



Commentary

Skin aging revisited



Skin aging is both preventable and treatable, which is the major theme for this issue of *Clinics in Dermatology*. Skin aging is a topic worth revisiting, because it concerns our patients who wish to stay and feel younger-looking as time marches on. *Clinics in Dermatology* has presented variations on the subject on various occasions.^{1–3} Since the publication of these issues, there has been recently an explosion of new knowledge on the understanding of the mechanisms of skin aging and its management, emerging to be translated in clinical practice.

Eleven contributions have been assembled herein, to update readers on new advances in the field of skin aging, divided into those contributing to the understanding of skin aging mechanisms and those who report on the management of skin aging.

Understanding mechanisms of skin aging

The skin represents the first bearer of marks of time as well as an easily accessible model for the assessment and determination of the involved molecular mechanisms. One study⁴ in this issue describes the deterioration of important skin functions in intrinsic and extrinsic aging and the resulting clinical manifestations. These mirror several internal age-associated diseases, such as neurodegenerative, cardiovascular, skeletal and endocrine or metabolic skin diseases. The authors report on current molecular data, which indicate that skin aging, especially intrinsic aging, mirrors age-related deficiencies in the entire human body. These data and the development of new biologic technologies highlight the importance of the skin in aging research, which is likely to enable future interdisciplinary projects on internal diseases.

Another contribution⁵ reports on the predictability of the skin aging process, despite that the human appearance does not always correlate with chronologic age; for example, rare genetic disorders are characteristic for physical and cognitive stagnation. Ideally, it would be desirable to slow down the aging process with the hope of looking younger longer and improving good health and longevity. Evidence that this may

become possible results from data showing increases in average human life expectancy over the past century and the development of protective strategies against environmental influence, including sunscreens, healthy lifestyle, and use of antiaging skin products. Stem cell therapy may also play a role in future aging therapy.

This issue includes a review⁶ the different aspects of the genetics of skin aging. Several genome-wide association studies have identified single nucleotide polymorphisms; especially, *MC1R*, *SLC45A2*, and *IRF4* had genome-wide significant associations with skin aging in Caucasians, whereas ethnic variations may occur. On the other hand, epigenetic changes in DNA methylation taking place with age across various tissues, including the skin, may play a role in the individual speed of aging. At last, differential gene expression in aging is a hot topic for current research, with an increasing number of studies exploring how changes in gene expression relate to extrinsic and intrinsic aging within the epidermis, dermis, and other tissues of the human body. Progressive changes of gene expression occur in the skin from age 20 to 74 years, with an acceleration in the 60s and 70s.

Because it is the result of two overlapping processes, aging is didactically classified in “intrinsic” and “extrinsic” types. Intrinsic structural changes occur as a consequence of physiologic aging and are genetically determined; extrinsic relates to exposure to harmful events and habits, for example, smoking, bad diet, alcohol consumption, lack of sleep, stress, sun exposure, and environmental pollution. Aging may be decelerated by improving bad habits or covering signs of aging with various esthetic methods and food supplements. Another review⁷ details the current knowledge on stem cells and their ability to exhibit telomerase activity, to self-renew, and to differentiate into all three embryonic tissues. This challenges aging as a process which can possibly be reversed. Stem cells can promote regeneration of aged tissues and organs by replacing apoptotic and necrotic cells with healthy ones, and they have antiinflammatory and antiapoptotic properties by paracrine secreting growth factors and cytokines on the site of administration. Autologous adipose-derived stem cells are the most promising because they can be easily harvested in large

numbers with minimally invasive liposuction and, as such, represent a powerful tool in antiaging and regenerative medicine.

One report⁸ is about dermal aging, which can be linked to a great number of complications in routine dermatologic conditions with slow wound healing as an example of a severe complication in the elderly. This may be attributed to aged dermal fibroblasts that modify the tissue microenvironment via a shift in their soluble factors and extracellular matrix repertoire. This senescence-associated secretory phenotype can explain the particular proclivity of aged skin to develop malignancies.

Another contribution⁹ reports on the disturbance of structures and functions of the skin barrier during aging, such as the skin barrier structure, the permeability barrier function, the epidermal calcium gradient, epidermal lipid synthesis, stratum corneum lipid processing, cytokine production and response after insults, stratum corneum acidity and hydration, and the antimicrobial barrier. Patients with diabetes also show changes in the skin barrier similar to those in aged skin, and the characteristics of the skin barrier are very similar.

The term “dermatoporosis” was introduced a decade ago to highlight the need to pay attention to the problems posed by premature skin aging beyond esthetic considerations. People with this condition have a thinner skin that becomes fragile, tends to tear, and may lead to deep dissecting hematomas in the final stages, corresponding to a medical emergency. A review¹⁰ summarizes various studies that have demonstrated a high prevalence of dermatoporosis in the elderly, with women being more exposed than men. They present a scoring system for dermatoporosis, providing different strategies to treat and prevent this skin condition, as well as to how to follow up patients over time.

Management of skin aging

Ethnic skin is quickly emerging as the norm as the population becomes more diverse. Because there is a projected rise in the number of aging adults, one study¹¹ examines structural and functional variation of aging in ethnic skin types by contributions primarily found through PubMed with supplemental textbook chapters. Caucasian, African American, East Asian, and Hispanic skin has distinguishing features of aging, but all populations share dyspigmentation, rhytides, and skin laxity. Increased melanin content predisposes skin of color to a greater degree of hyperpigmentation, but skin thickness may protect against rhytides formation. Tailored prevention and treatment are also paramount in attaining favorable outcomes for this growing cohort.

Basal cell carcinoma (BCC) is the most commonly diagnosed type of skin cancer. BCCs are especially prevalent in the elderly population, given their association with cumulative sun exposure and other risk factors. Another contribution¹² outlines the geriatric concepts related to

the care of older adults with BCCs. They describe how a patient’s life expectancy can be estimated and combined with tumor characteristics to determine lag time to benefit, a concept to better understand whether patients experience the efficacy of a treatment within their life span. Further, they review the possibility of current BCC overdiagnosis and summarize the effectiveness, benefits, and risks of common treatments for BCCs, noting that all treatment modalities have special considerations when administered to older adults, but nonsurgical treatments might be preferable for older adults with a limited life expectancy. Ultimately, they argue that the decision of whether and how to treat a BCC should be the result of shared decision-making between the provider and the patient, and the decision should take into account not only tumor characteristics, but also patient values and preferences.

Smooth, wrinkle-free skin is associated with supposed attractiveness, youthfulness, and health, whereas rhytides have a negative effect on one’s perceived appearance, image, and self-esteem. Noninvasive esthetic procedures, such as laser or light therapy, have been used to achieve and attain a more youthful appearance. This issue includes a review¹³ of the wide range of laser types and devices available for the regeneration and healing of skin. Lasers and light sources for skin rejuvenation involve the removal of aged skin tissue via thermal heat from high-powered devices, which stimulate the surrounding tissues to recover through natural wound-healing processes. In contrast, photobiomodulation, which makes use of low energy lasers or light-emitting diodes, uses no heat and has shown positive effects in the reduction of wrinkles and improving skin laxity.

Aging skin shows wrinkles, uneven tone, loss of elasticity, and thinning. Skin health is considered one of the principal factors representing overall “well-being” and the perception of “good health” in humans. The last contribution¹⁴ reports on antiaging strategies that have been developed during the last decades to combat both aging signs and dysfunction. Understanding the mechanism behind skin aging is required for elucidation of the mechanism of action, and hence, the potential benefits of the claimed antiaging products. In this review, preventive measurements, cosmetologic strategies, photoprotection (systemic antioxidants or ultraviolet filters), and the mechanisms of action and the effectiveness of topical pharmaceutical agents, such as antioxidants (vitamins, polyphenols, and flavonoids) and cell regulators (retinols, peptides, hormones, and botanicals), are presented.

Skin functions deteriorate with aging and this results in the development of disorders and diseases, which jeopardize life quality or sometimes even life itself. Awareness of the pathophysiology of age-associated skin alterations and diseases as well as of preventive measurements to avoid skin damage is the first step for successful, healthy aging. Research to understand aging corroborates the best prevention of age-associated diseases including cancer.¹⁵ We hope that this issue of *Clinics in Dermatology* fulfills your educational expectations and wish you an interesting read.

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References

1. Serri R, Iorizzo M. Combating aging skin. *Clin Dermatol* 2008;26:105.
2. Wollina U. Geriatric dermatology. *Clin Dermatol* 2011;29:1-2.
3. Marinović B. The mature patient: Geriatric dermatology. *Clin Dermatol* 2018;36:107-108.
4. Zouboulis CC, Makrantonaki E, Nikolakis G. When the skin is in the center of interest—an aging issue. *Clin Dermatol* 2019;37:296-307.
5. Malik A, Hoenig LJ. Can aging be slowed down? *Clin Dermatol* 2019;37:308-313.
6. Flood KS, Houston NA, Savage KT, Kimball AB. Genetic basis for skin youthfulness. *Clin Dermatol* 2019;37:314-321.
7. Godic A. The role of stem cells in anti-aging medicine. *Clin Dermatol* 2019;37:322-327.
8. Strnadova K, Sandera V, Dvorankova D, et al. Skin aging: the dermal perspective. *Clin Dermatol* 2019;37:328-337.
9. Choi EH. Aging of the skin barrier. *Clin Dermatol* 2019;37:338-347.
10. Kaya G, Kaya A, Sorg O, Saurat J-H. Dermatoporosis, a prevalent skin condition affecting the elderly: current situation and potential treatments. *Clin Dermatol* 2019;37:348-352.
11. Venkatesh S, Maymone MBC, Vashi NA. Aging in skin of color. *Clin Dermatol* 2019;37:353-359.
12. Sreekantaswamy S, Endo J, Chen A, Butler D, Morrison L, Linos E. Aging and the treatment of basal cell carcinoma. *Clin Dermatol* 2019;37:375-379.
13. Hourel NN. The use of lasers and light sources in skin rejuvenation. *Clin Dermatol* 2019;37:360-366.
14. Zouboulis NN, Ganceviciene NN, Liakou AI, Theodoridis A, Elewa R, Makrantonaki E. Aesthetic aspects of skin aging, prevention, and local treatment. *Clin Dermatol* 2019;37:367-374.
15. Zouboulis CC, Makrantonaki E. Clinical aspects and molecular diagnostics of skin aging. *Clin Dermatol* 2011;29:3-14.