REJUVENATION OF THE AGING BODY

SURGICAL AND NONSURGICAL TREATMENTS

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Anatomy of body aging

Aging can commonly be described as a progressive, subtle impairment of biological functions that proceeds in each individual in a non-homogenous manner. In the same person, organs age at a different rate that is influenced by multiple factors, including their genetic make-up, lifestyle choices, and environmental exposures. The gradual decline in organ functionality reduces the ability to maintain homeostasis, resulting in an increased vulnerability to environmental challenge, and a higher risk of disease and death. The aging process, underpinned by a set of highly conserved mechanisms, is extremely complex, involving the interplay of many biological and physiological variables. Understanding its physiology is imperative to allow populations to grow old healthily and with a good quality of life, by developing specific interventions to prevent or slow down the natural aging process (**Table 2.1**).

Musculoskeletal aging

Musculoskeletal aging is detrimental to many bodily functions and involves tissue atrophy, loss of function in muscle, bone, tendon, ligament, intervertebral disk, and articular cartilage (Collino et al. 2014). Sarcopenia, a term describing the loss of muscle mass and strength, is driven by alterations in the metabolic and contractile functions of the muscle fibers. This process, particularly evident around the seventh decade of life, leads not only to decreased total body

Table 2.1 The physiological process involved in the aging process

Body system	Indication
Myoskeletal	Sarcopenia Osteoporosis Osteoarthritis Height loss/posture change
Adipose	Increase in fat mass Reduction of subcutaneous fat Increase in ectopic fat deposits
Vasculature	Reduced angiogenesis Decreased number of vessels
Skin	Decrease in collagen/elastin Discoloration Dryness Loss of sensory perception Limited vitamin D production

mass but also affects posture, gait and height. Cross-sectional studies comparing young and old muscle have shown that muscle mass is lost at a rate of 0.64–0.70% per year in women and 0.80–0.98% per year in men, with loss of muscle strength being 2–5 times greater than loss of mass (Mitchell et al. 2012). Age is also the most prominent risk factor for the initiation and progression of osteoporosis and osteoarthritis. Osteoporosis, characterized by compromised bone mass and strength, predisposes an individual to an increased risk of fractures. Bone tissue is modulated throughout the lifespan, but bone mineral acquisition peaks at around 20 years of age (Nordin 2008). Aging is also a major contributor to the development and progression of osteoarthritis (OA), a joint disease where biochemical changes and mechanical stress leads to the breakdown of joint cartilage. Stiffness, pain and decreased movement are typically seen in middle-aged to elderly people (Englund 2010).

Fat and connective tissue distribution

Fat mass and adipose tissue, the connective tissue laden with adipocytes that serves as an energy depot, mechanical pad and thermal insulator, are also influenced by age. Increased fat mass and redistribution of body fat with simultaneous accumulation of trunk and lower body fat and a decrease of subcutaneous adipose tissue are both associated with the aging process (Zamboni et al. 2014). The increase and redistribution of total fat mass peaks around the age of 65 years and is thought to be independent of associated body changes such as sarcopenia (Prentice & Jebb 2001). Computed tomography (CT) studies evaluating age-related body fat redistribution have demonstrated that subcutaneous fat located in the face, thighs and calves decreased while ectopic fat deposits in the abdominal, liver, pancreas, cardiac and intramuscular area increased (**Figure 2.1**) (Kotani et al. 1994).

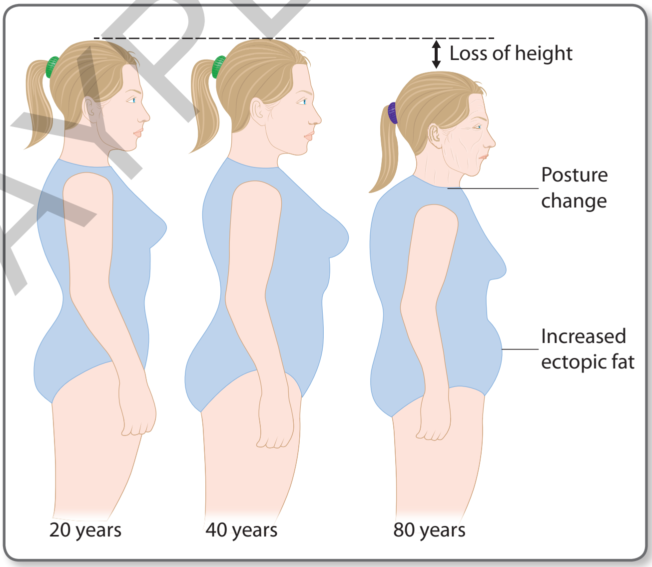

Figure 2.1 Major manifestations of aging on the body.

Vascular aging

Two main features characterize the vasculature of aging skin: reduction in the number of capillaries and vessels and variation in the vasculature distribution. Reduction in vasculature is most likely due to a process of gradual absorption and absence of the growth factors that stimulate angiogenesis. Decreased vessel size and vessel density accelerates around the age of 60 years and a progressive decline of the capillary network, which brings oxygen to the dermis, subsequently triggers its degradation. Thinning of the upper dermis accentuates the appearance of the underlying vessels, thus telangiectasia and varicose veins are common manifestations in the elderly (Bowes & Goldman 2002).

Aging skin

Skin undergoes many deleterious changes with the passing of time, such as atrophy, decreased elasticity, uneven pigmentation and impaired metabolic and reparative responses (Rittié & Fisher 2015). The dermal collagenous extracellular matrix, which confers strength and resiliency to the skin, undergoes gradual fragmentation. The elastin and collagen I network that constitutes the bulk of the dermis degrades and the matrix fibers lose their orderly organization, contributing to wrinkle formation. Flattening of the dermal-epidermal junction compromises epidermal resistance to shearing force, increases epidermal fragility and limits the flux of nutrients (including protective lipids in the stratum corneum) between the dermis and epidermis. This result in dry skin and a decrease in the barrier function of the skin. Thermoregulation, another key function of the skin, is also affected by the aging process, due to a reduced rate of sweating. Melanocytes in the basal layer of the human epidermis and the bulb of the hair follicles are evenly distributed in young individuals and produce melanin, which confers skin photoprotection. The aging process, however, affects both their activity and their number, leading to a net loss of around 10–20% of melanocytes per decade of life. Since this phenomenon does not progress in a homogenous manner, hypopigmenation, hyperpigmentation, ephelides and actinic keratosis are common manifestations in aged skin (Shlivko 2013). Additional skin changes associated with age are a decrease in sensory perception, limited capacity of vitamin D synthesis and loss of subdermal fat, which contributes to skin wrinkling and sagging.

Pathophysiology of aging

The physiology of the aging process is determined by both intrinsic and extrinsic factors (**Figure 2.2**).

Intrinsic factors

Intrinsic aging is largely defined by genetics, whereby fine-tuned molecular and physiologic degradation programs proceed in the whole body. Endogenous antioxidant mechanisms, such as glutathione transferase and superoxide dismutase enzymes, decline with age,

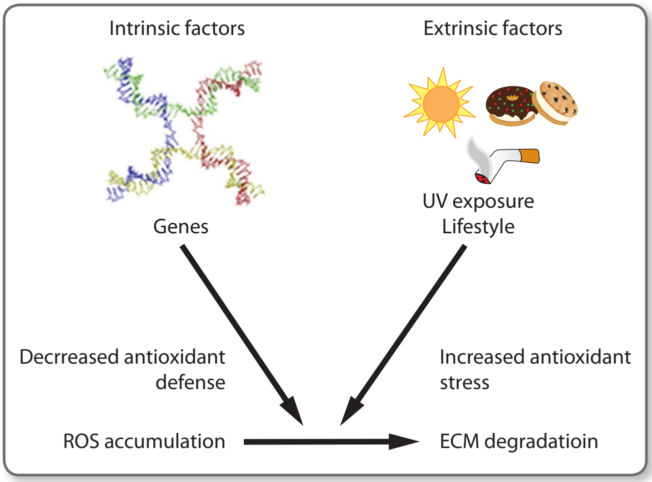

Figure 2.2 Intrinsic and extrinsic factors of aging.

allowing the accumulation of reactive oxygen species (ROS). These ROS can damage DNA and trigger cellular senescence and apoptosis. Telomeres, a stretch of nucleotides at the end of the chromosomes that are thought to be associated with maintenance of cellular health, also progressively shorten with age, leading to increased vulnerability to disease and tissue deterioration (Dangi-Garimella 2014). With age, growth factor (GF) levels involved in the body's inherent repair and proliferative mechanisms [(platelet-derived growth factor (PDGF), vascular endothelial growth factor (VEGF), transforming growth factor-β (TGF-β), epidermal growth factor (EGF)] decrease, with subsequent reduction of synthesis of new collagen, elastin, and glycosaminoglycan. Hormone changes also play a significant role in intrinsic aging. Disruption of the hypothalamic–pituitary–gonadal axis in women, which results in a steep decline in estrogen levels, leads to significant acceleration in the aging process with prominent skin aging and metabolic changes being some of the manifestations. Human growth hormone and dehydroepiandrosterone (DHEA) levels also decrease and can serve as biomarkers of aging (Baulieu 2000).

Extrinsic factors

Extrinsic skin aging occurs when external factors are involved, chiefly ultraviolet (UV) exposure, but also lifestyle choices such as the use of tobacco, poor nutrition and a lack of exercise.

Ultraviolet light exposure

Chronic exposure to the sun's ultraviolet light leads to profound effects on the skin known as photoaging. Ultraviolet B (UV-B) light penetrates the epidermis and is responsible for erythema and sunburn, whereas UV-A light penetrates into the dermis and is responsible for most of the skin damage associated with photoaging. UV light triggers molecular changes such as transactivation of transcription factors that induce gene upregulation, such as metalloproteinase (MMP). MMPs degrade collagen, elastin and other dermal extracellular matrix components, which are subsequently replaced with irregular and abnormal elastic material leading to the skin texture changes, formation of wrinkles, folds and furrows. A study comparing photodamaged versus sun-protected skin showed a decrease of 20% in total collagen in the sun-exposed skin (El-Domyati et al. 2002). Deterioration of the dermis leads to disorganization of vascularization, causing vessels to become visible at the skin surface as telangiectasia.

Smoking

Tobacco smoking is also strongly associated with accelerating aging in both women and men. The presence of nicotine decreases capillary blood flow to the skin, oxygen and nutrient deprivation then leading to deterioration and extracellular matrix degradation (Leow & Maibach 1998). The subsequent loss of vasculature contributes to wrinkling and discoloration. Smoking also leads to increased keratinocyte dysplasia, free radical formation and skin roughness. Wrinkle formation was found to be three times greater in smokers than in non-smokers, with a significant increase in the risk of wrinkles after 10 years (Farage 2008).

Lifestyle

Poor nutritional choices and a sedentary lifestyle are important factors that can advance the aging process. Reduced physical fitness impairs regeneration and remodeling of musculoskeletal tissue and encourages excess ectopic fat deposition. Nutrient deficiency such as lack of protein leads to increased muscle catabolism while suppressing fat breakdown. A diet lacking antioxidants such as vitamins E, C, D, B1, B12 and bioactive compounds (polyphenols, carotenoids, phytosterols) can also allow excess accumulation of ROS and reinforce the intrinsic aging process.

Facial aging

Aging affects every single part of the human body without discrimination, but the face is the first to present signs of aging. This is likely due to the fact that the face is the most exposed part of the body – from UV light to air pollutants; all external factors reach the face first. Facial anatomy is also unique in the sense that it comprises independent compartments that age separately from each other despite their close proximity. In youth, the face appears as a smooth, dynamic structure with very little shadowing between different anatomical regions. The process of aging brings changes in facial skin thickness, the composition of subcutaneous tissue, contours of the facial skeleton, and location of facial ligaments, leading to facial aesthetic unit separation, which has been found to play a significant role in the perception of facial aging (**Figure 2.3**) (Tan et al. 2015).

Selective resorption of the facial skeleton at specific sites occurs with age, including the superomedial and inferolateral aspects of the

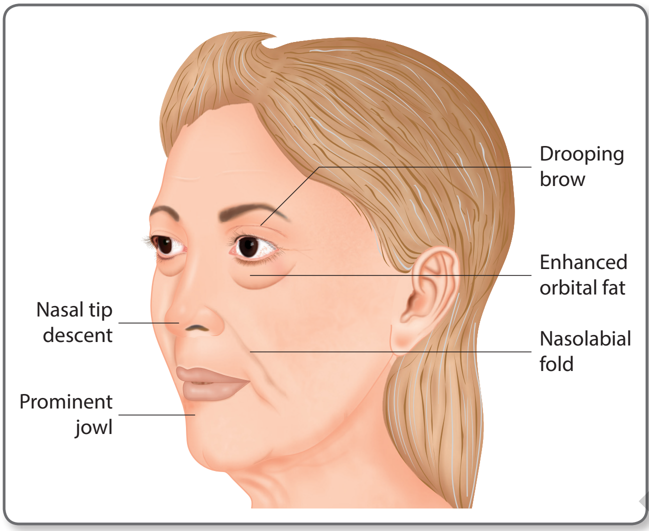

Figure 2.3 The key features of facial aging.

orbit, the medial suborbital and pyriform areas of the maxilla, and the prejowl area of the mandible. As the periosteum retrudes, facial muscles, fat and ligaments are repositioned. Ascension of the brow position leads to a 'drooped look' and recession of the superomedial orbital rim enhances the medial orbital fat pad. Descent of the nasal tip causes attachments between the upper and lower lateral cartilages to weaken, thus lengthening and enlarging the nose. In the midcheek, loss of projection of the maxilla leads to the development of the tear-trough deformity, malar mounds, and prominent nasolabial folds. In the lower face, reduced skeletal projection of the mandible lead to the appearance of a more prominent jowl (Mendelson & Wong 2012).

Prevention of aging

The fountain of youth – that is, any means that can prevent the consequences of intrinsic and extrinsic aging and increase longevity – has been pursued since the early centuries BC. From mythical tales to recent scientific studies, strategies have been identified and validated for their efficacy in delaying the aging process (**Table 2.2**).

Diet and exercise

A healthy diet, adequate sleep and exercise is essential to preserve the body's intrinsic regenerative, proliferative and repair mechanisms. A diet rich in fiber, monounsaturated fatty acids and antioxidant rich foods is associated with longevity and can offer protection against the development of several chronic diseases. Good nutrition and physical activity such as weight bearing exercise are also fundamentally important for musculoskeletal health, as several studies have demonstrated that both factors can delay muscle and bone atrophy and age-associated fat redistribution.

Table 2.2 Examples of strategies to delay the aging process

Anti-aging strategy	Examples
Lifestyle	Avoidance of smoking, sun exposure and stress Regular exercise Healthy, balanced diet Adequate sleep
Topical agents	Antioxidants Hormones replacement therapy Growth factors, PRP, stem cells
Non-invasive procedures	Chemical peels Laser/light devices Radiofrequency Dermal fillers (HA, CaHA, PLLA)

CaHA, calcium hydroxylapatite; HA, hyaluronic acid; PLLA, poly-L-lactic acid; PRP, platelet-rich plasma

Cosmeceuticals

Agents combining the functions of a cosmetic and a drug, known as cosmeceuticals, are commercially available and contain active ingredients that can prevent or reverse aging. The most commonly used and evaluated are antioxidants and sunscreens. Broad-spectrum sunscreens that block both UV-A and UV-B light are efficient measures to protect the skin and prevent the dramatic effects of photoaging. In a recent randomized clinical trial, a cohort of 903 participants randomized to either daily or discretionary use of broad-spectrum sunscreen use showed that individuals who used sunscreen daily did not show skin aging compared to those in the discretionary group (Hughes 2013).

Tretinoin and anti-oxidant vitamins

A derivative of vitamin A, tretinoin, has been extensively studied and conclusively shown to reduce the signs of photoaging by simultaneously stimulating dermal fibroblasts and suppressing MMP formation. Tretinoin can also prevent and reverse age-related changes in sun-protected skin as shown in a study in which, after 9 months of daily treatment with topical tretinoin cream 0.025%, the epidermis was shown to thicken, and collagen and elastin levels increased (Brenner & Dascalu 1991). Topical application of antioxidant vitamins B, C and E has also been shown to promote collagen production and interfere with the breakdown of the skin matrix.

Hormone treatments

Hormone replacement and supplementation is another strategy to prevent aging. The most profound effects are illustrated in postmenopausal women whose skin is significantly improved with estrogen replacement therapy or topical estradiol application. Growth hormone and DHEA (the precursor of androgen and estrogen) therapies also have vocal advocates for their impact on longevity and antiaging benefits. However, no clinical trial has supported these claims and their use remains controversial.

Growth factors

Growth factors, platelet-rich plasma (PRP) and stem cells that secrete growth factors comprise a new, growing area of research in aging prevention. PDGF, VEGF, TGF-β and EGF, with their pleiotropic effects on physiologic processes that regulate cell regeneration, are included in topical formulations and clinical studies are continuously evaluating their efficacy. Although data is preliminary and not of the highest level of evidence, it is clear that technological advances will soon harness the potential of these agents to delay aging (Fabi & Sundaram 2014).

Other techniques and treatments

Cosmetic medicine currently has an expansive armamentarium of approaches – both minimal and noninvasive – to encourage tissue regeneration, repair and growth. Driven by a goal to ameliorate aesthetic conditions and 'restore' youth, these procedures may also prevent and delay the aging process. Chemical peels, laser and light devices and radiofrequency instruments for skin rejuvenation aim at selective destruction of damaged tissue allowing the natural wound healing processes to restore a new healthy layer of skin. Highly effective in combating extrinsic aging such as photoaging, these strategies can also delay intrinsic aging by stimulating the local accumulation of growth and other restorative factors. Soft-tissue fillers can also trigger molecular and cellular processes with anti-aging effects. Hyaluronic acid (HA), calcium hydroxylapatite (CaHA) and poly-L-lactic acid (PLLA) all have bio-stimulatory properties that activate fibroblasts to repair and rejuvenate the local tissue (Gancevicien e & Liakou 2012).

Conclusion

Advances in our understanding of the physiologic mechanisms that drive the aging process, the extrinsic and intrinsic factors that contribute to it and the consequences to the face and body are allowing numerous options to impede and even prevent it. Aesthetic dermatology is taking its place in the forefront of aging research by inventing and scientifically evaluating devices, procedures, local and systemic therapies that can soon grant 'healthy cosmetic aging' to all.

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Thanks to advances in nonsurgical treatments and minimally invasive techniques, practitioners of aesthetic medicine are able to offer a wide range of options to patients seeking a naturally rejuvenated appearance.

Rejuvenation of the Aging Body: Surgical and Nonsurgical Treatments is a practical guide to the principles of aesthetic medicine and the clinical application of the interventions on offer. The book focuses on the techniques used to treat each region of the body and manage special indications such as cellulite. From neck to toe, each chapter describes the most suitable techniques using before and after photographs to demonstrate the beneficial results of each treatment.

Extensively illustrated and written in a practical, clinically-oriented style, *Rejuvenation of the Aging Body* is the ideal reference for physicians and surgeons at all levels who wish to employ the latest body rejuvenation techniques in their daily practice.

- Covers the whole body, from rejuvenation of the neck, hands, chest and trunk, to the lower extremities
- Discusses the full range of techniques including ultrasound, laser treatments, topical therapies and small molecule injectable biologics
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