

Review Article

Signs of skin aging: a review

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ABSTRACT

Skin aging is a complex process affected by both internal and external factors, leading to changes in skin structure and function. The connection between signs of skin aging and age is intricate, involving genetic, environmental, and lifestyle influences. However, relying solely on chronological age fails to accurately predict skin aging due to the complex interplay of these factors. Interventions such as retinoids show promise in altering skin aging processes, questioning the exclusive use of chronological age for predictions. Skin aging goes beyond appearance, reflecting deeper changes in skin function and structure. Therefore, comprehensive strategies including sun protection and topical treatments are essential for managing aging effects. In essence, understanding the intricate nature of skin aging and adopting holistic approaches tailored to individual factors are vital for promoting skin health throughout life.

Keywords: Skin aging, Intrinsic aging, Extrinsic aging, Treatment strategies, Prevention

INTRODUCTION

Skin aging is a complex, multifaceted process characterized by various structural and physiological changes in the skin, driven by both intrinsic and extrinsic mechanisms.¹ Intrinsic aging refers to the natural aging process that occurs over time, regardless of external factors. It is linked to genetic elements and characterized by programmed aging and cellular senescence. These processes are mainly instigated by internal oxidative stress and cellular harm. This type of aging leads to gradual changes in skin appearance and function, including reduced elasticity, thinning of the skin, and the appearance of fine lines.² Intrinsic aging is also characterized by biochemical degenerative processes that naturally occur with age, impacting the skin's healing capabilities and leading to morphological changes at all levels of aged skin.³ Extrinsic aging, on the other hand, results from environmental factors and lifestyle choices that accelerate the skin's aging process. Major contributors to extrinsic aging include chronic exposure

to ultraviolet (UV) light, particularly from sunlight, which is a primary cause of environmentally induced skin aging. Other factors such as longer wavelength radiation, air pollution, and exposure to chemicals also significantly contribute to extrinsic aging by generating reactive oxygen species (ROS), leading to DNA damage, loss of collagen, wrinkle formation, and overall deterioration of skin health.^{4,5} Extrinsic aging is additionally aggravated by lifestyle elements like smoking and inadequate nutrition, which have the potential to amplify the skin's aging progression beyond its inherent natural pace. Both intrinsic and extrinsic aging mechanisms mutually impact each other and cooperate to hasten the observable indications of aging, underscoring the importance of addressing both categories via preventative actions and therapies to uphold skin well-being and aesthetics.

Understanding the signs of skin aging is crucial due to the multifaceted nature of the aging process, involving intrinsic and extrinsic mechanisms that lead to structural and physiological changes in the skin.¹ Both natural and

photoaging share common biochemical mechanisms that result in altered skin structure and function, such as decreased collagen production and increased collagen degradation.⁶ Environmental elements such as UV radiation wield considerable influence in triggering morphological changes in the skin, resulting in profound wrinkles, laxity, and roughness. With advancements in molecular biology, newer insights into combating skin senescence have emerged, emphasizing the importance of tailored anti-aging therapies that address epidermal dysfunction, dermal matrix aberrations, and other age-related skin problems.⁷ As the population ages, dermatology faces the challenge of addressing the increasing prevalence of dermatoses associated with aging skin, necessitating specific recommendations for skin protection and medication use in elderly patients.

Intrinsic aging, influenced by genetic background and time, leads to dryness, atrophy, wrinkles, pigmented lesions, hypopigmentation, and elastosis.⁸ Extrinsic aging contributes to skin aging by inducing damage such as genomic instability, epigenetic alterations, and mitochondrial dysfunction. Ethnic variations also play a role in the manifestation of aging signs, with dark spots, loss of elasticity, volume, and rhytids being common across different skin types.⁹ Studies comparing Black African and Caucasian women revealed differences in facial wrinkles, pores, and skin tone, with Caucasians showing more advanced signs of aging, while Black Africans exhibited delayed aging signs but with exceptions like deeper pores and uneven skin tone. Dermal atrophy and aging are associated with collagen reduction, leading to dryness, hypo/hyperpigmentation, and diminished elasticity.¹⁰

SIGNS OF SKIN AGING

Fine lines and wrinkles

Fine lines and wrinkles are primarily caused by factors like UV exposure, aging, and gravity, leading to dermal matrix deterioration and skin contour deformities.¹¹ These wrinkles can be classified as dynamic (e.g., forehead lines) and static (e.g., nasolabial folds).¹² Prevention strategies involve antioxidants, sunscreens, and innovative dermal fillers with enhanced longevity and injectability.¹³ Different treatments, such as botulinum toxin and hyaluronic acid fillers, have demonstrated significant effectiveness in managing facial wrinkles.

Age spots

Age spots, also known as solar lentigines, are pigmented lesions that develop on sun-exposed skin due to chronic sun exposure. The development of age spots involves the accumulation of aged cells in the skin, characterized by lipofuscin bodies and altered keratinocyte proliferation.¹⁴ Mechanisms like the mis repair accumulation aging theory and the inhibition of lipofuscin formation contribute to their development. Treatment options include topical compositions with skin-whitening agents

and wrinkle-reducing agents.¹⁵ Notably, 10-hydroxystearic acid (HSA) has shown efficacy in reducing age spots by modulating collagen levels, MMP-1 expression, and p53 protein levels, acting as a PPAR α agonist. Understanding these mechanisms and utilizing targeted treatments can help prevent and manage age spots effectively.

Sagging

Loss of skin elasticity and sagging skin can result from various factors such as aging, weight loss, and postoperative complications like liposuction. Studies have highlighted the role of collagenous fibers in subcutaneous tissue, known as the retinacula cutis, in maintaining skin elasticity and preventing sagging. Various treatments address loss of elasticity and sagging skin. Botulinum toxin A injections into specific facial muscles effectively correct facial flaccidity and sagging post-masseter reduction, yielding high patient satisfaction and significant improvement. Poly-L-lactic acid (PLLA) applications enhance dermal thickness and skin flaccidity, proving effective and safe for inner arm skin laxity.^{16,17} Research on sagging skin mechanisms highlights the importance of the subcutaneous collagenous fiber network, where a denser structure correlates with better elasticity and reduced sagging.

Skin roughness

Skin roughness can stem from various factors, including diseases like pellagra, aging, and environmental damage. Pellagra, historically linked to maize consumption in Italy and the US, presented as rough skin among other symptoms.¹⁸ Physicians employ skin roughness as a diagnostic marker for various conditions such as warts, psoriasis, and distinguishing between benign and malignant skin lesions. Treatments for rough skin include compositions containing sodium chondroitin sulfate for skin moisture enhancement and wrinkle reduction.¹⁹ Understanding the causes and utilizing appropriate treatments can help in managing and preventing rough skin texture effectively.

Dry skin

Dry skin, also known as xerosis, is a prevalent skin condition influenced by factors like hydration, sebum content, and environmental elements. It can impact wound healing, exacerbate skin disorders, and affect quality of life. Causes of dry skin include intrinsic and extrinsic factors like aging, sunlight exposure, and chemical exposure. To address dry skin, a skin treatment glove has been developed, allowing for improved moisturizer retention and breathability.²⁰ Prevention and treatment strategies involve complete emollient therapy, which can aid in managing dry skin and enhancing skin appearance. Clinical pathways have been established to guide healthcare professionals in preventing and treating dry skin effectively. Overall, understanding the causes,

types, prevention, and treatment options for dry skin is crucial for maintaining skin health and quality of life.

Telangiectasia, skin pigmentation and skin volume loss

Telangiectasia on the skin, characterized by small dilated blood vessels near the skin surface, can appear due to various reasons such as sun damage and genetic disorders like hereditary hemorrhagic telangiectasia (HHT).²¹ Prevention involves sun protection to reduce long-term damage. Treatment options include sclerotherapy, laser therapy, intense pulsed light treatment, micro phlebectomy, thermocoagulation, and pulsed dye laser for HHT lesions.²² Overall, understanding the causes, types, and available treatments is crucial for managing telangiectasia effectively.

Skin pigmentation changes can result from various factors like genetics, UV exposure, medications, and skin diseases.²³ These changes manifest as hyperpigmentation (excess pigment) or hypopigmentation (reduced pigment) disorders like albinism, melasma, vitiligo, and post-inflammatory hyperpigmentation. Post-inflammatory hyperpigmentation (PIH) is a common acquired hypermelanosis triggered by inflammation, trauma, or procedures, particularly affecting individuals with skin of color.²⁴ PIH entails the presence of hyperpigmented patches in areas of inflammation, with more pronounced and enduring effects observed in individuals with darker skin tones. Treatment options for pigmentation disorders include anti-inflammatory medications, antioxidants, tyrosine inhibitors, and various plant extracts with anti-pigmentary effects.²⁵ Prophylaxis strategies for PIH encompass pretreatment and post-treatment approaches like topical agents and photoprotection. Photobiomodulation therapy (PBMT) using light sources has shown promise in treating both hypo and hyperpigmentation disorders by influencing melanin production and skin rejuvenation.

Loss of skin volume significantly contributes to facial aging, impacting every layer of the face. Factors such as aging, exposure to sunlight, and genetic predisposition can contribute to volume depletion, resulting in a sunken or drooping appearance. To counteract this effect, treatments like soft tissue fillers, fat transfers, and injections of hyaluronic acid gel are frequently employed to replenish lost volume. Additionally, techniques involving collagen stimulation, muscle control with botulinum toxin, and procedures like microlaser peels can help improve skin volume and overall facial cosmesis. Preventative measures include sun protection with sunscreens and antioxidants to mitigate volume loss caused by environmental factors.²⁶

Relationship between signs of skin aging and age

The relationship between signs of skin aging and age is multifaceted, involving both intrinsic and extrinsic factors that contribute to the visible and functional deterioration of the skin over time. Intrinsic aging is

manifested as fine wrinkles, loss of skin elasticity, and changes in the extracellular matrix components such as collagens and elastin, which are crucial for maintaining skin's structural integrity and function. Extrinsic factors, notably UV exposure, lead to photoaging, which exacerbates the aging process, causing more pronounced skin damage including severe wrinkles, laxity, and a rough-textured appearance. Research has shown that the dermal-epidermal junction (DEJ) flattens with age, leading to an increased likelihood of skin tears and breakdown under mechanical shear loads, indicating a direct correlation between structural changes in the skin and the aging process.²⁷ Additionally, the decrease in dermal water content and the expression levels of aquaporins (AQPs), which are critical for skin hydration, further contribute to aging-related skin dryness.²⁸ The aging process also affects skin's biomechanical properties, with intrinsic aging causing a decline in skin resilience and elasticity. This is further exacerbated by photoaging, which leads to significant loss of biomechanical function. Moreover, the accumulation of advanced glycation end products (AGEs) in the skin has been shown to correlate with age and is a significant marker of skin aging, affecting skin elasticity and blood perfusion.²⁹ Interestingly, studies have also identified a link between perceived age and cutaneous microcirculation, with individuals looking younger than their chronological age exhibiting higher microcirculation reactivity.³⁰ Furthermore, the relationship between skin atrophy and bone loss during aging suggests a systemic aspect of aging, where changes in skin can impact other bodily systems.³¹ The relationship between signs of skin aging and age is complex, involving both intrinsic genetic factors and extrinsic environmental exposures. These factors collectively contribute to the structural, functional, and perceptual changes observed in aging skin.

Limitations of chronological age as a predictor of skin aging

Chronological age, while a fundamental measure, has limitations as a predictor of skin aging due to the complex interplay of genetic, environmental, and lifestyle factors that influence the aging process. Research has shown that chronological aging and photoaging share fundamental molecular pathways, yet they manifest differently across individuals due to varying degrees of sun exposure and skin pigment, highlighting the environmental impact on skin aging beyond mere chronological age.³² Furthermore, the study of skin characteristics in middle-aged offspring of nonagenarian siblings versus their partners revealed no significant effect of familial longevity on skin aging, suggesting that genetic predisposition to longevity does not necessarily translate to slower skin aging.³³ The development of an objective, easy-to-apply method to assess biological skin age, which considers appearance and function, indicates that biological skin age can diverge significantly from

chronological age, being influenced by factors such as body mass index and hormonal status.³⁴

This divergence is further supported by the creation of a photonumeric scale for African-Americans to evaluate chronological skin aging, which identified increased age and greater body mass index as contributors to intrinsic skin aging, underscoring the role of lifestyle factors.³⁵ Moreover, the difference between biological and chronological age has been proposed as an indicator of skin aging, with research linking skin cell profile parameters to this difference, suggesting that individualized skin treatment strategies could be based on assessing this gap. Advanced imaging techniques and machine learning have also been employed to quantify skin aging, providing a data-driven approach that can differentiate between younger and older skin, indicating the potential for more nuanced aging assessments beyond chronological age. Additionally, the efficacy of topical treatments like retinoids in slowing the chronological aging of the skin by reducing matrix metalloproteinases (MMP) levels and enhancing procollagen synthesis underscores the ability to influence the biological mechanisms of skin aging, thus questioning the notion of chronological age as the sole predictor. Collectively, studies underscore the limitations of using chronological age as the sole predictor of skin aging, advocating for a multifaceted approach that considers biological, environmental, and lifestyle factors.^{32,36}

Aesthetic and functional impact of cutaneous aging

The aesthetic and functional impact of skin aging is multifaceted, involving both visible changes and alterations in skin's biomechanical properties. Aesthetically, skin aging manifests as fine lines, wrinkles, loss of elasticity and volume, rough-textured appearance, and uneven pigmentation, notably marked in photoaged skin. These changes are not merely cosmetic but reflect deeper structural and functional deteriorations. For instance, intrinsic aging leads to a biomechanical decline, with skin losing resilience and elasticity due to histological changes such as effacement of rete ridges and disorganization of papillary dermal elastic fibers. Extrinsic factors like UV exposure exacerbate these effects, causing severe loss of biomechanical function, evidenced by increased fatigue, hysteresis, and viscous "creep" in photo exposed sites. Functionally, aging skin experiences a reduction in its barrier function, elastic and mechanical properties, and vascular reactivity. This is partly due to epidermal thinning, increased MMP expression leading to collagen loss, and the impact of environmental factors such as pollution. The skin's ability to repair itself diminishes, with a noted decline in lipid content affecting the permeability of no lipophilic compounds and reducing the efficacy of topical medications.³⁷ Additionally, the skin immune system undergoes senescence, diminishing its ability to counteract infections and increasing the frequency of autoimmune and neoplastic diseases. Age-related changes

in skin mechanics, such as decreased stiffness and elastic recoil, significantly impact the aesthetic perception of skin, linking microstructural alterations with macroscopic changes. Addressing these changes requires an integrated approach, combining topical and systemic interventions to optimize aging towards healthy skin. This comprehensive understanding underscores the importance of both medical and cosmetic interventions in managing the aesthetic and functional impacts of skin aging.

Prevention and treatment of skin aging

The prevention and treatment of skin aging involve a multifaceted approach that addresses both intrinsic (chronological) and extrinsic factors, such as ultraviolet radiation, pollution, smoking, and stress. To combat these effects, various strategies and compounds have been identified. Sun avoidance and the use of sunscreens that protect against both UVB and UVA rays are primary preventive measures against photoaging.³⁸ Additionally, antioxidants play a crucial role in preventing skin aging by neutralizing free radicals and thereby reducing oxidative stress. For treatment, topical application of retinoids has been proven to reverse mild to moderate photodamage by enhancing collagen production and skin renewal.³⁹ Moreover, understanding the clinical, biochemical, and molecular changes associated with aging has led to the development of various interventions aimed at reducing, postponing, or repairing the effects of intrinsic aging and extrinsic environmental injury. In summary, the prevention and treatment of skin aging require a combination of protective measures against UV radiation, the use of antioxidants, and the application of compounds that promote skin renewal and repair. These strategies collectively address the complex biological process of skin aging.⁴⁰

CONCLUSION

Skin aging is a multifaceted process influenced by intrinsic and extrinsic factors, leading to structural and functional changes in the skin. The relationship between signs of skin aging and chronological age is intricate, with biological, environmental, and lifestyle factors influencing the aging process. Limitations of chronological age as a predictor of skin aging underscore the importance of considering individualized factors and employing advanced techniques like imaging and machine learning for more nuanced assessments. Moreover, the effectiveness of interventions such as retinoids in modulating skin aging pathways challenges the deterministic view of chronological age as the sole predictor, highlighting the need for comprehensive approaches.

The aesthetic and functional impact of skin aging extends beyond cosmetic concerns, reflecting deeper structural and functional deteriorations. Prevention and treatment strategies encompass a range of approaches, including sun protection, antioxidant therapy, and topical retinoids,

aimed at preserving skin health and mitigating the effects of aging. In conclusion, understanding the complexity of skin aging and implementing holistic approaches that consider individualized factors are essential for promoting skin health and well-being across the lifespan.

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