SOWIŃSKA, Teresa, ŁABUDA, Mikołaj, SŁOJEWSKA, Aleksandra, KOTKOWIAK, Agata, MENTEL, Oliwia, BOGUCKA, Adrianna, SZEMA, Agnieszka, KRÓLIKOWSKA, Klaudia, SIKORA, Jakub and KNYCHALSKA, Karolina. Hair Loss: Pathogenesis and Prevention: A Literature Review. Quality in Sport. 2025;41:59999. eISSN 2450-3118.
https://doi.org/10.12775/QS.2025.41.59999
https://apcz.umk.pl/QS/article/view/59999

The journal has been 20 points in the Ministry of Higher Education and Science of Poland parametric evaluation. Annex to the announcement of the Minister of Higher Education and Science of 05.01.2024. No. 32553.
Has a Journal's Unique Identifier: 201398. Scientific disciplines assigned: Economics and finance (Field of social sciences); Management and Quality Sciences (Field of social sciences).
Punkty Ministerialne z 2019 - aktualny rok 20 punktów. Załącznik do komunikatu Ministra Szkolnictwa Wyższego i Nauki z dnia 05.01.2024 r. Lp. 32553. Posiada Unikatowy Identyfikator Czasopisma: 201398.
Przypisane dyscypliny naukowe: Ekonomia i finanse (Dziedzina nauk społecznych); Nauki o zarządzaniu i jakości (Dziedzina nauk społecznych).

The authors declare that there is no conflict of interests regarding the publication of this paper.
Received: 01.04.2025. Revised: 25.04.2025. Accepted: 04.05.2025. Published: 10.05.2025.

Hair Loss: Pathogenesis and Prevention: A Literature Review

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ABSTRACT

Introduction and purpose:

Hair loss, clinically referred to as alopecia, represents a significant dermatological challenge that impacts millions of people worldwide. This disorder can lead to significant psychosocial distress, affecting self-esteem and quality of life across different age groups and genders. Its multifactorial etiology involves genetic predispositions, hormonal imbalances, immune-mediated mechanisms, and environmental influences. This literature review focuses on the latest reports on the pathogenesis of hair loss and summarizes current strategies for its prevention.

State of knowledge:

Hair loss occurs when the normal hair growth cycle is disrupted, leading to premature shedding. Genetic predisposition, especially in androgenetic alopecia, increases follicle sensitivity to hormonal changes. Androgens shorten the growth phase and thin hair, while estrogen decline in women can worsen hair loss. Other hormones such as growth hormone, prolactin, melatonin, cortisol, and thyroid hormones also play key roles in hair maintenance. Stress elevates cortisol, which can push hair into its resting phase earlier than normal. Immune responses in conditions like alopecia areata result in the body attacking its own hair follicles. Environmental pollutants and nutritional deficiencies further compromise hair structure. Preventive measures- such as balanced nutrition, stress management, and topical treatments- can help maintain healthier hair.

Conclusion:

By deepening our understanding of the pathogenesis of hair loss, we can enhance our ability to diagnose the condition and identify its underlying causes. Given the diverse etiologies, each patient should be evaluated individually, with treatment tailored to the specific findings of their examination.

Key words: alopecia; pathogenesis; prevention; hair follicle.

INTRODUCTION

Hair loss is a condition that not only affects the physical appearance of an individual but also has profound psychosocial consequences[1]. While several forms of alopecia exist—from androgenetic alopecia to alopecia areata—the underlying mechanisms and optimal treatment strategies can vary considerably [2,3]. Over recent decades, research has uncovered multiple molecular pathways that contribute to hair follicle cycling and regeneration. Advancements in

genomics, endocrinology, and immunology have provided insights into the role of genetic markers and hormonal dynamics in the pathogenesis of hair loss [4,5].

This literature review is organized into two primary sections: pathogenesis and prevention. Special emphasis is placed on understanding the underlying causes of hair loss, as determining its pathogenesis is crucial for effective treatment. Therefore, any intervention should be preceded by a thorough examination and accurate diagnosis. Moreover, factors such as diet, medication usage, hair care routines, and the patient's medical and family history must be carefully considered to tailor an appropriate treatment plan [6,47].

DESCRIPTION OF THE STATE OF KNOWLEDGE

1. Pathogenesis of Hair Loss

The hair follicle cycle plays a crucial role in the process of hair regeneration. Follicles undergo several phases: anagen (growth), catagen (regression), and telogen (resting). Disruptions in this cycle, caused by genetic, hormonal, or environmental factors, can result in premature entry into the telogen phase, leading to excessive shedding [7].

1.1 Genetic and Molecular Mechanisms

Genetic predisposition is a major determinant in conditions such as androgenetic alopecia. Variants in several genes, including those that regulate androgen receptors, have been associated with increased susceptibility to hair loss [7]. Recent studies have further elucidated molecular signaling pathways involved in hair follicle cycling. Disruptions in these pathways can impair the regenerative capacity of hair follicles, leading to premature transition from the anagen phase to the telogen phase[8]. Variations in DNA sequences, including single nucleotide polymorphisms (SNPs), microsatellite repeats, and structural mutations, play a role in determining susceptibility to hair loss [9]. Familial studies underscore the importance of inherited predispositions, further complicated by epigenetic modifications [10].

1.2 Hormonal Influences

Hormones play a central role in controlling hair growth by interacting with specialized receptors inside the dermal papilla cells (DPCs) of hair follicles. Their influence can differ depending on the region of the body [11,12].

Androgens

Androgens are key hormones that regulate hair growth through their interaction with specific receptors located in the DPC of hair follicles [5]. When hormones like dihydrotestosterone (DHT) bind to these receptors, they trigger changes in gene expression and signaling pathways within the follicle. In scalp regions, this process can lead to a shorter growth (anagen) phase and gradual miniaturization of the hair follicle. Over time, this results in the transformation of thicker, terminal hairs into finer, less pigmented hairs—a process central to androgenetic alopecia. Interestingly, while androgens cause hair thinning on the scalp, they promote the development of coarser terminal hairs in other androgen-sensitive areas, such as pubic, axillary, and facial hair [13]. The level of circulating androgens is a key factor in patterned hair loss. Clinical observations indicate that in the absence of testosterone, such as in eunuchs or castrated boys, the typical male pattern baldness does not develop [14].

Estrogens

Estrogens have a significant impact on hair follicle activity by binding to highly specific local receptors and extending the anagen phase, which enhances hair growth [15]. With menopause, the natural decline in ovarian follicles leads to lower levels of both estrogen and progesterone, which can contribute to various skin and hair issues [16]. This reduction is associated with an increased occurrence of female pattern hair loss, highlighting estrogen's role in promoting hair growth. Additionally, the underlying causes and treatment approaches for conditions like hair loss and unwanted hair growth differ between postmenopausal and premenopausal women [17,18]. During pregnancy, high estrogen levels may help extend the hair's growth

phase, while a drop in estrogen after childbirth is believed to trigger a phase of increased hair shedding, commonly known as postpartum hair loss [19,20].

Prolactin

Prolactin, a hormone most commonly known for its role in lactation, also appears to have a complex influence on hair growth. Although its precise function in hair follicle regulation is not fully understood, several observations offer insight into its potential role [21,22].

Elevated prolactin levels, as seen in conditions of hyperprolactinemia, are often linked to a hair loss pattern that resembles androgenetic alopecia. This situation is frequently accompanied by other signs such as menstrual irregularities, infertility, acne, and excessive hair growth in unwanted areas. One proposed mechanism is that high prolactin levels may stimulate the adrenal glands to produce more androgens, which can negatively impact hair follicles. Conversely, in some cases- particularly in young men with early-onset balding- lower than normal prolactin levels have been reported, suggesting that both an excess and a deficiency of prolactin can disrupt the normal hair cycle. Maintaining a balanced level of prolactin seems to be crucial for healthy hair growth, although the exact thresholds and mechanisms remain an active area of research [22].

Growth Hormone

Growth hormone (GH) plays a significant role in maintaining healthy hair by regulating the activity of hair follicle cells. It promotes the production of key growth factors, such as IGF-1, which in turn encourage hair follicles to transition from a resting phase into an active growth phase. When GH levels are optimal, they support the proliferation and differentiation of these cells, ensuring a robust hair cycle. However, a deficiency in GH can disrupt this balance, potentially leading to weakened follicle function and hair thinning or loss [23]. Clinically, conditions with excessive GH levels, like acromegaly, are associated with increased hair growth and hirsutism [24]. Conversely, inadequate GH signaling, exemplified by Laron syndrome, often correlates with alopecia and hair follicle abnormalities [25].

Melatonin

Melatonin, a hormone primarily known for regulating sleep cycles, has been found to have a positive impact on hair health [26]. The information appears to be well supported by current research. Melatonin's receptors have been detected not only on hair follicle cells but also in other skin components such as sweat glands, blood vessels, keratinocytes, and fibroblasts. This widespread presence suggests that melatonin can influence multiple aspects of skin and hair physiology. Studies indicate that melatonin can promote hair pigmentation by increasing the number and activity of melanocytes. It may also help maintain or even extend the growth (anagen) phase of the hair cycle, which is key to improving hair density and reducing hair loss [27]. Additionally, melatonin's activation of antioxidant pathways (such as through Nrf2) provides protection against oxidative stress- a major contributor to hair follicle damage [28,29].

Cortisol

Stress impacts hair health through a cascade of hormones that include CRH, ACTH, and cortisol—key players in the body's stress response system. When stress occurs, CRH is released from the hypothalamus, which in turn prompts the pituitary gland to produce ACTH. ACTH signals the adrenal glands to secrete cortisol [30]. These hormones can directly influence hair follicles by triggering an early end to the growth phase and impeding hair shaft development. In simple terms, high stress levels lead to a quicker shift of hair follicles into a resting state, which can result in thinning hair or hair loss [31].

In certain conditions like alopecia areata, elevated stress hormones may also disrupt the immune balance of hair follicles, making them targets for immune attacks. Meanwhile, in androgenetic alopecia, stress hormones can interfere with factors that normally promote hair growth. Additionally, excessive cortisol may degrade important skin components around the hair follicle, further contributing to hair loss. Overall, these stress-related hormonal changes underscore how both acute and chronic stress can adversely affect hair health [32].

Thyroid hormones

Thyroid hormones influence both the anagen and telogen phases by promoting cellular proliferation and metabolic activity within the hair follicle. During development, these

hormones guide proper follicle differentiation, in adulthood they help sustain the anagen phase, ensuring robust hair growth [33].

When thyroid hormone levels become imbalanced, hair loss can occur through different mechanisms. In hypothyroidism, low hormone levels lead to reduced cell division and a shortened growth phase, resulting in diffuse thinning and increased shedding. On the other hand, hyperthyroidism can induce oxidative stress by increasing the production of reactive oxygen species, which may damage hair follicle cells and disrupt the normal cycle. Additionally, thyroid hormones affect hair pigmentation by stimulating melanin production, so imbalances may also alter hair color [34,35].

1.3 Inflammatory and Immune Mechanisms

Beyond hormonal factors, immune-mediated responses play a critical role in certain forms of alopecia, particularly alopecia areata [32]. Aberrant T-cell responses and cytokine imbalances contribute to the inflammatory milieu that targets hair follicles [36]. Emerging evidence suggests that specific T-cell subpopulations may mediate the destruction of follicular structures [37]. Oxidative stress, resulting from an imbalance between reactive oxygen species and antioxidants, further exacerbates inflammation and follicular damage [38]. In response, endogenous antioxidant mechanisms may be activated, although these responses are often insufficient to counteract chronic inflammatory insults [39].

1.4 Environmental and Lifestyle Factors

External factors such as exposure to pollutants, nutritional deficiencies, and chronic stress have been linked to hair loss. Environmental pollutants may trigger inflammatory cascades that adversely affect scalp health [40]. Nutritional inadequacies, particularly deficits in proteins, vitamins, and minerals, can compromise the structural integrity of hair fibers [41, 47]. Moreover, chronic stress influences neuroendocrine pathways that may accelerate hair shedding [31]. Lifestyle habits—including smoking and irregular sleep patterns—are additional risk factors that modulate hair follicle health [42]. Cigarette smoking has been associated with a greater risk of developing alopecia areata. This may occur because the

toxins in cigarette smoke promote a pro-inflammatory cytokine environment and lead to an excess buildup of free radicals, both of which can compromise the normally protected status of hair follicles [43]. Various medications—including chemotherapeutic agents, biologics, and other immunomodulators—can trigger different types of alopecia [44].

2. Prevention Strategies

Prevention of hair loss involves strategies aimed at optimizing nutritional status, managing stress, and employing topical agents to sustain hair follicle health.

2.1 Nutritional Interventions

Adequate nutrition is a cornerstone for healthy hair growth. Micronutrients such as biotin, vitamin D, and essential minerals (e.g., zinc and iron) are critical for maintaining follicular metabolism and structure [45,46]. Diets rich in antioxidants and proteins have been associated with improved hair density and reduced shedding [47]. Balancing nutritional intake can thus serve as both a preventive and supportive measure against hair loss [48].

2.2 Lifestyle and Stress Management

Chronic psychological stress is a well-documented trigger for hair loss. Integrative approaches that include cognitive-behavioral therapy, mindfulness techniques, and regular physical activity have shown benefits in reducing stress-related alopecia [49]. Behavioral modifications, such as improved sleep hygiene and stress management practices, contribute positively to overall scalp health and can attenuate neuroendocrine responses that otherwise precipitate hair loss [50,51]. Quitting smoking is also an important preventive measure for maintaining hair health [52].

2.3 Topical Preventive Agents

Topical treatments, particularly those containing minoxidil, have long been employed as a first-line preventive measure in early hair loss. These agents function by prolonging the anagen phase of the hair cycle and improving blood flow to the scalp [53]. In addition, various natural extracts with anti-inflammatory and antioxidant properties are under investigation as adjuncts to conventional therapy [54].

CONCLUSIONS

Hair loss is a multifactorial condition driven by a complex interplay of genetic, hormonal, and inflammatory processes, with environmental and lifestyle factors further modulating its onset and progression. In conclusion, a deep understanding of these underlying mechanisms not only enhances our ability to diagnose and treat hair loss at its earliest stages but also paves the way for the development of more targeted and effective prevention strategies. Integrative approaches- combining medical therapies, nutritional support, and lifestyle modifications- offer the most promise for mitigating progression and improving overall hair health. As research continues to unravel the intricate cellular and molecular pathways involved, future therapeutic innovations are expected to provide personalized interventions that can significantly enhance quality of life for those affected.

DISCLOSURE

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- Receiving funding: Not applicable.

All authors have read and agreed with the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: Not applicable.

Acknowledgements: Not applicable.

Conflicts of Interest: The authors declare no conflict of interest.

Declaration of the use of generative AI and AI-assisted technologies in the writing process.

In preparing this work, the authors used ChatGPT for the purpose of improving language and readability. After using this tool, the authors have reviewed and edited the content as needed and accept full responsibility for the substantive content of the publication.

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