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Review

Age-related hair changes in men: Mechanisms and management of alopecia and graying

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ABSTRACT

The appearance of human scalp hair is often tied to perceptions of youth and virility, especially in men. Hair loss, or alopecia and hair graying are commonly associated with advancing age and are frequently a source for emotional distress and anxiety. Our understanding of the complex molecular signals and mechanisms that regulate and influence the hair follicle has expanded in recent years. By harnessing this understanding we are poised to address the esthetic concerns of aging hair. Additionally, changes in the hair follicle may be a reflection of systemic senescent signals, thus because of its accessibility, the hair follicle may serve as an important research tool in gerontology. In this review, the most current knowledge and research regarding mechanisms of androgenetic alopecia, senescent alopecia, and graying are discussed, as are extrinsic factors that may contribute to hair changes with age. Evidence based management strategies for treatment of age-related hair changes are also reviewed.

Contents

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1. Introduction

The hair follicle is a unique structure in that it undergoes continuous cycles of growth (anagen), resorption (catagen), and rest (telogen) from birth until death. During anagen, each individual hair follicle produces a new hair shaft. The size, length and pigment of the hair shaft vary depending on the location on the body and can change under the influence of biologic signals. The reason for the relative abundance of scalp hair compared to body hair in humans is not completely understood. Perhaps because of this prominence, the appearance of human scalp hair is often tied to perceptions of youth and virility, especially in men. Thus alopecia and graying, which are almost universal with advancing age, are often a source of anxiety and distress.

Follicular stem cells are responsible for regeneration of the hair follicle with each new cycle and recapitulate many of the signals of embryologic development. Various factors are known to influence and alter the regenerating hair follicle with advancing age. Androgens are the most extensively studied modulator of the hair follicle. However non-androgen senescent signals as well as extrinsic factors such as ultraviolet light and smoking are also likely to influence the function and fidelity of the hair follicle. Hair graying occurs as a result of alterations to the melanocytes, or specialized pigment-producing cells, that are associated with each hair follicle. Newer studies have shed light on the critical role of reactive oxygen species that lead to loss of melanocytes and pigment production.

2. Androgen mediated hair loss: androgenetic alopecia

Androgenetic alopecia (androgenetic alopecia), also known as male pattern hair thinning or male pattern balding is the most well recognized cause of hair thinning. Although there is no clear demographic data, it is often stated that up to 50% of men will manifest some degree of androgenetic alopecia by age 50 [1]. There is significant variation among the races with the greatest penetrance in Caucasians and the least among Africans [2]. Although extensive genetic studies have not been done, a polygenetic inheritance of baldness is suspected given the high prevalence of the trait, the strong concordance between family members, and the fact that risk increases with the number of relatives already affected and the fact that risk increases with the number of relatives already affected [3–7].

In men with androgenetic alopecia, large caliber hairs become progressively finer and thinner (miniaturized) leading to decreased coverage of the scalp; in some cases the hairs become so fine that they are barely visible to the eye. In those who are genetically susceptible, hair miniaturization can begin as early as the teens, twenties and thirties [8]. Interestingly, these changes occur only in certain regions of the scalp, specifically the frontal hairline, the top of the scalp and the crown or vertex scalp; the follicles along the sides and back of the scalp are spared even in men with extensive balding. These regional variations in patterns of scalp hair thinning may reflect differences in embryologic scalp patterning [9], levels of hormonal receptors [10] or other factors that may influence follicular growth [11].

Pathophysiologically, androgens mediate and drive the follicular transformation in androgenetic alopecia. There is a substantial increase in the local, or follicular, transformation of testosterone to dihydrotestosterone by the enzyme 5α-reductase [12]. Dihydrotestosterone, which has a five times higher affinity for the androgen receptor compared to testosterone, triggers specific genes that then lead to the gradual miniaturization of genetically programmed hair follicles [13].

The effects of androgens on the follicle have, for the most part, been studied in men under the age of 50. It is suspected that to some extent, hair loss in later years is mediated by both androgen as well as non-androgen signals. This idea is supported by the observation that there is a progressive decline in testosterone levels with advancing age with some reports suggesting that up to 25% of men over age 70 meet laboratory criteria for hypogonadism [14–16]. Additionally, tissue activity of 5α-reductase in the scalp decreases with age. This pervasive waning of circulating androgens and androgen activity suggests that non-androgen-related hair thinning may be an important factor in age-related hair thinning.

3. Non-androgen mediated hair loss: senescent alopecia

Various reports have suggested that decreased hair density and diameter occur with advancing age [17–21]. Such hair thinning is often identified as a marker of systemic senescence in humans and other mammals. In support of this concept, it is observed that patients with progeria, who have genetically programmed premature senescence, show a phenotype of hair loss [22].

The following criteria have been proposed for making the diagnosis of senescent alopecia: (1) hair thinning that does not become apparent until after approximately 50 years of age and (2) no family history of androgenetic alopecia [19,23,24]. Alternate terms that have been used include “late onset” or “age-related” hair thinning. In reality, senescent alopecia likely coexists with androgenetic alopecia in many patients. Clinically, the hair thinning in senescent alopecia is often described as being diffuse when seen in its “pure form” but having both a diffuse and patterned thinning when seen in combination with androgenetic alopecia [24,25]. Histologically, there is follicular downsizing or miniaturization of the follicle in both androgenetic alopecia and senescent alopecia [26].

Although androgenetic alopecia and senescent alopecia share many clinical and histologic features, the mechanisms by which follicular downsizing and miniaturization occur has recently been shown to be distinct [27]. Microarray comparison of age-matched subjects with androgenetic alopecia, senescent alopecia and normal controls without hair loss has shown that androgenetic alopecia is associated with altered expression of genes known to be required for hair follicle cycling. In stark contrast, the transcriptional profile of senescent alopecia reveals changes in the complex phenomenon of alternative splicing, oxidative stress response, and apoptosis, which are characteristic of aging tissues [27]. This difference in mechanism has significant implications in terms of treatment of hair loss at different ages. Further characterization of these senescent pathways may lead to attractive therapeutic targets for treatment of senescent alopecia, but may also prove to be useful markers of other systemic senescent processes.

4. Extrinsic factors (chemicals, heat, ultraviolet light, smoking)

The hair is made primarily of keratin bundles that are compacted together and surrounded with an outer cuticular layer to form a rope-like structure that is flexible yet strong. Sulfur crosslinks within the keratin provide for the strength of the hair. The outer cuticle resembles overlapping shingles on a roof and forms the “armor” that protects the underlying hair shaft. The quality and caliber of the hair shaft, or hair fiber decreases with age and can significantly affect how the hair is perceived [28]. Additionally, the aged hair fiber is more susceptible to damage and breakage from a variety of external insults, the general term for which is “weathering.”

Although extensive hair styling is not as common in men as in women, various hair care techniques may not be well tolerated with advancing age. Heat, coloring agents, and chemicals used for