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Biology of Hair Growth and Influence of External Factors (Ecology, Stress, Nutrition)

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Abstract

In the article the biological mechanisms of hair growth are examined and the influence of external factors ecology, chronic stress, nutrition and nutraceuticals on their growth is assessed. The study is based on a systematic literature review with emphasis on original works concerning the molecular mechanisms of hair growth. A descriptive meta-analysis of the results of other publications as well as clinical trials was conducted and a data integration scheme for multidisciplinary prognosis of alopecia risks, incorporating biochemical and physiological parameters, was developed. Data were systematized on how air pollution, ultraviolet radiation and heavy metals disrupt the functions of the dermal papilla and the phase balance of the hair cycle. The molecular pathways of stress-induced hair loss via HPA axis hyperactivity, neuropeptide signaling and local inflammation are described. A conclusion is drawn on the necessity of a comprehensive multifactorial approach and monitoring of nutritional status for personalized therapy of hair loss. The information presented in this work will be of interest to specialists in trichology and dermatophysiology investigating molecular and cellular mechanisms of hair growth in the context of endocrine and immunological interactions. The material will also be valued by experts in ecotoxicology and nutrition seeking to integrate data on the impact of polluted environments, chronic stress and macro- and micronutrients into the development of preventive and therapeutic strategies to maintain physiological homeostasis of the hair follicle.

Keywords: *Hair Growth, Hair Cycle Phases, Environmental Factors, Chronic Stress, Nutrition, Nutraceuticals, Telogen Effluvium, Anagen Phase, Dermal Papilla, Vitamins And Minerals.*

INTRODUCTION

Hair as corneous appendages of the skin perform not only an aesthetic but also a vital protective function, safeguarding the scalp from thermal and mechanical insults. Their condition also serves as a marker of overall health: deterioration of hair structure and growth rate frequently correlates with metabolic and endocrine disorders [1, 3].

Current understanding of hair follicle biology is based on its described cyclic functioning — anagen, catagen and telogen — as well as on a complex network of signaling pathways governing transitions between these phases. An integrative model accounting for cross-talk was presented by Natarelli N., Gahoonia N., Sivamani R. K. [3], demonstrating that the command center of growth is localized in the dermal papilla and is sensitive both to systemic hormonal stimuli and to local damaging factors. These observations resonate with the monograph of Trüeb R. M., Trüeb R. M. [9], which considers cycle biology through the prism of nutritional status: protein, iron, zinc and vitamin D deficiencies shorten anagen duration and increase the percentage of follicles in telogen. At the molecular level oxidative stress is viewed as a trigger of premature catagen transition and graying; O'Sullivan J. D. B. et al. [10] showed depletion of the melanocytic pool and disruption of the cellular clearance mechanism upon accumulation of reactive oxygen species.

Nutritional factors according to the Moscow Department of Health portal [2] determine hair growth rate through the balance of macro- and micronutrients: a complete spectrum of amino acids, ω-3 polyunsaturated fatty acids and antioxidants support active keratin synthesis whereas a high-glycemic diet enhances androgen production and induces follicular miniaturization. Practically the same dependencies, but with emphasis on regional deficiency profiles, are discussed in the Russian clinical educational review How to Improve Hair? [1]. Experimentally, the positive effect of plant sterols inhibiting 5-α-reductase was demonstrated by Kang X. et al. [7]; addition of pumpkin seed oil rich in Δ7-phytosterols normalized the DHT/testosterone ratio and restored the balance of proliferation and apoptosis in target cells.

Alongside metabolic stimuli the external environment (ultraviolet radiation, pollutants, thermal and chemical exposure) constitutes an independent modifier of shaft structure. Lazarchik N. [4] identified that repeated exposure to temperatures >200 °C or alkaline agents disrupts the disulfide framework, reducing cysteine content to 30 % of

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the original level; restoration is possible through combined application of low-molecular-weight amino acids and peptide reductants. The oxidative component of such damage is also linked to premature catagen, underscoring the cross-influence of environmental factors and endogenous aging pathways.

Therapeutic interventions can be divided into synthetic and phytogenic. Liquid-crystalline nanocapsules with minoxidil described by Fresta M. et al. [5] optimize drug deposition at the follicle orifice and in an in vivo model prolong anagen 1.7-fold compared to a traditional lotion. Panahi Y. et al. [6] in a randomized comparison demonstrated an equivalent but slower (by the sixth month) increase in hair density with 2 % rosemary oil relative to 2 % minoxidil, highlighting the role of anti-inflammatory and antioxidant components of phytotherapy. Hyun J. et al. [8] describe how Morus alba activates dermal papilla cells via Wnt signaling and increases vascular endothelial growth factor expression, inducing follicular transition to anagen within 48 h in culture.

Thus despite numerous data on iron and vitamin D deficiencies randomized studies confirming the clinical efficacy of their supplementation in telogen effluvium remain insufficient: reviews note positive correlations but no clear evidence base [9]. Secondly models of oxidative stress vary: some authors interpret it as a primary trigger of graying [10], others as a secondary effect of shaft damage [4]; the lack of a unified standard for quantitative assessment of ROS in the follicle hinders consensus. Thirdly extrapolation of in vitro results to clinical practice is complicated by a scarcity of long-term multicenter randomized controlled trials. Finally the combined influence of urban aeropollutants and psychosocial stress on cortisol receptor expression in the dermal papilla as well as epigenetic modifications of follicular cells in response to seasonal and circadian fluctuations remains poorly studied.

The aim of the study is to analyze hair growth biology considering the multifactorial impact of external conditions (ecology, stress, nutrition) and to propose a methodology for their systematic analysis.

The scientific novelty lies in the formulation and justification of the hypothesis of a synergistic effect of environmental toxins, chronic stress and nutrient deficiency on the anagen phase of the hair cycle through co-modulation of NADPH oxidases, NF-κB and Wnt/β-catenin pathways as well as in the development of an integrative multidisciplinary scheme for predicting alopecia risk based on comparative meta-analysis of biochemical and physiological markers.

The authorial hypothesis is based on the premise that interaction of environmental toxins, cohort stress and nutrient insufficiency leads to synergistic disruption of anagen mechanisms in the hair follicle through modulation of NADPH oxidases, NF-κB signaling and Wnt/β-catenin pathways.

The study is based on a systematic literature review with selection of original works on molecular mechanisms of hair growth. A descriptive meta-analysis of results from other publications and clinical trials was conducted and a data integration scheme for multidisciplinary alopecia risk prediction was developed incorporating biochemical and physiological parameters.

Biology of Hair Growth

Hair constitutes an independent organ of the skin, each of which is formed by a hair follicle provided with its own blood vascular network, innervation, sebaceous gland and arrector pili muscle. On the scalp of an adult human there are approximately 100 000 hairs [2]. The hair root is located deep within the dermis, in the hair bulb, and receives nutrients through the vascular hair papilla, whereas the visible supradermal part — the hair shaft — is a fully keratinized structure. In transverse section of the shaft three main layers are distinguished:

- Cuticle — the outer layer of keratin scales providing mechanical and chemical protection;
- Cortex — the middle, most voluminous layer, consisting of ordered keratin fibers containing melanin, which determines hair color
- Medulla — the central region, comprising not yet fully keratinized, living cells [1].

Figure 1 depicts the structure of hair.

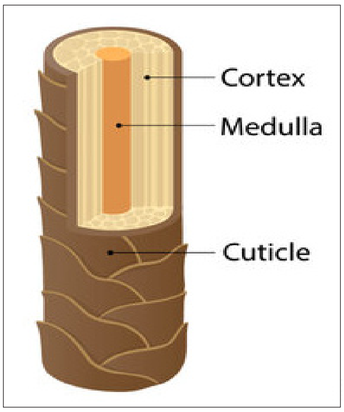

Fig.1. Hair structure [4].

Hair growth is regulated by the cyclical alternation of four phases, occurring independently in each follicle and repeating 15–30 times during life [3]:

1. Anagen (active growth phase), lasts from 2 to 8 years (in men – up to 3 years, in women – up to 5 years);
2. Catagen (transitional follicle regression) – approximately 2–3 weeks;
3. Telogen (resting phase) – up to 3 months;
4. Exogen (old hair shedding) – the concluding stage of hair loss and follicle preparation for a new anagen [3].

For clarity, the hair growth cycle will be presented in Figure 2 below.

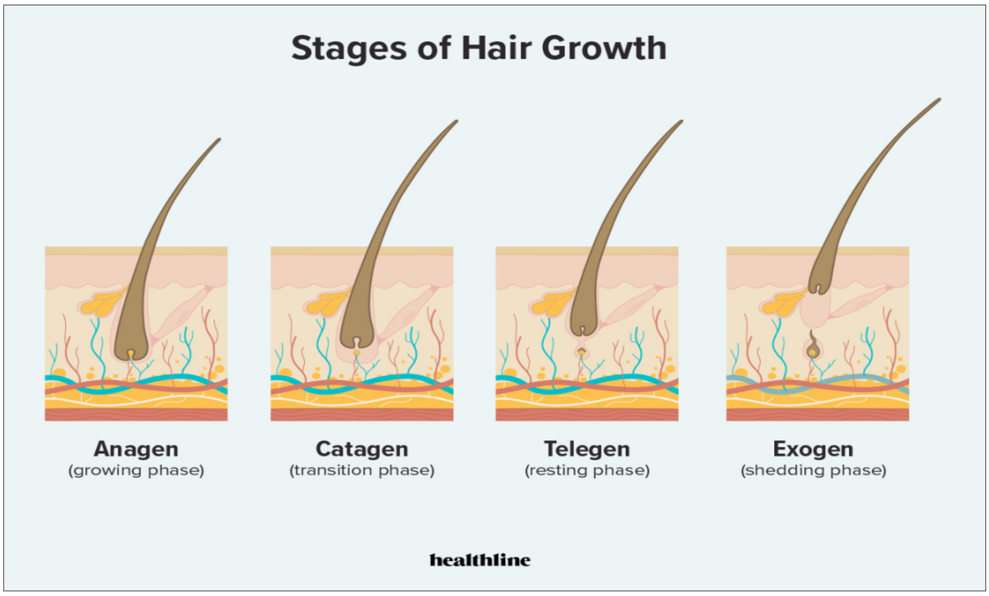

Fig.2. The hair growth cycle [4].

The majority of the hair coat (≈85 %) is in the anagen phase, ≈1 % in the catagen phase and ≈14 % in the telogen phase, which ensures uniform hair renewal without noticeable thinning [5].

Below, Table 1 presents the phases of hair growth.

Table 1. The main phases of hair growth and their characteristics (compiled by the author based on the analysis [1-3]).

Phase	Duration	Hairshare (%)
Anagen	Men: up to 3 years; women: up to 5 years	≈85
Catagen	≈2–3 weeks	≈1
Telogen	Up to 3 months	≈14
Exogen	A fewdays (shedding)	—

The variable duration of the anagen phase determines the maximum hair length: in humans it ranges from 2–8 years, whereas, for example, in eyelashes it lasts only 2–3 months. The duration and balance of the phases are controlled by complex molecular cascades (Wnt/β-catenin, TGF-β, FGF), disruption of which is sufficient to trigger a premature transition to catagen or prolongation of telogen, leading to enhanced hair shedding (telogen effluvium) or reduced hair growth.

Influence of Environmental Factors

Environmental factors exert a significant impact on hair growth and the health of hair follicles through mechanisms of oxidative stress, toxic load and microcirculation impairment.

Numerous epidemiological studies associate increased concentrations of particulate matter ($PM_{2.5}$ and PM_{10}), NO_2 and SO_2 in urban air with a rise in patient visits for hair loss. In a study of Chinese cities a direct correlation was found between daily $PM_{2.5}$ levels and hospitalizations for telogen effluvium: each additional 10 μg/m^3 of $PM_{2.5}$ was associated with a 5 % increase in hair loss cases [3]

Regarding damage mechanisms particulate matter is inhaled and penetrates the scalp microcirculation, stimulating the generation of reactive oxygen species (ROS) that damage matrix keratinocytes of the follicle and promote premature transition to telogen [2, 6]. Pollutants induce the expression of pro-inflammatory cytokines (TNF-α, IL-6) in the scalp, leading to degradation of connective tissue surrounding the follicle and fibrosis of the hair-bearing area

Prolonged exposure to cadmium, lead, arsenic and chromium via water and air results in accumulation of these elements in hair bulbs and the hair shaft. In hair analysis of middle-aged residents of industrial zones concentrations of lead (Pb) and cadmium (Cd) were 2–3 times higher than control values and were associated with increased risk of overt telogen effluvium [1, 7]. Cd and Pb inhibit pyruvate carboxylase and other sulfhydryl-dependent enzymes, impairing energy metabolism in follicle matrix cells. As and Cr form DNA adducts and induce apoptosis of matrix cells in the hair germ, which shortens the anagen phase [8, 9]

Excessive insolation causes photodegradation of keratin and lipids of the hair cuticle, increasing brittleness and contributing to mechanical damage [10]. Moreover prolonged exposure to high temperatures and low humidity leads to transepidermal water loss, desegregation of intercellular lipids and subsequent fragility of the hair shaft

Further in Table 2 the factors and their mechanisms of influence on hair growth are demonstrated

Table 2. The main environmental factors and their mechanisms of influence on hair growth (compiled based on the analysis [3]).

Factor	Mechanismofaction	Clinicaleffect
Air pollution ($PM_{2.5}$)	↑ reactive oxygen species (ROS), pro-inflammatory cytokines; damage to keratinocytes	Telogeneffluvium, hairthinning
Heavy metals (Cd, Pb)	Inhibition of sulfhydryl-dependent enzymes; formation of DNA adducts; apoptosis of cells	Shortening of anagen, follicular alopecia
UV radiation	Photodegradation of keratin; oxidation of hair shaft lipids	Increasedbrittleness, splitends
Climate (aridity)	Transepidermal water loss; degradation of cuticular lipids	Fragility, lossofelasticity

Environmental factors - from air pollution to the accumulation of heavy metals and excessive insolation—induce oxidative and inflammatory responses in the scalp, disrupting the normal hair growth cycle. Comprehensive exposure assessment and the development of protective strategies (air filtration, drinking water quality control, photoprotection) are important directions for the prevention of alopecia in urbanized regions.

Role of Chronic Stress

Chronic stress is one of the factors disrupting the balance of hair cycle phases, leading to premature transition of anagen to catagen and activation of telogen effluvium. Its pathogenesis is mediated by hyperactivity of the hypothalamic-pituitary-adrenal (HPA) axis, local neuropeptides and stress hormones, as well as alteration of the extracellular matrix structure of the hair follicle.

Under chronic psychoemotional stress there is increased secretion of corticotropin-releasing hormone (CRH), ACTH and cortisol. A persistently high cortisol level:

- induces catabolism of proteoglycans (versican, decorin), vital for the structural integrity of the hair papilla;

- reduces synthesis of hyaluronan and glycosaminoglycans, decreasing the volume of the follicular dermal matrix

- enhances apoptosis of matrix keratinocytes via activation of caspase-3.

Clinically this manifests as telogen effluvium and hair thinning on average 3–6 months after the onset of the stressful event [1, 8]

Substance P (SP), released from peripheral sensory nerve endings, plays a key role in the mechanisms of stress-induced hair loss:

- SP stimulates proliferation of mast cells and their degranulation, releasing histamine and prostaglandins, causing perifollicular inflammation;

- SP-mediated upregulation of NF-κB expression enhances production of IL-1β and TNF-α in dermal papilla cells

- Direct application of SP to the skin of mice models stress-induced alopecia, shortening the anagen phase by 20–30 %.

Below in Table 3 the main stress mediators, their sources and effects on the hair follicle are systematized.

Table 3. The main stress mediators, their sources and effects on the hair follicle (compiled by the author based on the analysis [1, 3, 7, 10]).

Mediator	Source	Molecular mechanism	Impact onhaircycle (%)
Cortisol	Adrenalcortex	↓ Proteoglycans (versican, decorin); ↑ caspase-3	Anagen ↓ by 25–35 %
Substance P	Sensory C-nociceptors	↑ Mast cell degranulation; ↑ NF-κB; ↑ IL-1β	Anagen ↓ by 20–30 %
Neuropeptide Y	Hypothalamus, limbic system	↑ Angiotensin II; ↓ tissue microcirculation	Catagen enhancement
CRH	Hypothalamus	↑ ACTH → ↑ cortisol	Shift of anagen to catagen

Thus chronic stress, mediated by HPA-axis imbalance and neuropeptides, induces premature catagen and stimulates telogen effluvium via oxidative stress, extracellular matrix degradation and perifollicular inflammation. Stress management and modulation of corticosteroid and neurotransmitter pathways represent promising therapeutic avenues for stress-induced alopecias.

The Significance of Nutrition and Nutraceuticals

Dietary regimen and specific nutraceuticals (dietary supplements with biologically active components) are of decisive importance for maintaining the phase balance of hair growth and the integrity of the hair follicle. Insufficiency of macro- and micronutrients leads to a decrease in matrix cell proliferation, loss of structural components of the shaft, and premature transition into telogen.

Since hair consists of more than 90 % keratin—a protein rich in sulfur-containing amino acids (cysteine, methionine)—a sufficient intake of protein and all essential amino acids is required to ensure keratin synthesis. Protein–calorie resource deficiency leads to telogen alopecia, a decrease in hair shaft thickness, and reduced follicular density. Administration of L-cystine together with pantothenic acid against a background of balanced protein intake resulted in a 15 % increase in the proportion of hairs in the anagen phase ($p < 0.01$) after six months of therapy

Polyunsaturated fatty acids (PUFAs) of the omega-3 and omega-6 classes are components of follicular dermal cell membranes and exert anti-inflammatory effects by inhibiting 5α-reductase and stimulating the synthesis of growth factors (FGF-7, VEGF). When the omega-6/omega-3 ratio decreases to less than 4:1, an 8 % increase in the proportion of follicles in the telogen phase and an approximately 10 % reduction in hair thickness are observed. Clinical trials demonstrate that administration of 1.5 g EPA + DHA per day for four months reduces the intensity of hair loss by 23 % compared with placebo ($p < 0.05$)

Trace elements play a key role in maintaining hair growth and hair follicle function. Iron serves as a cofactor for tyrosine hydroxylase and ribonucleotide reductase; when serum ferritin is below 30 μg/L, the risk of telogen alopecia increases by 40 %. Zinc is necessary for the formation of S-disulfide bridges in keratin; at concentrations below 70 μg/dL, a 15 % decrease in hair density is noted. Selenium is a component of glutathione peroxidase and protects the follicle from oxidative stress; however, intake exceeding 2 mg/day induces hair loss in 72 % of cases

Modern phytonutraceutical and complex supplements include marine collagen and fish-derived peptides, which extended the anagen phase by 12 % and increased hair density by 18 %. Polyphenols—extracts of rosemary, hops, and capsaicin—are capable of inhibiting 5α-reductase, improving scalp microcirculation, and enhancing VEGF expression in the dermal papilla

Mesotherapeutic approaches, in particular injections of platelet-rich plasma (PRP), demonstrate an increase in the telogen-to-anagen phase ratio by 22 % compared with control, confirming their efficacy in stimulating hair growth [1-3]

Thus, timely correction of diet, normalization of macro- and micronutrient levels, and intake of rational nutraceuticals (amino acid complexes, PUFAs, vitamin D and biotin in deficiency, combined polyphenolic preparations) contribute to hair strengthening, extension of the anagen phase, and reduction of hair loss. To achieve maximal effect, individualized selection of dosages and combined formulations via monitoring of serum markers (ferritin, 25(OH)D, Zn) is required

CONCLUSION

Air pollution ($PM_{2.5}$, heavy metals), ultraviolet radiation and chemical toxicants induce oxidative stress and chemokine-mediated inflammation of the scalp, leading to premature transition of follicles into catagen and telogen Prolonged elevation of cortisol and substance P disrupts extracellular matrix synthesis, stimulates perifollicular inflammation and apoptosis of matrix keratinocytes, provoking telogen effluvium

Adequate intake of protein/amino acids, polyunsaturated fatty acids, vitamins (A, D, B_7, C, E) and minerals (Fe, Zn, Se) supports proliferation of hair matrix cells, antioxidant defense and phase balance. In deficiency, selective nutriceuticals (L-cysteine, EPA/DHA, retinyl palmitate, cholecalciferol) demonstrate clinical efficacy in prolonging anagen and reducing shedding

For optimization of alopecia treatment the following are required:

- Early diagnosis of nutritional deficiencies and pilotrichological markers

- Environmental correction (minimization of exposure to pollutants, UV protection)

- Stress management (psychotherapy, adaptogens)

- Personalized nutritional support and use of evidence-based nutriceuticals in therapy of hair loss

A comprehensive multidisciplinary approach will ensure prolonged improvement of hair condition and prevention of recurrence of hair loss.

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