) presentation in women is female pattern hair loss (FPHL), which is diffuse reduction in hair density affecting the mid and frontal regions of the scalp with preservation of the frontal hairline. Male-pattern balding is undoubtedly an androgen-dependent genetically determined trait. It appears that dihydrotestosterone (DHT) diminishes the anagen phase of the hair follicle by binding to androgen receptors, resulting in terminal hair transforming into thinner and shorter vellus hair over time. According to scientific studies, the tendency for hereditary hair loss is mainly transmitted through the mother via the androgen receptor (AR) on the X chromosome. As men can only inherit the X chromosome from their mother, the "risk" of suffering alopecia is more closely related to the mother or maternal grandfather than the father. However, other hereditary factors may also cause baldness and can be tested for, using saliva.

The lab workup for hair loss initially includes CBC, CMP, free T3, TPO antibodies, ferritin, B-12, total testosterone, FSH, and estradiol at minimum. I have started to add a HbA1c and fasting insulin level in some patients as insulin resistance, obesity, diabetes, and metabolic syndrome can cause hair loss in men and women. Insulin resistance and hyperinsulinemia participate in the development of AGA by producing local androgens from cholesterol and enhancing local conversion of testosterone to DHT. Obesity and insulin resistance also increases 5-alpha-reductase, which in turn increases more DHT. Age, alcohol, obesity, medications, and sedentary lifestyle increase aromatase activity, lowering T and raising E. Increased DHT, lowered testosterone, and elevated estradiol levels contribute to hair loss in genetically predisposed men and women. Hypothyroidism is associated with lower levels of sex hormone binding globulin, which may result in higher levels of free androgens that can exacerbate AGA.<sup>4</sup>

In general, treatment options should include overall health improvements such as adding a probiotic, DIM (natural DHT blocker), ADK (D3 helps hair growth), and correcting any thyroid deficiency. Specifically for men suffering from androgenic alopecia, prescription treatments were ranked in efficacy in a network meta-analysis of 23 trials. The results of this analysis indicated that 0.5mg/day of oral dutasteride had the highest probability of being the most efficacious, followed by these agents in decreasing order of efficacy: 5mg/day of oral finasteride, 5mg/day of oral minoxidil, 1mg/day of oral finasteride, 5% topical minoxidil, 2 % topical minoxidil, and 0.25mg/day of oral minoxidil<sup>5</sup> (see Figure 1).

The efficacy of topical minoxidil (MX) alone on female pattern hair loss is limited. A study done on 120 non-menopausal women followed for 6 months showed that hair density increased the most in the 5 % minoxidil plus 12 sessions of micro-needling compared to the 5% MX plus oral spironolactone group (80-100mg daily) or the 5% MX group alone. MX is a regulator of potassium ion channels with vasodilatory effects that increase the duration of the anagen phase and induces angiogenesis surrounding hair follicles, thereby contributing to the conversion of miniaturized hairs to terminal hairs. The most common adverse events of MX include scalp pruritus and irritation. Spironolactone competitively inhibits androgen binding to intracellular receptors and is especially helpful among patients with signs of hyperandrogenism. The most common adverse effects in the Spironolactone group were menstrual disorders, hyperkalemia, and edema of the limbs though rare. In another study following 166 women for 18 months with FPHL, 74% of the patients receiving spironolactone (110 mg average daily dose) reported stabilization or improvement in their hair. Epidermal thickness and follicle diameter were increased in the micro-needling group. It has been hypothesized that the trauma generated by the needle penetration induces the release of platelet derived growth factor, epidermal growth factor, and activation of the hair matrix thru the Wnt/B-catenin pathway. Micro-punctures caused by the micro-needling may also facilitate the penetration of the topical medications<sup>6</sup> (see figure 1).

**Figure 1. Treatment Options for Hair Loss**

Condition	Onset	1 <sup>st</sup> Line Treatment	2 <sup>nd</sup> Line Treatment
Telogen effluvium (TE)	Fast	None/Time	None/Time
Androgen Alopecia (AGA)	Slow		
Male		0.5mg/day of oral dutasteride	5mg/day of oral finasteride
Female		5% Minoxidil + 12 micro-needling sessions	5% Minoxidil + Spironolactone 80-100mg QD

In summary, hair loss is a common complaint of patients undergoing pellet therapy, thus it is important that providers understand how to evaluate and treat it. Although, testosterone therapy is often blamed for a patient's hair loss or thinning, it is lack of hormone optimization that is more often associated with this untoward cosmetic outcome. This summary provides an overview of the two most common causes of hair loss and provides a comprehensive approach to the most effective treatments for your patients.

<sup>1</sup> Glaser RL, Dimitrakakis C, Messenger AG. Improvement in scalp hair growth in androgen-deficient women treated with testosterone: a questionnaire study. *Br J Dermatol*. 2012 Feb; 166(2): 274-278.

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<sup>2</sup> Glaser R, Dimitrakakis C. Testosterone therapy in Women: Myths and misconceptions. *Maturitas*. 2013; 74: 230-234.

<sup>3</sup> Qiu Y, Zhou X, Li Y. Systemic Review and Meta-analysis of the Association Between Metabolic Syndrome and Androgenic Alopecia. *Advances in dermatology and venerology*. 2022 Dec;102:1-7.

<sup>4</sup> Famenini S, Slaught C, Duan L, Goh C. Demographics of women with female pattern hair loss and the effectiveness of Spironolactone therapy. *J AM Acad Dermatol*. October; 73(4): 704-706.

<sup>5</sup> Gupta AK, Venkataraman M, Talukder M, Bamimore MA. Relative Efficacy of Minoxidil and the 5- $\alpha$  Reductase Inhibitors in Androgenetic Alopecia Treatment of Male Patients: A Network Meta-analysis. *JAMA Dermatol*. 2022 Mar 1;158(3):266-274.

<sup>6</sup> Liang X, Chang Y, Wu H, Liu Y, Zhao J, Wang L, Zhuo F. Efficacy and Safety of 5% Minoxidil Alone, Minoxidil Plus Oral Spironolactone, and Minoxidil Plus Microneedling on Female Pattern Hair Loss: A Prospective, Single-Center, Parallel-Group, Evaluator Blinded, Randomized Trial. *Front Med (Lausanne)*. 2022 Jul 11;9:905140.