

## Light Therapy — A Promising Option for Menopausal Hair Loss

By Karen Clark, MD

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A woman's hair is important to her identity and self-esteem. Even temporary conditions of hair loss, thinning, or texture change can become significant sources of anxiety and even anguish, with all of their potential for negative downstream effects on body, mind, and relationships. In this light, a physician's duty to understand maladies and render aid demands a working knowledge of the causes of and treatments for unwanted hair changes among women.

Few men celebrate the onset of male pattern baldness, but for most it's a grudgingly accepted and quite common mark of maturity. But women have different expectations for themselves, and society—fairly or not—expects different things from them. Although about two-thirds of women may experience some level of alopecia or thinning related to menopause,<sup>1</sup> women of any age are not commonly seen without their hair; when they are, it's usually the result of a bold style choice, not hair loss. For those whose hair loss is not a style choice, the experience can be devastating. Instead of merely signifying the end of youth, for some women, the loss of hair quality or hair itself can feel like the death of femininity, or even identity.

### Perimenopause, Hormones, and Hair

While some hair and scalp conditions can indicate a serious health concern, the majority of mature women's hair problems result from female pattern hair loss (FPHL) caused by hormonal fluctuations due to menopause and age. This places androgenetic alopecia squarely in the geriatrician's bailiwick.

Perimenopause, the time of transition between the reproductive years and the postreproductive years, begins for most women in their 40s, but earlier for some. Estrogen levels, along with periods, typically fluctuate during this time. The first symptoms of menopause may also manifest during this time, including



insomnia, vaginal dryness, uterine bleeding, hot flashes, and hair loss. There's wide variability in the severity and duration of these symptoms, but perimenopause can last between four and eight years, according to the North American Menopause Society. Once a full year has elapsed since her last period, a woman has left the perimenopausal phase and passed into menopause proper.

As estrogen and progesterone production wane in the body, so do their positive effects on hair, leading to slower growth and thinning. Unlike men of a similar age, women's hair tends to thin in shaft size and density more than actual balding, though bare patches do happen for some. Hair can be affected anywhere on a woman's head and may even shed in distressing clumps when washed or brushed. As estrogen and progesterone levels diminish, this leaves the hair follicle subject to the hormonal influence of androgens alone, which causes follicles on the head to shrink and eventually dislodge. And, as if she didn't have enough to worry about already, your perimenopausal patient may respond to increasing androgenic hormones by developing more facial hair. This is generally just a few sprouts or light peach fuzz, but don't expect her to be happy about it.<sup>2</sup>

### **Other Causes**

Hair loss for women at midlife is nearly always hormone related, but less common causes must also be considered, including disease, stress, certain medications, and improper nutrition. A thorough blood count and thyroid tests can help rule in or out such factors.<sup>2</sup>

Stress-related hair loss, or telogen effluvium, can occur in response to extreme trauma, whether emotional or physical, usually manifesting one to three months after the experience. Triggers can include stress, major surgery, and childbirth; the condition is more common in women due to its association with plasma iron levels and medication changes.

Another nonhormonal cause of hair loss is traction alopecia, also more prevalent in women. It results from trauma to the hair follicles caused by braids, hair extensions, and tightly pulled hair styles that stress the hair. Alopecia areata—an inheritable autoimmune disease affecting about 6 million Americans—can also cause hair loss.<sup>3</sup>

### **Menopause, Hair Loss, and Emotional Health**

Before making a diagnosis or suggesting tests or treatment, the canny physician knows to carefully question and listen to each patient to best determine the scope of her physical and psychological symptoms. In the case of perimenopausal hair loss, this interactive communication is paramount. It's something a time-pressed clinician might be tempted to dismiss, as it is, after all, no threat to health and "merely" a mark of maturity. This temptation should be avoided, regardless of the physician's gender, because a woman's hair is important.

Beyond signifying youth, fertility, beauty, and feminine identity, a woman's hair is a platform for self-expression that is, for the most part, totally under her control. It can be grown long, cut short, colored, curled, and flipped this way and that, all at a woman's whim or after her deep consideration. When this familiar freedom is curtailed, a certain voice is silenced, and others notice. The fact that hair loss occurs for a normal and natural reason does nothing to diminish the angst associated with this change in a woman's appearance, especially given today's youth-based culture.

Compounded by genetic inclinations, personal history, and the many other stressors in life, hair loss can be a factor in the onset of depression for at-risk women. As such, it must be taken seriously. Women distraught over their condition can wind up avoiding social engagements, retreating from relationships, and using unhealthy coping mechanisms such as overeating or self-medicating.

For all these reasons, hormonal hair loss in women nearing or past menopause should be acknowledged, addressed, and treated. The good news for patients and their geriatricians is that help is available. A number of techniques, devices, lifestyle changes, counseling, and medicines have proven effective at mitigating the problem, and sometimes eliminating symptoms entirely.

### **Medical Approaches**

In the United States, minoxidil, the only over-the-counter medication for patterned hair loss approved for use by men and women, is sold as a liquid or foam in 2% or 5% strengths. It's believed that by prolonging the anagen phase, minoxidil enlarges the hair shaft, possibly by calcium channel-opening activity. The patented foam is expensive though, and can be tricky—not to mention sticky—for patients to apply. It takes some work to use it. Patients should be told that stopping the medication can cause hair loss to resume and that they will experience a paradoxical worsening of hair loss for a month as follicles are stimulated to transition from telogen to the anagen phase.

Its efficacy as treatment for FPHL is supported by a systematic review and meta-analysis of randomized trials that found that women treated with topical minoxidil (1%, 2%, or 5% formulations) were more likely to report clinically significant hair regrowth than were women in placebo groups.<sup>4</sup> The mean increase in hair counts in treated areas was higher in treated women vs those in placebo groups. A subsequent randomized trial of minoxidil 5% foam and placebo also supports the efficacy of minoxidil.<sup>5</sup>

All three formulations of minoxidil on the market (2% solution, 5% solution, and 5% foam) are effective. Doctors tend to use the higher concentration, but none of the four trials that compared minoxidil 2% with minoxidil 5% found a significant difference in efficacy between the two. Minoxidil 5% foam is associated with fewer side effects such as scalp pruritus, dandruff, and sideburn hypertrichosis compared with twice-daily application of 2% solution.<sup>6</sup> Treatment with minoxidil takes at least four months to show visible

effects. Patients should use the product for at least 12 months to determine inefficacy.<sup>7</sup> No matter what remedy or combination of remedies patients ultimately use, they will need to use them forever.

Second-line agents used for FPHL are those that inhibit androgen production or action, such as spironolactone, finasteride, cyproterone acetate, and flutamide. They are used more often for women with FPHL related to hyperandrogenism and those who respond poorly to monotherapy with minoxidil. Of these, finasteride is used most often.

Finasteride is a 5-alpha-reductase inhibitor type 2 that blocks the conversion of testosterone to dihydrotestosterone, thereby reducing the effects of dihydrotestosterone on hair follicles. In studies of finasteride, about 90% of men had halted loss and 65% had partial regrowth over six months.<sup>8</sup> Few investigations have evaluated the efficacy and safety of finasteride in women with FPHL, and existing studies show mixed results.

One 12-month, placebo-controlled, randomized trial of 137 postmenopausal women with FPHL and normal serum androgen levels found that treatment with finasteride 1 mg per day did not seem to be of benefit.<sup>9</sup> Uncontrolled studies utilizing higher doses of finasteride (2.5 or 5 mg per day) have suggested that finasteride may be of benefit in some women without hyperandrogenism.

Conflicting data also exist regarding the value of finasteride in hyperandrogenemic women with FPHL. Experts note additional studies are necessary to clarify the population of women with FPHL who may benefit from treatment. The agent is usually well tolerated by women.<sup>10-12</sup>

### **Light Therapy**

Patients with patterned hair loss have experienced some success with in-office energy-based devices such as fractional lasers and at-home low-level laser therapy (LLLT) devices. There are now almost 50 devices according to FDA's 510(k) premarket notification list that are classified as laser—comb, cap, or hair products intended for growth of scalp hair.<sup>13</sup>

Whether it's called LLLT, low-level light therapy, or photobiomodulation, the premise is that nonthermal, low-intensity light of specific wavelengths triggers biochemical changes in the scalp. As a result of light's absorption into cellular photoreceptors, downstream alterations set off signaling cascades.<sup>14</sup> Distinct wavelengths of light have been known to have various biological effects on humans. Low-powered lasers and some LEDs with a wavelength in the red to near-infrared region of the spectrum (660 nm–905 nm) have been shown clinically to be effective for pain, inflammation, and tissue repair.

LLLT was discovered by a happy accident when in the 1960s a Hungarian scientist found that low-level laser induced hair growth and improved wound healing.<sup>15</sup> It's theorized that when LLLT is applied to the scalp, it acts to increase the number of hair follicles as well as hair's tensile strength. This is likely

achieved through improved microvascular circulation, reduced inflammation, and increased cell energy in the form of adenosine triphosphate.<sup>16</sup>

Research indicates that LLLT can stimulate anagen reentry in telogen hair follicles, prolong the duration of the anagen phase, increase the rates of proliferation in active anagen hair follicles, and prevent premature catagen development.<sup>17</sup> These effects may be induced via increased blood flow, cytokine and growth factor induction, and direct keratinocyte stem cell or dermal papilla cell stimulation.<sup>18,19</sup>

Original LLLT devices contained red light-emitting laser diodes (eg 655 nm) and were deployed in dermatology practices via various methods such as overhead panels, bonnets, and caps. In the late 1990s, LLLT was made available for in-home use with the earliest hair growth device—a comb—FDA cleared in 2007. It was reported that patients using the comb had a greater increase in mean terminal hair density compared with those using a sham device.<sup>20</sup> Without uniform light delivery, however, and due to the fact that the user has to adjust the treatment area, patient compliance is spotty.

Today, light-based hair regrowth devices come in a variety of helmet shapes and laser types as well as technical features, not to mention price points. Most important, they have some level of clinical evidence; the literature shows that LLLT devices have an excellent safety profile with accumulating evidence backing their efficacy.

Clearly, however, long-term, high-quality studies comparing devices in diverse populations are lacking.<sup>21</sup> High-quality randomized controlled trials and/or head-to-head trials between drugs and devices are required to clarify these findings and develop new algorithms and protocols for treatment.<sup>22</sup> At the very least, a growing body of peer-reviewed evidence can be consulted when discussing treatment options. It's very likely that a combination of approaches, started as early as possible, will be necessary to give patients the highest chance of success.

### **LLLT Clinical Research Highlights**

Investigators evaluated the use of 655-nm red light and 780-nm infrared light applied once daily for 10 minutes on 24 men with androgenetic alopecia. Global photography and phototrichogram were also evaluated. Following 14 weeks of treatment, there was increase in hair density on both the vertex (145.1/cm<sup>2</sup> vs 137.3/cm<sup>2</sup> pretreatment, <0.005) and occiput (163.3/cm<sup>2</sup> vs 153.3/cm<sup>2</sup>, <0.005) as well as anagen/telogen ratio (vertex: 84.7 vs 79.7 pretreatment and occiput: 91.9 vs 89.6 pretreatment). Further, 83% of the patients said they were satisfied with the treatment.<sup>23</sup>

One product, a 655-nm at-home-use comb was studied on androgenetic alopecia patients who used it for six months, five to 10 minutes, every other day. Hair regrowth and increased hair tensile strength was measured using a proprietary instrument and removal of three typical terminal hairs from a 1-cm<sup>2</sup> area. Hair count was performed within a 1-cm<sup>2</sup> space created within a mold that was prepared around the area

of greatest alopecia. There was greater improvement in tensile strength in the vertex area for men and temporal area for women; however, all patients had improvement. Both men and women had substantial improvement in hair count (for temporal area: 55% in women and 74% in men; in vertex area: 65% in women and 120% in men).<sup>24</sup>

The same device was also tested in a double-blind, sham device—controlled, multicenter, 26-week trial randomized study of 110 men with androgenetic alopecia. Patients used the device three times per week for 15 minutes for a total of 26 weeks. The investigators reported significantly greater increase in mean terminal hair density in patients using the device vs sham device group. Patients' subjective assessment at 26 weeks revealed significant improvements in overall hair regrowth, slowing of hair loss, thicker-feeling hair, better scalp health, and hair shine.<sup>20</sup>

### **Medical Grade LEDs**

Recently, investigators have been considering LED light sources in terms of their ability to deliver discrete bands of light, tunable across the entire visible light spectrum. Slightly broader bands of LED light can enhance cellular metabolism by increasing the absorbance spectrum. LEDs have been associated with increased adenosine triphosphate, upregulation of nitric oxide production, the induction of transcription factors, alteration of collagen synthesis, angiogenesis stimulation, and increased blood flow. Some obvious advantages of LEDs include their safety, small size, and light weight, facilitating easy at-home use. This approach offers the ability to irradiate a large area of tissue with minimal power and lower energy cost per milliwatt.<sup>25</sup>

Not all LEDs are equal, and notably, high-quality LEDs with useful lives up to 50,000 hours can deliver 125-degree viewing angles that allow for large overlapping cones of light and deep skin penetration. Newer hair growth devices use LEDs to boost coverage and make them easier to use—and they claim better results than laser-alone devices.

This advancing technology is of interest, as it appears to represent an efficient use of energy and the technology stands to benefit men and women, regardless of their hair loss pathology. A double-blind randomized controlled trial of men with androgenetic alopecia using a helmet containing 21 5-mW lasers (655 ± 5 nm), and 30 LEDs every other day (67.3 J/cm<sup>2</sup>, 25 minutes treatment) for 16 weeks reported a 35% increase in hair growth.<sup>26</sup>

Another 24-week, randomized, double-blind, sham device—controlled multicenter trial among men and women investigated the efficacy of a helmet-type LLLT device combining 650 nm laser with 630 and 660 nm LEDs (total energy density—92.15 mW/cm<sup>2</sup>, 47.9 J/cm<sup>2</sup> for 18 minutes). Even though mean hair thickness (12.6 ± 9.4 vs 3.9 ± 7.3 in control group, =0.01) and hair density (17.2 ± 12.1 vs -2.1 ± 18.3 in control group, =0.003) increased significantly in the treatment group, there was no prominent difference in

global appearance between the two groups.<sup>27</sup> Findings from a different study were in accordance with these results where LLLT increased hair count and shaft diameter; however, blinded global images did not support these observations.<sup>28</sup>

### **Dual-Wavelength LED Light Therapy**

Many variables are in play when it comes to evaluating the best approach to harnessing penetrating light. Skin type and proper irradiance levels to maximize hair growth are two important factors. Device manufacturers continue to evaluate potential synergies that can be exploited through color mixing and seek optimal wavelengths of light to use in combination with other therapies. To establish appropriate protocols, there must first be adequate and well-controlled clinical trials.

Of note, one recently FDA-cleared, at-home light therapy approach represents the first all-LED, dual-wavelength light therapy device. The system uses a novel color combination of dark orange (620 nm) and red light (660 nm) to stimulate more nitric oxide production in the scalp. The user must activate the cap through a validated mobile app, once daily for 10 minutes, thereby enhancing compliance. Preliminary results from a controlled, double-blind, parallel study (not yet released at press time) found treated individuals, who were at least 80% compliant, had an average of more than 21 more hairs per cm<sup>2</sup> vs users of a placebo device (16 weeks post baseline).<sup>29</sup>

### **Conclusion**

Because therapies such as LLLT and dual-wavelength LED light therapy are natural and chemical-free, physicians can feel comfortable suggesting them to patients. Setting appropriate expectations is crucial, as patients should be made to understand that arresting hair loss is a win. When started as early as possible and used in combination with complementary therapies, results can be improved.

It's important to be upfront with patients, letting them know that a lot remains unknown about hair loss, and patients should be cautioned against using expensive and unproven products that they may find online. When it comes to compounded medications or shampoos, for example, it is important to use an established and reliable compounding pharmacy with a known pharmacist. These items are best pursued through a physician's office rather than purchased online without guidance.

It's wise to recommend psychotherapy to patients in need of additional support. Women with hair loss can be significantly distressed and truly struggling with its consequences in terms of their overall emotional well-being. Older patients are more receptive to counseling than they were just 10 years ago.

Feeling bad about oneself doesn't have to be a part of aging. Although women's transition into menopause and beyond can be a challenge on many levels, hair loss is one that doctors are getting better at managing.

Karen Clark, MD, is in practice at Chapel Hill Gynecology in North Carolina. She is a fellow of the American Congress of Obstetricians and Gynecologists, and is board-certified by the American Board of Obstetrics and Gynecology. She is a North American Menopause Society Certified Menopause Practitioner, one of only five in the Triangle area of North Carolina. Clark reports the following relevant disclosure: She is a member of the Revian professional affiliate program. She may be reached at [kclarkmdnc16@outlook.com](mailto:kclarkmdnc16@outlook.com).

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