Ro J Prev Med. 2023, sept; 2 (3): 31–36

THE AGING PROCESS

Mădălina-Nicoleta Mitroiu[1], Roxana Elena Bohîlțea[1,2]

[1] Department of Obstetrics and Gynecology, Filantropia Clinical Hospital, Bucharest, Romania
[2] Department of Obstetrics and Gynecology, 'Carol Davila' University of Medicine and Pharmacy, Bucharest, Romania

Abstract

Aging represents the progressive deterioration of physiological integrity. This natural process leads to atrophy, decreased elasticity, and impaired metabolic and reparative responses in the skin. There is an increasing emphasis on "healthy aging." Chronic sun exposure leads to recurrent damage caused by the sun's ultraviolet light, known as photoaging. Environmental factors, in addition to sun exposure, also play a role in photoaging. Numerous studies have confirmed the role of cigarette smoke in accelerating skin aging. There are treatment options available for both types of aging.

Keywords: *aging, photoaging, sun protection, retinoids, botulinum toxin, filler injections, laser therapies*

Introduction

Aging is the progressive deterioration of physiological integrity, resulting in reduced functional capacity in the body. This is a significant risk factor for chronic human diseases, including cardiovascular conditions, diabetes, neurological degeneration, and cancer. Therefore, a growing emphasis on "healthy aging" raises essential questions in medicine. In recent years, unprecedented progress has been made in aging research, particularly in the discovery that the pace of aging is at least partially controlled by genetic components and various biological processes (1). In this article, we will address the topic of skin aging, attempting to divide this process into two main categories: physiological aging and photoaging.

What is skin aging?

It is a natural process that leads to atrophy, decreased elasticity, and impaired metabolic and reparative responses in the skin. These changes are distinct from causes like sun exposure, known as "photoaging," which we will address separately (2). The epidermis becomes thinner, and the dermo-epidermal junction flattens, increasing skin fragility due to tensile stress. Any traumatic action on the skin of older people, such as removing an adhesive film like a bandage, can cause detachment of the epidermis as the dermo-epidermal junction is weaker in this age group. Additionally, bleeding in the space between the epidermis and dermis can occur quickly (3).

The dermo-epidermal junction loses its architecture, reducing the available area for transferring nutrients, such as lipids, from the protective stratum corneum. This leads to the appearance of xerosis or dry skin and compromises the barrier function (3).

Reduced cell division of keratinocytes results in slowed epidermal renewal. This leads to a slower and prolonged migration of the basal layer of the skin towards its surface (3). Changes in cellular composition occur, reducing the number of melanocytes, immunologically active Langerhans cells, and an overall 50% reduction in nail growth (4).

Skin Changes Associated with Aging:

Decreased dermal vascularization leads to thinning and a decrease in the biosynthetic capacity of resident fibroblasts (5). These changes result in delayed wound healing. With advancing age, dermal collagen decreases by up to 75%, with the remaining collagen being fragmented and disordered (6). In the fourth age, there is a significant decrease in elastin biosynthesis, leading to the degradation of the elastic fiber network in the skin. Loss of hydration and skin elasticity occurs with changes in dermal glycosaminoglycan macromolecules (7). Loss of subdermal fat reduces thermal insulation, decreasing the ability of older individuals to retain heat. Tonic vasoconstriction and decreased sweat gland production capacity contribute to temperature regulation disruption with aging (8,9). Sensory perception of the skin decreases, especially in the lower limbs (10). Another critical role of the skin is vitamin D synthesis. This process, which occurs under the action of ultraviolet rays in the dermis, decreases with aging (11). A decrease in subdermal fat, which provides support for the skin, leads to wrinkles and laxity and increased susceptibility to trauma (12). Many age-related changes in sun-protected skin, such as thigh skin, appear reversible after topical administration of all-trans retinoic acid. After nine months of daily treatment with 0.025% tretinoin, the epidermis thickens, capillaries reappearance increases, and collagen and elastin content increases (13).

Chronic sun exposure leads to the appearance of recurrent damage caused by the ultraviolet light of the sun, known as photoaging. Photoaging causes most of the undesirable cosmetic skin changes. The changes that occur include the disorganization of cells in the epidermis, cellular dysplasia, and the appearance of atypical cells. In the dermis, the appearance of elastosis, amorphous aggregates of elastic fibers, a decrease in collagen content, and inflammatory infiltration at perivascular zones are consequences of photoaging (13).

The appearance of photoaged skin is characteristic; it sags, wrinkles appear, and it becomes rough, with a greater tendency to develop telangiectasias and hyperpigmentation. All these changes are partially reversible through topical treatment with retinoic acid (13).

Risk factors for photoaging:

Advanced age, prolonged sun exposure for professional or recreational reasons, male gender, and equatorial geographic regions are some risk factors for photoaging. Regarding skin types, individuals with lighter and less pigmented skin are at higher risk for sun damage and skin cancer. The key risk factor for photoaging is the amount of sun exposure a person has over their lifetime.

According to an Australian study, changes in skin texture associated with moderate to severe photoaging have been observed in 72% of men and 47% of women under the age of 30. The severity of photoaging increases rapidly after age 30 (14). In populations with darker skin, wrinkles become evident only around the age of 50, and their severity is not as great as in people with lighter skin of the same age (15).

A series of factors have been implicated in photoaging. Still, the most important factor is exposure to ultraviolet rays, which leads to the loss of structural integrity of the dermal extracellular matrix. Both ultraviolet A (UVA) and ultraviolet B (UVB) rays are involved in photoaging. More significant damage occurs from UVA exposure. These can penetrate deeper into the dermis than UVB and are at least ten times more present than UVB in terrestrial sunlight (16).

Visible light also plays an essential role in the process of photoaging. It represents at least 40% of solar irradiation. This light penetrates deeper into the skin due to its longer wavelength compared to UV radiation. It leads to the production of proinflammatory cytokines. While greater melanin content in the skin protects patients against UV radiation, it intensifies the harmful effects of visible

light, especially in people with darker skin tones (17,18).
Environmental factors, in addition to sun exposure, also play a role in photoaging. Air pollution - pollutants such as lead, smoke, carbon emissions, industrial particles, automobile emissions (nitrogen oxide), sulfur oxide emitted from industrial processes, and ground-level ozone are factors that contribute significantly to this process of skin degradation over time (19-24). Several epidemiological studies support the contribution of these factors (25).
Cigarette smoke- the role of cigarette smoke in accelerating skin aging has been confirmed by numerous studies (26-28). The smoker's face is characterized by perioral and periocular wrinkles and a complexion with a grayish appearance.

How to prevent photoaging?

We have numerous weapons against this type of aging, which we will enumerate below.
Sun protection- is the first line of defense against photoaging for all skin types. This includes avoiding sun exposure, using sunscreen, and wearing protective clothing (29). UV rays have the highest intensity between 10:00 a.m. and 4:00 p.m. in the summer months and at high altitudes (30,31). Snow and water reflect up to 90% of UV rays, while shade reduces the amount of UV by 50-90% (32,33). The use of sunscreens, as well as a sun protection factor (SPF) of 30 or higher, can provide adequate protection. Therefore, in addition to sunscreen creams, clothes, hats, and sunglasses offer reliable protection against UVB and UVA radiation, being very easy to use (34,35). A strict routine of sunscreen application increases the risk of vitamin D deficiency. This can be easily corrected by oral vitamin D supplementation (36).
Regarding patients already affected by photoaging, it is crucial to consider various factors before choosing treatment. The degree of impairment, expectations, the patient's financial availability, and compliance with treatment are important factors.
Patients should be educated about the application of sun protection throughout the year.
Topical retinoids - are the first-line therapy for patients already suffering from photoaging. Among the topical retinoids used for the treatment of photoaging are tretinoin, tazarotene (a synthetic retinoid), and adapalene (a third-generation synthetic retinoid). There are several possible local reactions when starting treatment, and patients should be informed about them. Skin irritation, peeling, redness, burning, dryness, exfoliation, and stinging may occur. These common side effects of retinoid treatment often lead patients to discontinue treatment. This treatment should not be initiated or continued during pregnancy, as it is teratogenic.

Complementary Therapies:

Cosmetics - are a category of topical products that can be taken without a prescription. This includes vitamins, antioxidants, plant extracts, and hydroxy acids, which can be helpful to some extent in the treatment of photoaging (37).
Chemical peels involve applying caustic chemicals to exfoliate the epidermis at a controlled depth. The result is skin regeneration, reduced pigmented spots, and smoothing fine wrinkles.
Topical fluorouracil - is used primarily for patients with actinic keratoses. It promotes wound healing, epidermal lesion healing, dermal matrix remodeling, and overall improvement in skin appearance (37,38).
Photodynamic therapy uses light-sensitive drugs and a light source to destroy diseased cells. It improves skin appearance by reducing fine wrinkles and skin pigmentation. It is also a good modality for treating actinic keratosis.

Other invasive treatments:

Botulinum toxin injection - is an injectable neuromodulator derived from neurotoxins produced by Clostridium botulinum. These bacteria inhibit neurotransmission between peripheral nerve endings and muscle fibers, leading

to peripheral muscle paralysis. When appropriately used, botulinum toxin injection is an excellent method for improving cosmetic defects caused by muscle contraction. Its effects are temporary, with muscle function returning to normal within a few months (38,39).

Filler injections—hyaluronic acid, collagen, or fat - these methods help to smooth out wrinkles by filling. They can also be used when restoring lost tissue volume is necessary (40). Laser therapies - Non-ablative technology leads to dermal remodeling by improving skin laxity, resulting in We use radiofrequency devices, fractional lasers, and infrared lasers for this purpose (41). Ablative technology's mechanism is ablating the epidermis and superficial portions of the dermis. It also remodels the collagen in the deep dermis (41).

Conclusions

Aging is a natural process that affects both the skin's functionality and appearance, resulting in wrinkles, hyperpigmentation, and other specific signs. It is essential to approach each case individually, considering the degree of impairment, patient expectations, and financial availability. Patient education about sun protection is also crucial in preventing and managing photoaging. By implementing an appropriate skin care regimen and treatments, we can contribute to maintaining healthy and youthful skin, even as we age.

References

1. Cai Y, Song W, Li J, Jing Y, Liang C, Zhang L, Zhang X, Zhang W, Liu B, An Y, Li J, Tang B, Pei S, Wu X, Liu Y, Zhuang CL, Ying Y, Dou X, Chen Y, Xiao FH, Li D, Yang R, Zhao Y, Wang Y, Wang L, Li Y, Ma S, Wang S, Song X, Ren J, Zhang L, Wang J, Zhang W, Xie Z, Qu J, Wang J, Xiao Y, Tian Y, Wang G, Hu P, Ye J, Sun Y, Mao Z, Kong QP, Liu Q, Zou W, Tian XL, Xiao ZX, Liu Y, Liu JP, Song M, Han JJ, Liu GH. The landscape of aging. Sci China Life Sci. 2022 Dec;65(12):2354-2454. doi: 10.1007/s11427-022-2161-3.
2. Blokzijl F, de Ligt J, Jager M, Sasselli V, Roerink S, Sasaki N, Huch M, Boymans S, Kuijk E, Prins P, Nijman IJ, Martincorena I, Mokry M, Wiegerinck CL, Middendorp S, Sato T, Schwank G, Nieuwenhuis EE, Verstegen MM, van der Laan LJ, de Jonge J, IJzermans JN, Vries RG, van de Wetering M, Stratton MR, Clevers H, Cuppen E, van Boxtel R. Tissue-specific mutation accumulation in human adult stem cells during life. Nature. 2016 Oct 13;538(7624):260-264. doi: 10.1038/nature19768.
3. Ashcroft GS, Mills SJ, Ashworth JJ. Ageing and wound healing. Biogerontology. 2002;3(6):337-45. doi: 10.1023/a:1021399228395.
4. Yaar M, Gilchrest BA. Skin aging: postulated mechanisms and consequent changes in structure and function. Clin Geriatr Med. 2001 Nov;17(4):617-30, v. doi: 10.1016/s0749-0690(05)70089-6.
5. Varani J, Dame MK, Rittie L, Fligiel SE, Kang S, Fisher GJ, Voorhees JJ. Decreased collagen production in chronologically aged skin: roles of age-dependent alteration in fibroblast function and defective mechanical stimulation. Am J Pathol. 2006 Jun;168(6):1861-8. doi: 10.2353/ajpath.2006.051302.
6. Russell-Goldman E, Murphy GF. The Pathobiology of Skin Aging: New Insights into an Old Dilemma. Am J Pathol. 2020 Jul;190(7):1356-1369. doi: 10.1016/j.ajpath.2020.03.007.
7. Uitto J. The role of elastin and collagen in cutaneous aging: intrinsic aging versus photoexposure. J Drugs Dermatol. 2008 Feb;7(2 Suppl):s12-6. PMID: 18404866.
8. Anderson RK, Kenney WL. Effect of age on heat-activated sweat gland density and flow during exercise in dry heat. J Appl Physiol (1985). 1987 Sep;63(3):1089-94. doi: 10.1152/jappl.1987.63.3.1089.
9. Inbar O, Morris N, Epstein Y, Gass G. Comparison of thermoregulatory responses to exercise in dry heat among prepubertal boys, young adults and older males. Exp Physiol. 2004 Nov;89(6):691-700. doi: 10.1113/expphysiol.2004.027979.
10. Perry SD. Evaluation of age-related plantar-surface insensitivity and onset age of advanced insensitivity in older adults using vibratory and touch sensation tests. Neurosci Lett. 2006 Jan 9;392(1-2):62-7. doi: 10.1016/j.neulet.2005.08.060.
11. Holick MF, Matsuoka LY, Wortsman J. Age, vitamin D, and solar ultraviolet. Lancet. 1989 Nov 4;2(8671):1104-5. doi: 10.1016/s0140-6736(89)91124-0.
12. McCullough JL, Kelly KM. Prevention and treatment of skin aging. Ann N Y Acad Sci. 2006 May;1067:323-31. doi: 10.1196/annals.1354.044.
13. Griffiths CE. The role of retinoids in the prevention and repair of aged and photoaged skin. Clin Exp Dermatol. 2001 Oct;26(7):613-8. doi: 10.1046/j.1365-2230.2001.00892.x.
14. Green AC, Hughes MC, McBride P, Fourtanier A. Factors associated with premature skin aging (photoaging) before the age of 55: a population-based

study. Dermatology. 2011 Feb;222(1):74-80. doi: 10.1159/000322623.
15. Goh SH. The treatment of visible signs of senescence: the Asian experience. Br J Dermatol. 1990 Apr;122 Suppl 35:105-9. doi: 10.1111/j.1365-2133.1990.tb16134.x.
16. Yaar M, Gilchrest BA. Photoageing: mechanism, prevention and therapy. Br J Dermatol. 2007 Nov;157(5):874-87. doi: 10.1111/j.1365-2133.2007.08108.x.
17. Lim H, Kang S, Chien AL. CHAPTER 2: Photodamage in Skin of Color. In Watson REB, Griffiths CEM, editors, Cutaneous Photoaging. Royal Society of Chemistry. 2019. p. 31-57. (Comprehensive Series in Photochemical and Photobiological Sciences). doi: 10.1039/9781788015981-00031
18. Mahmoud BH, Ruvolo E, Hexsel CL, Liu Y, Owen MR, Kollias N, Lim HW, Hamzavi IH. Impact of long-wavelength UVA and visible light on melanocompetent skin. J Invest Dermatol. 2010 Aug;130(8):2092-7. doi: 10.1038/jid.2010.95.
19. Kim KE, Cho D, Park HJ. Air pollution and skin diseases: Adverse effects of airborne particulate matter on various skin diseases. Life Sci. 2016 May 1;152:126-34. doi: 10.1016/j.lfs.2016.03.039.
20. Li M, Vierkötter A, Schikowski T, Hüls A, Ding A, Matsui MS, Deng B, Ma C, Ren A, Zhang J, Tan J, Yang Y, Jin L, Krutmann J, Li Z, Wang S. Epidemiological evidence that indoor air pollution from cooking with solid fuels accelerates skin aging in Chinese women. J Dermatol Sci. 2015 Aug;79(2):148-54. doi: 10.1016/j.jdermsci.2015.04.001.
21. Krutmann J, Liu W, Li L, Pan X, Crawford M, Sore G, Seite S. Pollution and skin: from epidemiological and mechanistic studies to clinical implications. J Dermatol Sci. 2014 Dec;76(3):163-8. doi: 10.1016/j.jdermsci.2014.08.008.
22. Vierkötter A, Krutmann J. Environmental influences on skin aging and ethnic-specific manifestations. Dermatoendocrinol. 2012 Jul 1;4(3):227-31. doi: 10.4161/derm.19858.
23. Lanuti EL, Kirsner RS. Effects of pollution on skin aging. J Invest Dermatol. 2010 Dec;130(12):2696. doi: 10.1038/jid.2010.323.
24. Vierkötter A, Schikowski T, Ranft U, Sugiri D, Matsui M, Krämer U, Krutmann J. Airborne particle exposure and extrinsic skin aging. J Invest Dermatol. 2010 Dec;130(12):2719-26. doi: 10.1038/jid.2010.204.
25. Just M, Ribera M, Monsó E, Lorenzo JC, Ferrándiz C. Effect of smoking on skin elastic fibres: morphometric and immunohistochemical analysis. Br J Dermatol. 2007 Jan;156(1):85-91. doi: 10.1111/j.1365-2133.2006.07575.x.
26. Model D. Smoker's face: an underrated clinical sign? Br Med J (Clin Res Ed). 1985 Dec 21-28;291(6511):1760-2. doi: 10.1136/bmj.291.6511.1760.
27. Daniell HW. Smoker's wrinkles. A study in the epidemiology of "crow's feet". Ann Intern Med. 1971 Dec;75(6):873-80. doi: 10.7326/0003-4819-75-6-873.
28. Rigel DS, Taylor SC, Lim HW, Alexis AF, Armstrong AW, Chiesa Fuxench ZC, Draelos ZD, Hamzavi IH. Photoprotection for skin of all color: Consensus and clinical guidance from an expert panel. J Am Acad Dermatol. 2022 Mar;86(3S):S1-S8. doi: 10.1016/j.jaad.2021.12.019.
29. Wang SQ, Balagula Y, Osterwalder U. Photoprotection: a review of the current and future technologies. Dermatol Ther. 2010 Jan-Feb;23(1):31-47. doi: 10.1111/j.1529-8019.2009.01289.x.
30. Rigel DS, Rigel EG, Rigel AC. Effects of altitude and latitude on ambient UVB radiation. J Am Acad Dermatol. 1999 Jan;40(1):114-6. doi: 10.1016/s0190-9622(99)70542-6.
31. Kromann N, Wulf HC, Eriksen P, Brodthagen H. Relative ultraviolet spectral intensity of direct solar radiation, sky radiation and surface reflections. Relative contribution of natural sources to the outdoor UV irradiation of man. Photodermatol. 1986 Apr;3(2):73-82. PMID: 3703716.
32. Moise AF, Aynsley R. Ambient ultraviolet radiation levels in public shade settings. Int J Biometeorol. 1999 Nov;43(3):128-38. doi: 10.1007/s004840050128.
33. Hatch KL, Osterwalder U. Garments as solar ultraviolet radiation screening materials. Dermatol Clin. 2006 Jan;24(1):85-100. doi: 10.1016/j.det.2005.09.005.
34. Wang SQ, Kopf AW, Marx J, Bogdan A, Polsky D, Bart RS. Reduction of ultraviolet transmission through cotton T-shirt fabrics with low ultraviolet protection by various laundering methods and dyeing: clinical implications. J Am Acad Dermatol. 2001 May;44(5):767-74. doi: 10.1067/mjd.2001.112384.
35. Marks R, Foley PA, Jolley D, Knight KR, Harrison J, Thompson SC. The effect of regular sunscreen use on vitamin D levels in an Australian population. Results of a randomized controlled trial. Arch Dermatol. 1995 Apr;131(4):415-21. PMID: 7726582.
36. Kligman AM. Introduction: What is cosmeceuticals. In: Procedures in Cosmetic Dermatology Series: Cosmeceuticals, 1st ed, Draelos ZD (Ed), WB Saunders, Philadelphia 2005.
37. Sachs DL, Kang S, Hammerberg C, Helfrich Y, Karimipour D, Orringer J, Johnson T, Hamilton TA, Fisher G, Voorhees JJ. Topical fluorouracil for actinic keratoses and photoaging: a clinical and molecular analysis. Arch Dermatol. 2009 Jun;145(6):659-66. doi: 10.1001/archdermatol.2009.97.
38. DasGupta BR. Structures of botulinum neurotoxin, its functional domains, and perspectives on the crystalline

type A toxin. In: Therapy with Botulinum Toxin, Jankovic J, Hallet M (Eds), Marcel Dekker, 1994. p.15.

39. Donofrio LM. Fat distribution: a morphologic study of the aging face. Dermatol Surg. 2000 Dec;26(12):1107-12. PMID: 11134986.
40. Kim KH, Geronemus RG. Nonablative laser and light therapies for skin rejuvenation. Arch Facial Plast Surg. 2004 Nov-Dec;6(6):398-409. doi: 10.1001/archfaci.6.6.398.
41. Ross EV, Grossman MC, Duke D, Grevelink JM. Long-term results after CO2 laser skin resurfacing: a comparison of scanned and pulsed systems. J Am Acad Dermatol. 1997 Nov;37(5 Pt 1):709-18. doi: 10.1016/s0190-9622(97)70106-3.