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Theory and practice

Skin aging

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Abstract

Irreversible skin aging changes usually begin early in the second decade of life, though the external signs may be not visible for a long time. Skin aging is a complex biological process resulting from both intrinsic, or genetically programmed, changes that develop with time and extrinsic impacts caused by environmental factors. A number of extrinsic factors often act together with the physiological aging process. Extrinsic factors that prematurely age the skin are repetitive facial expressions, gravity, bad sleeping positions, smoking, etc. The external signs of skin aging are fine wrinkles, thin and transparent skin, pigment spots, loss of underlying fat, sagging skin, dry skin with or without itch, inability to sweat sufficiently, graying hair, hair loss, unwanted hair, thinning of the nail plate, disappearance of the nail half-moons, ridges. Changes and reduction of the blood vessels are an essential and permanent feature in the skin of elderly individuals.

It is not possible to stop or even appreciably slow down the intrinsic aging process, however everybody is able to attenuate the signs of premature aging by protecting skin from the sun, quitting smoking, eliminating harmful facial exercises, abolishing diseases influencing skin aging, etc.

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Introduction

While age-related skin changes usually begin at twenties, the external signs of intrinsic aging may be not visible for decades. These signs are fine wrinkles, thin and transparent skin, loss of underlying fat leading to hollowed cheeks and eye sockets, as well as a noticeable loss of skin firmness on the hands and neck, shrink of the skin due to bone loss, dry skin that may itch, inability to sweat sufficiently to cool the skin, graying hair, hair loss, unwanted hair, thinning of the nail plate, disappearance of nail half-moons, and ridges. Genes control how quickly the normal aging process unfolds.

A number of extrinsic factors often act together with the normal aging process to prematurely age the skin. Often premature aging is caused by sun exposure. Other external factors are repetitive harmful facial expressions, gravity, bad sleeping positions, smoking, wrong diet, etc.

Skin as an organ

Skin is the largest body organ of the integumentary system that guards underlying muscles and organs. It serves as a protective shield against harmful temperature,

light, injury, and infection. Skin also stores water, fat, vitamin D, senses painful and pleasant stimulation. Human skin is about 2 mm thick. On average, an adult has about 2 square meters of skin which weighs about 2.7 kg. The outer skin layer, the epidermis, is a tough layer that contains melanin protecting against the rays of the sun and giving the skin its colour, and elements of the immune system. The second layer (located under the epidermis) is called the dermis. It contains the network of blood vessels, nerve endings, sweat glands, sebaceous glands, hair follicles, and hair muscles. Under these two skin layers lies a fatty layer of subcutaneous tissue. Throughout the body, the skin's characteristics vary in thickness, colour, texture, hair follicles. Asian and African race skin exhibits increased dermal thickness, collagen, and melanin content as compared with Caucasian skin.

Physiological aging of the skin

Skin aging is a complex biological process resulting from both intrinsic, or genetically programmed, aging that occurs with time and extrinsic aging caused by environmental factors. The turning-point occurs in the menopause (andropause). The estrogen receptor has been detected on the cells of the skin. Accordingly, dermal cellular metabolism is influenced by the hypoestrogenoemic state of menopause, leading to changes in the collagen content and alterations in the concentration of glycoaminoglycans (GAG). A reduction in hydrophilic glycosaminglycans leads to a direct reduction in water content which influences the skin turgor. Decorin, the main proteoglycan in skin, has a small size with a core protein of approximately 40kDa and one chondroitin sulfate / dermatan sulfate glycosaminoglycan chain. The main function of decorin is to regulate the collagen matrix assembly. Reducing the length of the decorin, the GAG chain reduces the distance between collagen fibrils. Collagen becomes sparser and less soluble in intrinsically aged skin, but is thickened and more soluble in extrinsically aged areas. Changes in skin collagen lead to diminished skin strength.

Elastin, an important extracellular skin component, degrades slowly and accumulates damage with intrinsic aging. Increased synthesis of abnormally structured elastin occurs predominantly in photoexposed areas. This leads to an age-related accumulation of aberrant elastoic material clumped in the papillary dermis. Generally, age leads to an increased folding and decreased interaction of proteins with water. Despite increased GAGs in aged skin, these are abnormally deposited on the elastoic material and cannot interact properly with water. Hence, in aged skin, water is found in the tetrahedron form, bounded with similar rather than other molecules. Changes in the macromolecular metabolism of the dermis are a major factor leading to skin aging [1]. Specifically, the accumulation of elastosis material is accompanied by the degradation of matrix proteins, which is mediated by matrix metalloproteinase (MMPs) in skin aging. Molecular alterations in the dermis include decreased collagen synthesis, MMP induction, and abnormal accumulation of elastic fibers and proteoglycans [2–4].

The accumulation of abnormal elastic material, termed solar elastosis, is the prominent histopathologic alteration in photoaged skin [5, 6].

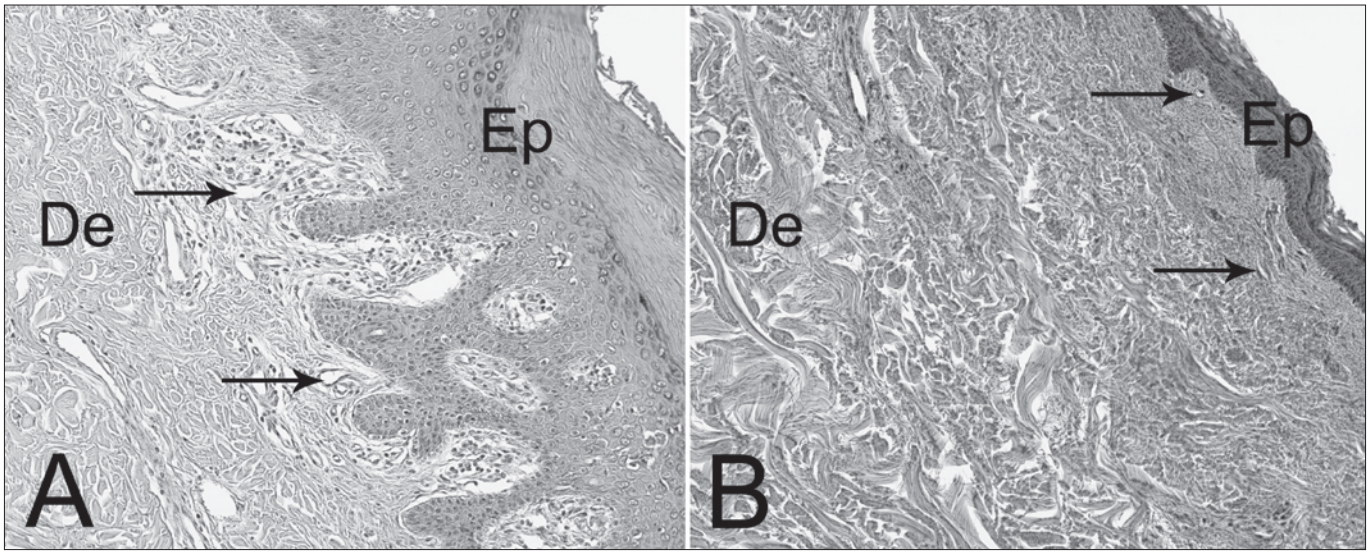

Figure. Human skin biopsies: from young patient (panel A) and aged patient with atrophic epidermis and dermal papillae, and scarce blood vessels (panel B). Stained with H & E, original magnification × 100. Ep – epidermis; De – dermis; arrows indicate some blood vessels

Lipid content appears to decrease with age, although the proportion of different lipid classes remains fairly constant [7]. A reduction of the microvasculature has been observed in the skin of all elderly individuals (Figure). Capillary blood flow velocity decreases significantly in postmenopausal women. Postmenopausal flushing is due to profound vasodilatation in the dermal papillae.

Hair growth is also influenced by the hormonal milieu, and consequently hair loss has been associated with the beginning of menopause [8]. The increased prevalence in the elderly of chronic wound-healing conditions, such as venous and diabetic ulceration, is firmly established.

The ageing process, both intrinsic and extrinsic, is also believed to be influenced by the formation of free radicals, also known as reactive oxygen species.

Wrinkling and pigmentary changes are directly associated with photo-ageing and are considered its most salient cutaneous manifestations. Skin aging and good looking depend on a variety of factors: lifestyle, diet, heredity and personal habits. While no one can stop or even slow down the intrinsic aging processes, everybody can prevent and hide the external signs of premature aging by protecting the skin from the sun, quitting smoking, eliminating bad facial exercises, etc.

Tobacco smoking and skin aging

Epidemiological studies demonstrated that tobacco smoking is one of the numerous factors contributing to premature skin aging. Other factors include age, sex, pigmentation, sun exposure history, and alcohol consumption [9–12]. Tobacco smoking exerts its deleterious effects on skin directly through its irritant components on the epidermis and indirectly on the dermis via blood circulation [10, 13]. The decreased moisture in the stratum corneum of the face contributes to facial wrinkling due to direct toxicity of the smoke. Pursing the lips during smoking with contraction of the facial muscles and squinting due to eye irritation from the smoke might cause the formation of wrinkles around the mouth and eyes [14]. Boyd et al. have reported that tobacco smoking enhances the effect of solar elastosis in subjects averaging 42 pack-years of tobacco smoking [15]. *In vitro* studies using cultured skin fibroblasts demonstrated that tobacco smoke extracts induce an increase in tropoelastin. This too might be a cause of premature skin aging.

Hot climate and skin aging

The skin is a highly exposed organ during vacation times, especially during travel to countries with subtropical and tropical climates. Prolonged stay in these countries significantly increases the risk of contacting rarely seen dermatoses such as leishmaniasis, larva migrans and myiasis. The bites of various flies may provoke itching and excoriations that may be infected with *Staphylococcus aureus* and / or hemolytic streptococci, resulting in impetigo, furunculosis or erysipelas. Elderly persons spending weeks in the tropical sun may develop drug-induced phototoxic or photoallergic rash due to concomitant medication for cardiovascular or rheumatic diseases. Acute sunburn is considered a short-lasting problem, but it increases the risk of malignant melanoma later. Mucocutaneous manifestations arising weeks and months after returning from vacation should raise suspicions of sexually transmitted syphilis and HIV.

Disease-caused acceleration of skin aging

There is a broad and diverse spectrum of vasculitic syndromes. These syndromes affect the skin with varying levels of associated systemic manifestations, running the gamut from a self-limited, localized, cutaneous phenomenon to a rapidly progressive, multiorgan disease. The majority of cases of cutaneous vasculitis show a neutrophilic small vessel vasculitis that can be either a primary (idiopathic) disorder (e. g., cutaneous leukocytoclastic angiitis) or a secondary disorder associated with drugs, infection (e. g., streptococcal infection, viral hepatitis) or underlying disease (e. g., connective tissue disease, malignancy) [16].

Sjögren's syndrome (SS) is an autoimmune disease characterized by exocrine gland involvement. The skin is affected in nearly half of SS patients. Cutaneous manifestations consist of xerosis, angular cheilitis, eyelid dermatitis, pruritus, cutaneous vasculitis (frequently manifesting as palpable purpura), and erythema annulare. Most of them are nonspecific and less severe than the oral, ocular, or musculoskeletal symptoms [17]. Skin manifestations can be observed in autoimmune diseases such as rheumatoid arthritis (RA), dermatomyositis (DM) and Behçet syndrome (BS). In RA, the most widely recognized skin lesion is the rheumatoid nodule. Other cutaneous manifestations can be observed either as non-specific or related to the disease itself and / or to the commonly used drugs. In DM, skin manifestations are frequent and include a heliotrope rash (blue-purple discoloration) on

the upper eyelids with edema, a flat red rash on the face and upper trunk, and erythema of the knuckles with a raised violaceous scaly eruption (Gottron rash). The most typical skin manifestations are nodular lesions which are commonly seen in BS and may be due to panniculitis (erythema nodosum (EN)-like lesions) or superficial thrombophlebitis [18].

Skin aging in progeria

Progeria, also known as the Hutchinson–Gilford syndrome, is an extremely rare inborn condition, initially reported by Johnathan Hutchinson in 1886 and further described by Hastings Gilford in 1904. Transmission is most likely from a sporadic autosomal dominant mutation. The patients usually appear normal at birth. Clinical manifestations are evident by the first or second year of life and include the physical characteristics usually associated with the elderly. Histopathologic changes occur primarily in the skin, bone, and cardiovascular tissues, while other organs appear to be unaffected. Current research suggests a genetically based underlying defect of hyaluronic acid that may possibly account for the entire process. Werner's syndrome (adult onset progeria) is also a rare form of autosomal recessive genodermatosis associated in almost 80% of cases with mutation of the WRN gene. Rapid aging syndrome is characterized by a short stature with skin and hair anomalies (early graying of the hair, alopecia, depilation, sclerosed skin), orthopedic complications (flat foot, hallux valgus and other joint deformations) as well as systemic signs (early cataract, premature and diffuse atherosclerosis, endocrinopathies [19, 20] and a high risk of certain types of cancer (sarcomas, myeloid blood dyscrasias).

Principles of the aged skin care

The dramatic increase in the aging population and the psychosocial impact of skin aging has created a demand for effective interventions. Intrinsic and extrinsic aging of the skin follow different pathways, but the end result is similar. Treatment options include cosmeceuticals, laser rejuvenation, chemical peels, and microdermabrasion. The advances that have been made in the past 25 years in the understanding of the clinical, biochemical, and molecular changes associated with aging have led to the development of many different approaches to reduce, postpone, and in some cases repair the untoward effects of intrinsic programmed aging and extrinsic environmental injury [21]. The architectural frameworks of the skin microcirculation are rather complex and change continuously with aging. In females, this decline in the effectiveness of skin repair mechanisms follows the menopause, and a series of clinical studies have identified estrogens as endogenous enhancers of healing processes. The administration of 17 beta-estradiol, either systemically or topically, has been shown to reverse the fundamental repair defects observed in postmenopausal women. By contrast, androgenic species retarded repair and interfered with the accumulation of the structural proteins that reconstitute the damaged dermis. Since estrogen-based hormone replacement therapy produces wide-ranging effects, not all of which are considered to be desirable, more recent studies have sought to identify downstream mediators of estrogenic effects in order to formulate better targeted strategies for improving skin repair in the elderly [22]. Preventing the effects of extrinsic aging involves using sunscreen – the right product used in the right amount, at the right time, in the right places [23]. Different cosmeceuticals include antioxidants, growth factors, peptides, anti-inflammatories / botanicals, polysaccharides, and pigment-lightening agents.

The correct use of moisturizers and cleansers is an integral component of the skin care regimen for any patient with skin problems. When used appropriately, these products not only improve skin hydration by reducing transepidermal water loss, but also help to restore the skin barrier and improve the aesthetic appearance of the skin. Proper moisturizing and cleansing are essential components of an overall skin treatment plan to ensure a satisfactory outcome in patients [24].

Growth factors, in addition to their crucial role in cutaneous wound healing, are also beneficial for skin rejuvenation. The antiaging effects of some skin creams is based on a mixture of human growth factors and cytokines, which was obtained through a biotechnology processes using cultured human fetal fibroblasts. Topical application of growth factors and cytokines is beneficial in reducing external signs of skin aging [25]. The response to cosmetic treatment modalities differs in patients of a darker skin pigmentation, and this needs to be recognized by the cosmetic and laser surgeon.

Antioxidants protect the cells from the damaging effects of oxygen-free radicals. Antioxidants include vitamins A, C, E and betacarotene, and are available in ointment, cream, lotion, and oral supplement forms. Some people use a vitamin-A based cream, or creams containing alpha-hydroxy acids, to diminish the appearance of

age spots and wrinkles. Laser treatments and bleaching are other options for removing age spots. Frequent moisturizing with an over-the-counter cream or lotion can relieve dry, itchy skin. Some conditions of aging skin, such as seborrheic keratoses, broken blood vessels, and purpura require no treatment. However, they can be removed or their appearance diminished if they become irritated or are unsightly. Actinic keratoses are removed from the skin.

Dermabrasion, laser resurfacing, chemical peeling, and some topical treatments can influence skin, giving it a smoother and refreshed appearance. Treatments administered for menopause, in particular hormone replacement therapy, alter its effects on the basic components of the skin. In conclusion, specific care and treatment do not stop natural aging processes in the skin, nevertheless, they can dramatically change the external sings of aging.

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ODOS SENĖJIMAS

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Santrauka

Negrįžtami odos pakitimai atsiranda gyvenimo trečiajame dešimtmetyje, tačiau jie dar ilgai lieka nepastebimi. Odos senėjimas – tai sudėtingas biologinis procesas, veikiamas genetinės organizmo programos bei išorinių veiksnių: veido mimikos, netinkamos padėties miegant, rūkymo ir kitų. Senstant atsiranda smulkių raukšlių, oda plonėja, tampa permatoma, pigmentuota, sukritusi, sausa, išvagota.

Neįmanoma sustabdyti odos senėjimo, sąlygoto vidinių procesų, tačiau jį galima sulėtinti, apsisaugant nuo saulės, nerūkant, vengiant žalingos mimikos, gydant odą veikiančias ligas.

Raktažodžiai:
oda, senėjimas