



Review Article

Breaking bald: Unraveling the mysteries of hair loss and modern treatments

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ABSTRACT

Alopecia, commonly known as hair loss, presents a multifaceted challenge affecting millions worldwide. Recent advances in hair loss treatment and prevention offer hope to individuals grappling with this condition. This comprehensive overview delves into the causes of hair loss, encompassing genetics, hormonal imbalances, nutritional deficiencies, stress, and underlying medical conditions. The COVID-19 pandemic has also revealed unique patterns of hair loss i.e., telogen effluvium, prompting ongoing research and therapeutic exploration.

Current treatment options, including medications like minoxidil and finasteride, surgical interventions such as hair transplants, and non-surgical techniques like laser therapy and platelet-rich plasma therapy, are examined in detail. While effective, these treatments come with limitations and potential side effects, necessitating careful consideration.

Looking ahead, researchers are exploring innovative approaches to combat hair loss, from targeted medications to gene therapies and stem cell-based interventions. Advanced delivery methods using nanotechnology and biomaterials hold promise for more effective and safer solutions in the future.

Recognizing the psychological impact of hair loss, this review emphasizes the importance of addressing the emotional aspects of this condition to enhance overall patient well-being. The future holds the potential for more holistic and successful treatments in the ongoing battle against hair loss, offering optimism to those seeking solutions.

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1. Introduction

Alopecia, often known as hair loss, describes the gradual thinning of hair on the scalp, which can be temporary or permanent. The primary type, "androgenetic alopecia," i.e., permanent hair loss from the scalp in certain patterns, causing baldness due to hormones (specifically androgen) and genetic factors. This interaction between hormones and genetics drives this specific hair loss type. Variations like

alopecia areata, identified by regrowth of bald patches; telogen effluvium, leading to abrupt hair shedding post events like childbirth or illness; and traction alopecia, originating from hair weakening due to tight hairstyles such as braids or ponytails, contribute to the diverse range of hair loss conditions.¹

While hair loss (alopecia) might not be categorized as a severe or life-threatening condition, the prospect of losing hair can result in considerable emotional distress, proving to be a distressing experience for individuals facing premature or significant hair thinning. Many people are

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open to exploring numerous options in their efforts to regain their hair or, at the very least, recapture a portion of their previously abundant locks.¹

Recent progress in the realm of hair fall treatment and prevention has instilled hope in individuals struggling with hair loss.² These advancements encompass a variety of interventions such as medication, hair transplant surgery, and hair restoration methods. Hair loss can induce notable psychological distress, with pattern hair loss affecting roughly 50% of males and 25% of females by the age of 50.³

One intervention that has displayed promising outcomes involves the use of medication, specifically minoxidil.⁴ Research has highlighted minoxidil's effectiveness in reducing hair shedding among individuals dealing with chronic telogen effluvium.⁵ Moreover, the topical application of minoxidil has gained approval from the US FDA for both men and women, rendering it a viable treatment avenue for androgenic hair loss.^{2,6,7}

In addition to minoxidil, another medication sanctioned by the US FDA for addressing androgenic hair loss in men is finasteride.⁷

The emotional and social ramifications of hair loss are frequently underestimated, as the medical dimensions of the underlying conditions are generally perceived as less severe. Focusing on the psychological aspects of androgenic alopecia can enhance overall patient well-being and contribute to more favorable treatment results.⁸

2. Materials and Methods

The methodology for developing this comprehensive document encompassed several essential steps. Firstly, an extensive literature review was performed, leveraging academic databases, research papers, and reputable online sources. The objective was to gather a diverse array of information pertaining to hair loss, encompassing its etiology, treatment options, psychological implications, lifestyle factors, and emerging research trends.

Subsequently, the data procured from these varied sources were meticulously collated and structured into cohesive sections, thereby creating a well-organized narrative on the subject matter. The document was thoughtfully segmented into paragraphs, each addressing distinct facets of hair loss, including its causes, potential treatments, and future prospects.

Moreover, a critical analysis was carried out to assess the accuracy and reliability of the information presented. Rigorous cross-referencing of data from multiple sources was undertaken to ensure coherence and eliminate potential bias.

Lastly, the document was diligently referenced to uphold transparency and credibility. Proper citations were thoughtfully incorporated to duly acknowledge the sources of information employed in each section, thereby adhering

to rigorous academic standards.

3. Discussion

3.1. Causes of hair fall (As shown in Figure 1)

3.1.1. Genetic causes

The genetic causes of hair loss are currently being investigated using genome-wide association and linkage analyses. It has been established that particular polymorphic hair follicle proteins are involved in the disorder by linking them to characteristics associated with hair loss. It is possible to get insights into the mechanisms underlying changes in hair texture by understanding how these protein changes result in phenotypic variances. Strong correlations exist between hair form and many polymorphisms in proteins expressed in the inner root sheath (IRS) of hair follicles. Hair loss and abnormal hair growth are also linked to genes expressed in the IRS, some of them including KRT74, lipase H, and the LPAR6/P2RY5 receptor for lysophosphatidic acid.

These genetic discoveries offer important information for comprehending the genetics of hair loss and associated hair features, advancing the study of hair loss and posing the possibility of new therapeutic strategies.⁹

3.1.2. Endocrine imbalances

Before birth, a molecular genetic mechanism that results in the development of hair follicles is regulated. Thyroid hormones, glucocorticoids, insulin-like growth factor-I, and prolactin are all hormones that influence hair development, albeit androgens are the most significant ones. Many hormones and their receptors play vital roles in the healthy advancement of this process. Additionally, retinoid X receptors and vitamin D receptors are useful for postpartum hair development.¹⁰

3.1.3. Nutrients

The health of the hair follicles depends on several micronutrients, including the vitamins A, and B complex (biotin, B12, and folate), C, D, iron, selenium, and zinc. Vitamin A levels should be balanced because too much can stunt hair growth. Lack of biotin affects cell signaling and can cause hair loss. Folate and B12 are essential for the synthesis of nucleic acids, which affects the growth of hair follicles. For those who suffer from hair loss brought on by iron deficiency, vitamin C improves iron absorption. Vitamin D controls keratinocyte growth, which may have an impact on the hair cycle. Iron is necessary for DNA synthesis in hair follicles because they divide quickly. Unbalances in selenium and zinc can also result in hair problems. For healthy hair, a balanced diet and professional guidance are crucial. Understanding the function of micronutrients in preventing and treating hair loss will require more study.¹⁰

3.1.4. Stress

Stress has numerous effects on hair, including hair loss. Telogen effluvium, which results in early hair shedding, can be brought on by it. In addition, it exacerbates pre-existing hair loss diseases like androgenetic alopecia (AGA) or alopecia areata, each of which has a unique underlying etiology. Additionally, stress brought on by hair loss itself can exacerbate the problem by creating a vicious cycle. According to studies conducted on mice, stress can impair hair growth and result in inflammation of the hair follicles, which involves chemicals like substance P and corticotropin-releasing hormone. If it applies to people, stress may cause considerable hair loss.¹¹

3.1.5. Lifestyle

Stress, lifestyle choices, and environmental factors including nutrition, sleep, smoking, and UV exposure all have an impact on how our cells function and how our genes are expressed, which determines our vulnerability to hair loss. Genetic history also plays a part. These causes can cause hair loss in varied degrees in even identical twins.¹²

3.1.6. Underlying medical condition

Many medical disorders can cause hair loss. The patient’s medical history is essential for making a diagnosis, especially in the six months before the onset of hair loss. Telogen effluvium is a transitory hair loss condition that can be brought on by conditions like endocrine problems, autoimmune diseases, high fevers, serious illnesses, surgery, pregnancy, crash dieting, and rapid weight loss. It’s crucial to perform thyroid screenings. Systemic Lupus Erythematosus (SLE), which manifests as photosensitivity and joint discomfort, can result in both scarring and non-scarring hair loss. Children’s hair problems may be related to other skin and neurological conditions. Additionally, taking height and weight into account can be important because disorders like polycystic ovary syndrome (PCOS), which is more prevalent in overweight people, may be connected to hair loss in women.¹³

3.2. COVID-19-induced hair loss

Observational studies in COVID-19 patients revealed increased pattern hair loss (HL) and telogen effluvium (TE). Suspected culprits include oxidative stress, hypoxia, psychological stress, and systemic inflammation. Stress hormones and pro-inflammatory cytokines disrupt proteoglycan metabolism, possibly mediating the link between COVID-19 and HL. To promote scalp angiogenesis, PRP and regeneration techniques like AD-MSCs, HFSCs, and LLLT are used. Encouraging angiogenesis and preventing cell ischemia are vital strategies for COVID-19-induced hair loss. PRP’s ability to release growth factors supporting dermal papilla cell survival via Bcl-2 activation and Akt signaling offers a



Figure 1: Causes of hairfall



Figure 2: Guide to hair fall solution

potential regenerative approach to enhance hair growth.^{14,15}

Another study found that hair loss may be reversible in COVID-19 patients but some patients took longer to recover. The severity of COVID-19 didn’t seem to affect the hair loss. Interestingly, more women experienced hair loss than men. The reason for hair loss in COVID-19 is not clear, but it might involve a pro-inflammatory substance called interleukin-6 and female hormones.¹⁶ Both the studies have their limitations like a smaller number of participants and no specific tests for hair loss. More research is needed to understand the cause and efficacy of PRP and regenerative therapies in COVID-19-induced hair loss.

3.3. The Psychological impact of hair loss

The emotional consequences of experiencing hair loss can be substantial, impacting both the mental and social aspects of an individual’s life. The effects of hair loss include lowered self-confidence, feelings of sadness, withdrawal

from social interactions, heightened anxiety, and an overall decline in mental well-being.¹⁷ This underscores the necessity for effective treatments and preventative measures for hair loss, not only to address the physical manifestation but also to support the emotional health of those affected by this issue.¹⁸ The use of medical interventions like minoxidil has displayed promising outcomes in lessening hair shedding and stimulating hair regrowth in individuals dealing with persistent telogen effluvium.¹⁹

3.4. Exploring minoxidil-A game-changer in hair fall treatment

Examining minoxidil as a transformative element in addressing hair loss underscores its crucial function in diminishing hair shedding and encouraging hair regrowth among those dealing with persistent telogen effluvium.²⁰ Research shows minoxidil can slow hair loss and promote regrowth in around 40% of men and 20% of women with genetic pattern baldness. However, its effects are temporary, and hair loss typically resumes when usage is stopped.²¹ Moreover, minoxidil's endorsement by the US FDA for both men and women underscores its effectiveness and safety in managing androgenic hair loss across a diverse spectrum of individuals. The effectiveness of finasteride in countering male pattern baldness is also worth noting.⁶

Finasteride stands as another medication greenlit by the US FDA for managing male pattern baldness. Studies have indicated that finasteride proficiently obstructs the enzyme responsible for converting testosterone into dihydrotestosterone, a factor known for advancing male pattern baldness.^{22,23}

3.5. Effectiveness of finasteride in treating male pattern baldness

Research findings have highlighted the strong efficacy of finasteride in addressing male pattern baldness. Various studies have provided evidence of finasteride's ability to impede the enzyme responsible for transforming testosterone into dihydrotestosterone, a factor linked to the advancement of male pattern baldness.²⁴ Furthermore, clinical trials have underscored finasteride's capacity to stimulate hair regrowth and diminish hair loss in individuals with male pattern baldness.² Two large meta-analyses found that finasteride consistently showed significant improvements in hair count, scalp coverage, and patient/investigator assessments versus placebo.²⁵ Nevertheless, it's essential to acknowledge that both minoxidil and finasteride come with limitations and potential side effects that need to be taken into account before commencing treatment.²⁶

The constraints and possible adverse effects linked to the utilization of minoxidil and finasteride in hair loss treatment should be carefully considered.²⁷ While

these treatments effectively encourage hair growth, they may lead to potential side effects like hypertrichosis and gynecomastia with low-dose minoxidil, and sexual-related issues with finasteride, including irregular ejaculation and reduced sperm volume.²⁷

3.6. Advancements in surgical interventions- hair transplant techniques

Beyond medication-centered treatments, progressions in surgical approaches have also had a notable impact on the domain of hair loss management. Innovations in surgical techniques, such as hair transplant procedures, have gained increasing popularity among those seeking a lasting resolution to hair loss.²⁸ These methods encompass the extraction of healthy hair follicles from donor regions, usually situated at the back of the head, followed by their relocation to areas afflicted by hair loss. Hair transplant procedures have demonstrated encouraging outcomes in reinstating hair growth and enhancing the overall aesthetic of individuals dealing with hair loss.²⁹ Furthermore, enhancements in hair transplant methodologies have resulted in outcomes that appear more natural and have reduced recovery periods for patients.^{28,30}

3.7. Non-surgical hair restoration techniques

In recent times, there have been notable strides in non-surgical techniques for restoring hair. These non-surgical methods have witnessed substantial advancements, presenting alternate avenues for individuals who may not be ideal candidates for medication or surgery, or who opt for less intrusive means of hair rejuvenation.³¹ These approaches encompass laser therapy, platelet-rich plasma therapy, peptide-hormone therapy, and micro-needling. Laser therapy employs low-level laser devices to invigorate hair follicles and stimulate hair growth. Laser therapy operates by activating hair follicles through photobiomodulation, where light energy is absorbed by cytochrome C oxidase. This triggers angiogenesis and speeds up the repair process. Platelet-rich plasma therapy involves infusing concentrated platelets from the patient's blood into the scalp, aiding in the stimulation of hair growth. Peptide hormones like Parathyroid Hormone-Related Peptide (PTHrP), IGF-1, and Prolactin influence hair follicle development and growth. PTHrP impacts morphogenesis through receptor activation. IGF-1 promotes hair follicle growth, with both insulin and IGF-1 affecting hair growth in vitro. Prolactin affects seasonal coat changes in animals and hair follicle cycles, potentially causing shedding. Prolactin receptor deletion in mice accelerates the initial hair cycle. Prolactin excess leads to hirsutism, while IGF-1 and insulin likely play roles in hair growth physiology.³²

Micro-needling constitutes another non-surgical technique, utilizing tiny needles to establish microchannels in the scalp, enhancing the absorption of topical hair growth products and prompting hair follicle activity.^{33,34}

All in all, progressions in hair fall treatment and prevention have expanded to provide a spectrum of choices for those seeking to tackle hair loss. These advancements encompass both surgical and non-surgical options, offering individuals a broader array of possibilities for managing hair loss concerns.³⁵ These enhancements have also led to improved outcomes, marked by natural-looking results, shorter recovery periods, and heightened patient satisfaction. The surging popularity of non-surgical hair restoration techniques like laser therapy, platelet-rich plasma therapy, and micro-needling presents alternative routes for individuals who might not be suitable candidates for surgical interventions or who favor non-invasive strategies for hair revitalization.^{34,36}

3.8. *Understanding androgenic hair loss and available treatment options*

Androgenic hair loss, commonly referred to as male pattern baldness, is a prevalent type of hair loss that impacts both men and women. This condition is characterized by the gradual reduction in hair thickness, length, and coloration. The underlying cause of androgenic hair loss is the shrinking of hair follicles due to their sensitivity to androgens. This specific type of hair loss is usually addressed using FDA-approved treatments like minoxidil and oral finasteride, which have demonstrated efficacy for addressing grades 1 and 2 of hair loss.³⁷ However, for individuals experiencing more advanced stages of hair loss (grade 3 and beyond), additional treatment possibilities might be required. Platelet-rich plasma therapy has emerged as a frequently employed approach for promoting hair regrowth in such instances. Additionally, techniques like micro-needling show the potential to enhance hair growth by facilitating the absorption of topical hair growth products and stimulating hair follicles. Furthermore, the utilization of low-level laser light therapy has been noted to encourage hair growth and is often used as a supplementary treatment approach.^{33,36,38,39}

3.9. *FDA approvals in the fight against hair loss*

In the field of hair loss treatments, the US Food and Drug Administration has approved two medications, namely finasteride and minoxidil, to be employed in the fight against hair loss.⁴⁰ These medications have undergone comprehensive testing and assessment to ensure their safety and effectiveness in addressing hair loss. It's important to acknowledge, however, that the impacts of finasteride and minoxidil are constrained and temporary, with their effectiveness being unpredictable.⁴¹ Additionally, these

medications are associated with undesirable side effects that can raise concerns. As a result, there exists a critical requirement for the development of novel and improved therapeutic approaches to prevent hair loss and promote hair growth.⁴⁰ The endorsement of finasteride and minoxidil by the US Food and Drug Administration signifies a noteworthy achievement in the ongoing battle against hair loss.⁴²

3.10. *Novel hair restoration technology*

Research demonstrates that using Tomorrow Labs HIF strengthening factor [HSF] hair restoration to treat AGA-related hair loss is risk-free and productive. Without any issues or negative consequences, it works for both genders. The substance is a water-soluble substitute for well-known hair-loss therapies like minoxidil and caffeine and provides quantifiable outcomes. Our clinical evaluation of [HSF] revealed a considerable reduction in hair loss and an increase in hair growth in people. Additionally, it enhances the condition of the scalp and hair. [HSF] is a novel and promising treatment for AGA with such encouraging results and no adverse skin responses.⁴³ Studies show gene uptake by hair follicles, with optimal results during early anagen onset. Intradermal SHH gene injections induce early anagen onset, potentially modulating the hair cycle. Gene correction methods could address hair abnormalities caused by mutations. Ex vivo delivery, like GFP-expressing adenoviral vectors, holds promise for lasting expression.⁴⁴

Although we can't currently cure hair loss in humans using bio-engineered hair follicles, we can explore possible hair growth treatments using human cell-based models. When evaluating various compounds that can encourage hair development, these models are simple to apply and trustworthy. These models can be used to screen for drugs that prevent the effects of hormones connected to hair loss by incorporating particular cells. We anticipate using human cell models becoming the industry standard for hair research as technology develops. We aim to gain a better understanding of hair regeneration in bald individuals by investigating the molecular properties of hair cells. This shift in focus will help us find more effective treatments and avoid wasting time on treatments that don't work well in mouse models.⁴⁵

3.11. *Pending innovations -future of hair fall treatment and prevention*

Despite the constrained effectiveness and undesired side effects linked to finasteride and minoxidil, researchers and scientists are actively exploring fresh avenues to combat hair loss. Their persistent efforts focus on devising innovative pharmacological treatments that surpass current options in terms of safety and efficacy.⁴⁶ These inventive solutions aim to address the fundamental triggers of hair

loss and promote sustainable hair regrowth. Among these advancements are targeted medications that obstruct specific enzymes or receptors involved in hair loss, gene therapies designed to rejuvenate hair follicle function, and stem cell-based interventions capable of regenerating hair follicles. Additionally, investigations are underway to assess the potential of nanotechnology and biomaterials in delivering therapeutic agents directly to hair follicles, offering more localized and precise treatment alternatives.^{29,47,48}

The emergence of these encouraging breakthroughs instills hope for a future where hair loss can be effectively averted and treated with minimal adverse effects. While the FDA approval of finasteride and minoxidil for hair loss treatment exists, their effectiveness remains limited and unpredictable, coupled with undesirable side effects. This underscores the immediate necessity for improved and modern therapeutic approaches to tackle the challenge of hair loss.⁴⁰

3.12. Lifestyle and prevention strategies

To maintain healthy hair and prevent excessive hair loss, incorporating lifestyle adjustments and preventive measures is essential. The issue of excessive hair loss is not only concerning physical appearance but also impacts emotional well-being.⁴⁹ Individuals can integrate a variety of lifestyle and preventive strategies into their daily routines to mitigate the risk of hair loss.

First and foremost, maintaining a balanced and nutritious diet is pivotal to promoting robust hair growth. A diet rich in vitamins, minerals, and protein can supply the necessary nutrients for strong and vibrant hair. Including lean meats, fruits, legumes, and leafy greens in one's diet can nourish hair follicles and stimulate healthy hair growth. Additionally, maintaining adequate hydration through sufficient water intake plays a role in sustaining hair quality.^{50,51}

Effective hygiene practices contribute significantly to hair loss prevention. Regularly washing the hair with a mild shampoo and conditioner helps keep the scalp clean and free from excess oil and dirt, which can clog hair follicles and contribute to hair loss.⁵²

Choosing a brush or comb with wide teeth or soft bristles can reduce hair breakage and minimize hair fall. Avoiding tight hairstyles like braids and ponytails that place strain on the hair is another measure to prevent hair loss. Furthermore, minimizing the use of hair dryers, curling irons, and straighteners can prevent damage to the hair shaft and, consequently, hair loss.^{53–55}

Maintaining a consistent exercise routine and effectively managing stress levels are crucial factors in preventing hair loss. Exercise improves blood circulation throughout the body, including the scalp, thereby promoting hair growth. Given that stress is a recognized contributor to hair loss, practices like yoga or meditation can aid in stress reduction

and, consequently, hair loss prevention. In conjunction with these lifestyle adjustments and preventive methods, certain home remedies and treatments can be employed. Utilizing natural products in DIY treatments is one such approach. Oils like coconut oil, castor oil, and almond oil can be applied to the scalp to strengthen and nourish hair follicles. Herbal remedies such as neem leaves and amla, traditionally used for centuries in East Asia, offer an alternative avenue for hair loss prevention and promoting hair growth. Various herbal therapies have demonstrated promising outcomes in terms of preventing hair loss and encouraging hair growth.^{56–59}

3.13. Natural products used for hair loss

Numerous studies (mainly randomized, placebo-controlled) have been conducted on plants and plant-derived compounds to confirm their efficacy in treating hair loss. Curcuma aeruginosa (pink and blue ginger), Serenoa repens (palmetto), Cucurbita pepo (pumpkin), Trifolium pratense (red clover), and Panax ginseng (Chinese red ginseng) are the herbs with the strongest scientific support against alopecia. Inhibition of 5 α -reductase is thought to be the main mechanism of action, with improved nutritional support and scalp blood flow also contributing.^{60,61}

A significant contributor to hair loss in humans is the enzyme known as 5-alpha-reductase. This enzyme plays a pivotal role in converting testosterone into dihydrotestosterone (DHT), which subsequently leads to the shrinking of hair follicles. A natural solution to this issue can be found in coffee berries, which contain beneficial compounds such as caffeine and chlorogenic acid. These compounds have been shown to exhibit the ability to hinder the activity of the 5-alpha-reductase enzyme, potentially countering the process of hair follicle miniaturization.^{62,63}

4. Limitations to the Overview

The methodology employed in creating this document possesses inherent limitations. Despite diligent efforts to ensure accuracy and reliability, the reliance on existing literature introduces the potential for bias or data inconsistencies, given the variations in research findings. Moreover, while providing a general overview of available hair loss treatments, the document does not encompass individual variations in treatment outcomes, influenced by genetic and hormonal factors. In addition, while recognizing the psychological impact of hair loss, this document does not delve extensively into the exploration of psychological interventions. Lastly, information pertaining to COVID-19-induced hair loss draws from observational studies, highlighting the need for further research to establish conclusive findings within this specific context.

5. Conclusion

Alopecia, or hair loss, can have a profound impact on individuals' lives, both physically and emotionally. Recent advances in hair loss treatment and prevention have expanded the options available to those affected, encompassing medications like minoxidil and finasteride, surgical interventions like hair transplants, and non-surgical techniques such as laser therapy and platelet-rich plasma therapy. The psychological aspects of hair loss are often underestimated but can significantly affect an individual's self-confidence and mental well-being. Recognizing and addressing these emotional aspects is essential for comprehensive patient care.

The causes of hair loss are diverse, including genetics, hormonal imbalances, nutritional deficiencies, stress, lifestyle factors, and underlying medical conditions. The COVID-19 pandemic has introduced new patterns of hair loss, highlighting the need for continued research and treatment options. While minoxidil and finasteride are effective treatments, they come with limitations and potential side effects, necessitating careful consideration by individuals seeking these treatments.

Looking to the future, researchers are exploring innovative approaches to combat hair loss, including targeted medications, gene therapies, stem cell-based interventions, and advanced delivery methods using nanotechnology and biomaterials. These advancements offer hope for more effective and safer solutions for hair loss in the future.

In summary, hair loss is a common and challenging condition that affects many individuals. Recent advancements provide optimism for those seeking solutions. Recognizing the multifaceted nature of hair loss and addressing its emotional impact will contribute to more holistic and successful treatments. Ongoing research is crucial in understanding emerging patterns, such as those related to the COVID-19 pandemic, and developing potential future treatments.

6. Source of Funding

None.

7. Conflict of Interest


None.

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