Lifestyle Factors Affect Skin Health

THE BODY'S LARGEST ORGAN FACES A BATTERY OF INSULTS EVERY DAY.

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Social perceptions and value judgments are often based on appearance. Dull, tired skin is indicative of aging. Wrinkles, under-eye puffiness, uneven skin tone and volume loss around eyes, mid face and lips add years to one's appearance. Aging is a complex phenomenon involving both intrinsic and extrinsic processes that contribute to a loss of structural integrity and physiological function of the skin. Factors contributing to aging can be divided into four main categories: biological, environmental, mechanical and lifestyle. We present here lifestyle and atmospheric factors which affect skin and overall health.

YOU ARE WHAT YOU EAT

Dietary factors and nutritional supplements certainly influence skin aging. Nutritional deficiencies can cause cutaneous signs such as dermatitis, alopecia and depigmentation. Frequent fast-food consumption is a major health concern since most fast food is rich in glucose, saturated fats, trans fats, simple carbohydrates, glycated proteins and sodium, and devoid of active antioxidants. When glycated proteins are consumed, they are absorbed in the gut with approximately 30% efficiency and circulate through the bloodstream. They are pro-inflammatory and accumulate on nucleic acids, proteins and lipids, promoting such widely diverse diseases as diabetic sequelae, pulmonary fibrosis and neuro-degeneration.[1]

Trans fats found in processed foods like margarine and fast food can clog arteries, which takes away elasticity from the skin. High glycemic index foods such as bread, chips, popcorn and cake are rapidly digested and absorbed which causes rapid spikes in blood sugar levels. These spikes affect biochemical functions like the insulin pathway and may affect blood vessels and accelerate the aging process. High blood sugar levels can affect collagen tissues and make skin vulnerable to lines and wrinkles.

Artificial colors enhance the visual appeal of food and nonfood products. Some synthetic colors, like tartrazine, have adverse effects on human health and especially young children. Tartrazine is an artificial lemon-yellow azo dye, recognized as E102 or C.I. 19140 or FD&C Yellow 5 and used for the coloring of food. Tartrazine may be found in nonfood products like soaps, cosmetics, shampoos and other hair products, crayons and stamp dyes. A diversity of immunologic reactions has been recognized in tartrazine consumption, comprising general fatigue, nervousness, migraines, clinical depression, purple skin spots and sleep disruption. Either consumption or cutaneous contact with a material containing tartrazine can produce symptoms of sensitivity.[2]

Pharmaceuticals are the major part of treatment of various

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disorders. Drugs can induce or enhance skin diseases such as phototoxicity, skin pigmentation, acne, itching and psoriasis. Drugs can cause hair disorders like alopecia. Penicillin, sulfa, phenyl-butazone and tetracycline are the most common drug inducing various skin disorders.[3]

Studies have clearly shown varying associations exist between tobacco or alcohol use, and skin photoaging and facial aging. Smoking generates free radicals which, in turn, damage skin repair mechanisms and reduce collagen and elastin synthesis, which leads to premature skin aging. In our studies, we saw a major decline in glutathione peroxidase clearly associated with smoking and alcohol. Smoking can also cause cutaneous micro vascular contraction that increases in relation to the duration and amount of exposure. Research shows alcohol dramatically affects appearance and skin features. Drinking alcohol causes dehydration, depleting skin blood's capillaries flow. Chronic alcohol consumption has detrimental impacts on skin health, impairing the skin's antioxidant defense system by decreasing dermal carotenoid concentrations. Alcohol also causes peripheral vasodilation, which can lead to dilated facial capillaries.[4]

STRESS & SKIN

The skin and the central nervous system share several neurotransmitters, hormones and receptors. Psychological stressors are known to trigger the immune system and have an influence on both innate and acquired immunity. A number of studies provide clear evidence that psycho-social factors such as depression and anxiety have a serious effect on the outcome of numerous medical conditions, including those of the skin. Psychological factors and stress can lead to skin conditions such as psoriasis, atopic dermatitis, acne, urticaria, pruritus and alopecia.[5]

Clinical observations have suggested that there is an intrinsic connection between psychological state and skin diseases. Chronic psychological stress stimulates the autonomic nervous system, renin-angiotensin system and the hypothalamic-pituitary-adrenal axis. Prolonged activation can result in chronic immune dysfunction, increased reactive oxygen species (ROS) production and DNA damage, which are known contributors to skin aging. Sleep deprivation affects features relating to the eyes, mouth, and skin. The investigators reported drooping eyelids; red, swollen eyes; dark circles under the eyes; pale skin, wrinkles/fine lines, and drooping corners of the mouth.

An analytic cross-section study was conducted on 400 subjects—200 patients with primary psychiatric disorders and 200 age- and sex-matched individuals free from primary psychiatric disorders. Researchers found that infectious skin diseases are the most common skin disease categories in psychiatric patients. Although psychogenic skin disorders occur exclusively in primary psychiatric disorder patients, it is much less frequent than the infectious skin diseases overall.[6]

Stress can lead to a variety of skin issues.

An Australian Longitudinal Study, conducted on 6,630 women, highlights that the relationship between skin disease and psychological morbidity in young women. It confirms that psychological morbidity (depression, anxiety and stress) is a factor in the causation of skin disease.[7]

Chronic diseases are major killers in modern era. Physical inactivity is a primary cause of most chronic diseases. Conversely, physical activity prevents and delays chronic diseases, implying such diseases need not be the outcome of life.

EXTERNAL FACTORS

Studies show that pollutants gain entrance to the skin by direct accumulation on the skin surface. Absorption via the hair follicles, inhalation, ingestion and circulation of pollutants in plasma penetrate dermal tissues. Pollution creates oxidative stress for skin. Air pollutants enter the skin via nanoparticles and generate quinones; i.e., redox cycling chemicals that produce ROS. This increase in the amount of ROS and free radicals within the cell and its mitochondria overcomes the skin's innate antioxidant defenses.

Most commonly, pollutants are generated through the burning of fossil fuels by vehicles and industries giving rise to components such as particulate matter (PM) and polycyclic aromatic hydrocarbons (PAHs). Additional pollutants are derived from a variety of unrelated sources, such as cigarette smoke, ultraviolet (UV) light, volatile organic compounds (VOCs), and tropospheric (ground level) ozone. Particulate pollut- ants with a diameter of 2.5mm or less (PM2.5) and 10mm or less (PM10) and nano particles are the main constituents of PM. PAHs and VOCs are mainly generated by power plants,

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industries, vehicles and domestic agricultural sources.[8]

Epidemiological evidence that exposure to traffic-related air pollution including PM, NOx and ground level ozone is associated with pigment spot and wrinkle formation in Caucasians and East Asians. Preliminary evidence suggests that at least some of these effects may be mediated via aryl hydrocarbon receptor (AhR) signaling in human skin.

Following short-term exposure to air pollution from a California wildfire, rates of clinic visits for both atopic dermatitis and itch were significantly increased among adults aged 65 years or older. This finding suggests that the skin of older adults has a greater vulnerability to air pollution, with rapid outcomes after short-term exposure to air pollution. The increased association of risk for pollution-induced skin exacerbations with older age may be due to age-related molecular processes affecting skin barrier function.[9]

The skin is the most exposed organ to the environment; therefore, cutaneous diseases are inclined to have greater sensitivity to climate. Global warming is responsible for a warm and humid environment which can encourage bacterial and fungal colonization, causing an increased incidence of skin infections. Global warming, deforestation and changes in precipitation are linked to variations in the geographical distribution of vectors of some infectious diseases; i.e., malaria, leishmaniasis and Lyme disease. Additionally, climate change can affect the ozone layer, cloud cover and relative humidity—all regulate the amount of UV radiation that reaches the earth's surface. More UV radiation increases incidence of melanoma, squamous cell carcinoma and basal cell carcinoma.[10]

TEMPERATURE CHANGE

Core body temperatures are almost universally maintained around 37°C and skin temperatures around 35°C. Hyperthermia, elevated core body temperature, occurs when elevated skin temperatures are sustained, which can result in death when core body temperatures reach around 42-43°C. While acclimatization can reduce the burden of heat, acclimatization only improves sweating mechanisms, and the cooling effects of acclimated people have limits. As relative humidity increases, the evaporative cooling effects of sweating decreases. Once relative humidity reaches 100%, sweating continues but evaporative cooling stops. Even acclimated or healthy humans face mortality with prolonged skin temperatures of 37-38°C. Thus, it is reasonable that sustained periods of time with HI > 35°C can be physically intolerable, and outdoor exposure to Wet Bulb Globe Temperature WBGTmax > 30 °C has been associated with increased mortality rates among vulnerable populations.[11]

Exposure to cold air causes thermoregulatory reactions like variations of behavior and physiological adjustments to keep thermal balance by either raising metabolic heat production through shivering or reducing heat losses consecutive to peripheral cutaneous vasoconstriction. A strong vasoconstriction can result in a fast reduction in hand and foot skin temperatures. This can damage tactile sensitivity, manual dexterity and muscle contractile features. Significant temperature reduction can also increase pain and sympathetic drive and decline gross motor function.[12]

AIR & WATER POLLUTANTS

Increasing globalization has led to congested metro cities and increased time spent in traffic during routine travel. Increased road traffic affects human health in several ways. Automobile emissions contain toxic chemicals that pollute the atmosphere. Road traffic emissions produce greenhouse gases that contribute to global warming. Vehicles emit a range of pollutants, including nitrogen oxide (NOx) and particulate matter (PM).[13] Humans are exposed to heavy metal toxicity through consumption of water containing metal. Heavy metals readily bioaccumulate in vegetables and enter through the food chain. Effects of heavy metal toxicity on human ranges from mild eye, nose and skin irritations to organ dysfunction such as cirrhosis, necrosis, low blood pressure, hypertension and gastrointestinal distress. Of course, some heavy metals such as iron, manganese and zinc are required in minute amounts for various biochemical processes. But other heavy metals, such as lead, cadmium and mercury, are of serious threat and considered foreign in the body. For example, water polluted with arsenic can cause cancer of the lungs, liver and bladder. Kidney and lung damage and bone fragility may result when cadmium-containing water is ingested. Exposure to lead can severely damage the brain and kidneys. In children, lead exposure even at very low concentration may hamper learning, cause memory loss, affect attention and response functions, and generally make children aggressive. The chemical form of mercury in the environment is also important in analyzing toxicity. The organic form of mercury, methyl mercury (MeHg) and dimethyl mercury (DMeHg), is known to be more toxic than inorganic mercury.[14] Mercury is present in the food chain.

UV & IR DAMAGE

Natural sunlight is polychromatic; therefore, its ultimate effects on the human skin are the result of not only the action of each wavelength separately, but also interactions among the many wavelengths, including UV, visible light and infrared (IR).

Excessive exposure to UV carries profound health risks, including atrophy, pigmentary changes, wrinkling and ma-

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lignancy. UV is epidemiologically and molecularly linked to the three most common types of skin cancer—basal cell carcinoma, squamous cell carcinoma and malignant melanoma.

Recent evidence indicates that IR and heat may induce premature skin aging, just like UV radiation. IR exposure of human skin stimulates the expression of MMP-1 and decreases type I procollagen expression in vivo. Acute IR irradiation also increases new, leaky vessel formation and induces inflammatory cellular infiltration. Heat energy, which increases skin temperature, also increases MMP-1, -3 and -12. It modulates elastin and fibrillin synthesis, resulting in the development of solar elastosis. Acute heat shock in human skin stimulates new vessel formation, recruits inflammatory cells and causes oxidative DNA damage.[15] Continuous UV radiation exposure induces oxidative stress in epidermal cells, causing cell damage, fat oxidation and cell inflammation.

Blue light is defined as light within the wavelength range of 400-500nm. The sun is the main source of blue light. It is also emitted by electronic devices, including computer monitors, flat-screen televisions, smartphones, tablets and fluorescent light bulbs. Changing lifestyles; i.e, less time spent outdoors and increased use of light-emitting diode and fluorescent lighting, have changed the pattern of blue light exposure in humans. In controlled clinical settings, blue light can be used to treat conditions such as psoriasis, atopic dermatitis and acne. Blue light is capable of producing various effects on the skin, including deleterious direct effects, such as hyper pigmentation and photo aging, and complex indirect effects, such as circadian rhythm modulation.[16] When formulating cosmeceuticals, we should focus on products which control exposure or decrease blue light effects.

Life is stressful. To reduce stress, eat well, avoid smoking and alcohol, and practice meditation. They will enhance quality of life and appear of skin. The best skin in the world is found in Asian countries where women have glowing skin through eating right and maintaining healthy life style. Further research should involve fast developing field of clean Ayurveda, an alternative system to bring balance to life. The Ayurvedic market is expected to approach $29 billion by 2030. It includes natural herbs, plant-based medicines and spices and is heralded as an alternate medicine devoid of side effects. ■

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Enhancing Skin Anti-Aging through Healthy Lifestyle Factors

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[1]

Abstract: Lifestyle health has been recognized as an evidence-based innovation that defines how everyday behaviors and routines influence the avoidance and therapy of illness and provides an important adjunctive component to overall health. Specifically, an approach with small changes over time can have a dramatic impact on the health and well-being of individuals not only, in general, but also can be applied to skin health. However, lifestyle health factors to improve skin well-being have not been discussed extensively and/or well promulgated. The narrative for this overview focuses on providing a summary for topic background information, but more importantly, presents four lifestyle factors that can improve dermal health [i.e., factor 1: nutrition—diet; factor 2: rest (sleep); factor 3: movement/physical exercise, and factor 4: social and community associations]. This was accomplished by identifying preceding journal reports/reviews covering especially the last five years (January 2018 to July 2023; 164 out of 205 references cited or 80%) using scientific search databases. The main conclusions of this overview encourage the concept that lifestyle health factors such as nutrition/diet, rest/sleep, movement/physical exercise, and community/social interactions support enhanced skin health and well-being with aging. Plus, social media interventions that aim to promote dietary, sleep and physical activity changes might be an application to improve skin health in the future.

Keywords: skin; anti-aging; health; lifestyle factors; diet; sleep; exercise; social interactions; polyphenols; vitamins

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1. Introduction

Everyone ages, the skin (being the largest organ of the body) is the most conspicuous visual indicator of aging, especially in the facial/neck and hand/arm/leg regions [1–3]. However, habits and actions (that may be positive or negative) have profound influences on short-term and long-term health and quality of life (QOL) [4,5]. This perspective is supported by numerous scientific studies and evidence-based guidelines for the prevention and/or treatment of age-related diseases [4–21]. For example, many studies have exam- ined factors such as: (a) good nutrition via dietary choices [4–10], (b) regular rest with good sleep cycles for restoration and managing stressors [4,5,7–10,13,14,21], (c) physical activity including moderate to vigorous exercise to enhance cardiovascular health and to manage/control body weight [4,5,7,9,10,15–17,21], and (d) the importance of positive social relationships to stay mentally/emotionally connected with community associations with ideals engaged in worthy activities among like-mined people [4,5,10,12,14,16,18–21].

The concept of lifestyle choices was first proposed in 1999 by James Rippe in the textbook "Lifestyle Medicine", which defined how daily habits and practices impact both the prevention and treatment of disease and provides an important adjunctive component to overall health [21]. In fact, a recent report presented at the annual meeting of the American Society of Nutrition 2023 looked at the lifestyle behaviors of nearly 720,000 military veterans between the ages of 40 to 99 years of age in the "Million Veteran Program", a longitudinal study designed to investigate the health and wellness of United States (US) veterans [21].

The investigators found that lifestyle habits (like the list of factors outlined above) build on each other and could add up to 24 years of life extension, enhancing longevity and the QOL [21].

While healthy lifestyle factors have been examined for the prevention and/or treat- ment of age-related disease, this paradigm has been lacking for skin aging. Thus, this narrative overview examines the latest existing knowledge about how lifestyle factors influence skin aging, and how different modalities of daily habits and choices coalesce to advance/build various components to boost skin anti-aging toward better overall health. Specifically, the purpose of this review is not to present comprehensive coverage, but to provide an updated general summary on: (a) aging, (b) skin aging, and the four factors that can influence skin aging such as (1) nutrition and dietary selections, (2) rest (sleep), relaxation/recovery/rejuvenation and protection against stressors, (3) movement (exercise- moderate to vigorous levels to improve cardiovascular, weight control and well-being), and (4) community (covering social and community associations) to "become" better in managing the challenges of aging. This overview identified previous journal articles and reviews (with emphasis over the past five years) from January 2018 through July 2023 using the keywords: lifestyle health/medicine, skin, dermal, human and/or using dif- ferent keyword combinations (retrieved from 1 July to 10 August 2023). The following databases were utilized: PubMed maintained by the US National Library of Medicine at the National Institutes of Health; Science Direct and Scopus by Elsevier and from Google Scholar. Also, background references (where appropriate) include the keywords: lifestyle health/medicine, diet, sleep, isolation, exercise, estrogens, skin aging, microbiome, phytoe- strogens, phytochemicals, polyphenols, and/or combinations (without a year-limit range for searching the background topics). This overview is based on previously conducted studies and does not contain new data/results of human participants or animals performed by the authors.

2. Skin Aging

2.1. Skin

Of all the organs, the skin is the most conspicuous to display signs of aging or dermal changes [1–3]. Skin covers an area of around 2 m^2 (however, more recent estimates account- ing for dermal pores suggests 25 m^2) and represents one-sixth of the total weight for an adult [2,3,22,23]. The skin serves a variety of functions such as acting as the body's initial barrier protecting against foreign agents (pathogens), ultraviolet (UV) light, chemicals, me- chanical or other injury, and it helps to maintain body temperature, prevent water loss from the body, produce vitamin D, detect/fight infections, and provides sensory information (touch, pressure, temperature, and pain-nociception) [2,3,22,23]. Trans-epidermal water loss (TEWL) has been determined to range from 120 to 240 g/m^2/day, which is important for skin hydration [24,25].

There are seven skin layers, which are displayed in Figure 1. In summary, the epider- mis is the major outer layer with keratinocytes as the major cell type (at 75–125 microns thick). The epidermis is further stratified into 5 distinct layers.

The first skin layer is the stratum corneum- keratinocytes become corneocytes, which are strong (dead keratinocytes) that provide barrier protection and prevents TEWL [2,3,22–25]. The water content of the stratum corneum (about 20–30%) is part of the natural moisturizing factor (NMF) array that maintains adequate skin hydration [2,3,22,23].

The stratum lucidum, the second skin layer is a thin, transparent layer of keratinocytes only found on the palms of the hands and soles of the feet [3,22].

The third layer- the stratum granulosum- contains glycolipids (keratohyalin granules) that keeps the skin layer together (these are filled with histidine and cysteine rich proteins to bind the keratin filaments together), along with desmosomal connections that help form a waterproof barrier [3,22,23,26] (see Figure 1).

Figure 1. Cartoon Structure/Component(s)/Layers of Human Skin. Note: the stratum lucidum is not shown because it is only found on the palms of the hands and soles of the feet.

The stratum spinosum, the fourth layer is 8 to 10 cells thick held together by sticky proteins called desmosomes, helping the skin be flexible and strong along with an abundant number of dendritic cells (Langerhans cells) for immune defense [3,22,23,27].

The fifth skin layer is the stratum basal- this is a single row of stem cells, continually producing keratocytes, and contains melanocytes (10–25% of the cells herein) [responsible for melanin pigment] [2,3,22,23].

The dermis represents the sixth layer comprised of collagen and elastin fibers, which are secreted by fibroblasts providing the structural components for flexibility and strength [1–3,22,23,28].

The dermis is composed of two regions or zones, the papillary dermis (that has fewer structural fibers and contains vascular networks that serve two functions-support the avascular epidermis with vital nutrients and thermoregulation) and the reticular dermis (that contains dense structural fibers, which provides the skin with overall strength and elasticity) [2,3,22,23] (see Figure 1).

The hypodermis (the seventh dermal layer) is the deepest situated below the dermis that contains adipose (fat) cells, hair follicles, nerve endings, sweat glands, bursa, loose connective tissue (collagen and elastin) and blood vessels (plus lymph vessels-immune function [2,3,22,23].

Finally, emerging evidence suggests that skin is a ‘neuro-endocrine-immune” organ [3], especially since advances in microbial research have linked chemical messengers (hormones) to the gut-skin microbiome to influence dermal health [23].

2.2. Skin: Chronological Aging and Photoaging Aging

Skin aging is a complex process due to chronological (intrinsic) and photoaging (extrinsic) mechanisms that have been reviewed elsewhere, but will be covered herein, in brief [1–3,29–35].

2.2.1. Extrinsic Skin Aging

Extrinsic aging is an important collateral factor in cosmesis, appearance, diagnosis, and management of the skin in aging individuals, which is due mainly to the chronic exposure to various environmental elements such as the sun (UV light including tanning bed), air/water pollution, smoking (vaping), diet/exercise/stress, lifestyle, repetitive mus- cle contractions (smiling, frowning, etc.), gravity, sleeping positions and cutaneous or general diseases/disorders [2,7,29,31,34,35]. However, the main environmental element associated with extrinsic aging is photo-aging (exposure to UV light) resulting in a cas- cade of cellular and molecular signaling mechanisms that increase oxidative stress and

inflammation [2,29,31,35,36]. These extrinsic aging factors may be independent of hormonal status and should be considered in the clinical management of aging skin [2,29,31,35,36].

2.2.2. Intrinsic Skin Aging

Intrinsic or chronological aging is a natural process caused by the accumulation of reactive oxygen species (ROS) resulting from oxidative cellular metabolism [36] and is influenced by genetics, metabolism, hormonal, immunological, cardiovascular, gastroin- testinal, psychogenic (involving stress or affective disorders), degenerative, or neoplastic disease [2,29,35,36].

In women, the skin thickens to 25 to 30 years of age, then there is a progressive declination of all skin layers during aging [2,29,30,35,36]. Chronological or intrinsic ag- ing is an inevitable biological process where deteriorating alterations in the production, quantity, and preservation of dermal cellular/protein elements takes place [2,29,32,35,36]. Throughout dermal aging, keratinocytes change shape, and the epidermal-dermal junction (rete pegs) becomes compressed, while there is a decline in the dermis thickness because of the deficit of collagen, elastin, and hyaluronic acid (elastosis). It is more noticeable in sun-exposed areas (solar elastosis) [2,29,32,36,37]. Skin turgor declines along with the increased appearance of fine lines/wrinkles, especially along normal areas of stress, gravity, and mechanical muscle contractions especially around the eyes and mouth [2,29,32,36]. Matrix metalloproteinases (MMPs) cause destruction of collagen and elastin fibers that in turn enhance mitochondrial oxidative stress and deletions of mitochondrial DNA via the c-Jun/AP-1 pathway in dermal fibroblasts [29–32] (see Figure 2).

Figure 2. Chronological aging via the loss of skin homeostasis/oxidative metabolism, photo-aging by exposure to UV light and extrinsic aging (due to external factors and lifestyle) through cellu- lar/molecular signaling mechanisms are shown. This diagram displays the sequence or production of reactive oxygen species (ROS) that is more commonly called oxidative stress (OS). Oxidative stress (OS) in the major factor associated with inflammation and alterations in the decline of collagen and elastin resulting in wrinkles. Abbreviations: Proinflammatory transcript factor (NFkB), AP-1 nuclear transcription element, Activator Protein—1 (AP-1), hyaluronic acid (HA), Tissue Inhibitor of Matrix Metallo-proteinase (TIMP) and Transforming Growth Factor beta (TGFβ). Estrogens and Selective Estrogen Receptor Modulators (SERMs) provide protection by binding especially to estrogen receptor (β) in chronological, photo-aging, and extrinsic aging. Adapted with permission from Lephart E.D. Naftolin, F. Factors Influencing Skin Aging and the Important Role Estrogens and Selective Estrogen Modulators (SERMs). *Clin. Cosmet. Invest. Dermatol*. 2022, 15, 1695–1709 [2].

Finally, blood vessels in the dermis become more fragile, leading to bruising (senile purpura), sebaceous glands produce less oil, sweat glands produce less sweat (challenging to keep cool), less subcutaneous fat layer reduces the ability to maintain body temperature and skin tags, pigmented spots (liver spots/lentigos) can appear with aging [2,29,31,33,36].

2.3. Hormonal Benefits/Changes with Aging (Estrogen in Women)

17β-Estradiol has numerous cutaneous benefits that are detailed elsewhere [2,38,39]. Recall 17β-estradiol is the most potent sex steroid hormone in humans and the major estrogen produced by the ovaries during the reproductive years [2,39,40]. 17β-Estradiol levels reach a maximum around the mid to late 20 s [2,39,40]. Interestingly, the levels of skin collagen and elastin also follow the estrogen profile during this interval. [2,38–42] (see Figure 3A,B). Around 30–35 years of age, estrogen levels begin to decline, and there are corresponding changes in the skin; wrinkles appear because of the declination in collagen and elastin fibers in the dermal layer (Figure 3A) [2,38–43].

Figure 3. (**A**) Upper Panel displays the progressive decrease in dermal collagen and elastin fibers and the appearance of fine lines and wrinkles with the passage of time. (**B**) Lower Panel displays the levels of ovarian 17β-estradiol levels (red histogram bars) in women from the late teenage years to seventy years of age. After menopause the low estrogen levels (not shown) are derived from the aromatization of androgens in peripheral fat tissue sites. The profile of collagen expression in skin with aging is displayed (green histogram bars) while the elastin levels (blue histogram bars) follow the pattern of ovarian estrogen production with aging. Adapted with permission from Lephart E.D. Naftolin, F. Factors Influencing Skin Aging and the Important Role Estrogens and Selective Estrogen Modulators (SERMs). *Clin. Cosmet. Invest. Dermatol.* 2022, 15, 1695–1709 [2].

17β-Estradiol production from the ovarian follicles declines after 35 years of age, and there is a progressive declination in estrogen levels by around 45 years [2]. Then there begins to be inconsistent oscillations in ovarian estrogen production as the follicles respond to gonadotrophins waves until they become exhausted with the onset of menopause (in the USA this milestone is around 51 years of age ± 4 years) [38,39,41,43] (Figure 3B). Af- ter menopause, estrogen production occurs not in the ovaries but at peripheral adipose tissue sites [36,38,39,43]. While it is known that skin cells can produce estrogens locally,

the aromatase enzyme activity is dramatically reduced to approximately 30-times lower than in premenopausal ovarian follicular tissue [39,44]. Also, it should be noted that androgens have a negative influence on skin cells especially on collagen and elastin via the 5α-reductase type I enzyme located in fibroblasts. This enzyme can counteract the positive estrogenic influence, especially after menopause [2,38,39,43]. The lack of estradiol and/or agonist influences by selective estrogen receptor modulators (SERMs) actions, es- pecially via ERβ activation, has been shown to account for the vivid loss in dermal fibers such as collagen and elastin causing atrophy, wrinkles, poor wound healing/barrier func- tion/hydration [2,38,39,43,45] (Figure 3A) The declination of skin components is heightened by intrinsic and extrinsic aging, which are reviewed elsewhere [2,29,36,38].

Estrogens send their chemical hormonal messages via estrogen receptors (ER) through- out the body. Notably, it has been reported that there is specific-tissue regulation of how ERs are synthesized in humans; also, it is known that ER beta is more abundant in the epidermis and fibroblasts (and in the scalp region) compared to ER alpha [2,38,46]. In fact, ER beta activation has been shown to promote wound healing and cellular/tissue restoration in human skin via dermal structures such as collagen and elastin that occur via
biomechanical processes [2,36,38,39,47–49]. Plus, ERβ agonists via SERM actions are known to provide similar positive actions on skin health compared to 17β-estradiol, which are seen in plant-derived molecules such as polyphenols (resveratrol, flavonoids and isoflavonoids, etc.) or phytoestrogens that selectively bind/activate ERβ in human skin [2,36,38,39,49,50]. Finally, the effects and benefits of 17β-estradiol on skin are shown in Figure 4.

Figure 4. Effects and Benefits of 17β-Estradiol on Skin. Adapted, in part, from VectorStock license 3,264,406 to ED Lephart.

2.4. Other Hormonal Influences on Skin

While 17β-estradiol is the most potent steroid hormone in the body, the skin is an endocrine organ that contains the biochemical enzymes for local hormone production to influence regional immune function [50,51]. Conversely, there are several hormones produced by the endocrine system from glands that secrete chemical messengers into the bloodstream that bind specific receptors in cells/tissues to maintain homeostasis, but other hormones are also known to influence the skin [36,50,52–55]. In addition to estrogens, androgens, cortisol (the stress hormone), progesterone and thyroid hormone are known to influence skin health (see Figure 5). Androgens along with cortisol are known to have a negative impact on skin where they decrease collagen and elastin, skin turgor, wound healing, and fibroblast viability, but increase MMPs, wrinkle formation and sebum production [2,36,38,39,54,55] (Figure 5). Progesterone like estrogens has positive influences on skin except that it stimulates sebum production [56–58]. Finally, thyroid hormone regulates the metabolic rate of the body and helps regulate epidermal cell proliferation,

differentiation, hair and nail growth, wound healing, and skin hydration by affecting the function of dermal fibroblasts [50,52,53]. Thus, while estrogens play a leading role in skin, other hormones also have a significant influence on dermal health (Figure 5).

Figure 5. Other Hormonal Influences on Skin.

3. Health Lifestyle Factors

3.1. Aging

Various health and governmental agencies worldwide devote a broad scientific effort to understand the nature of aging and to extend healthy active years that enhance the quality of life (QOL). Aging has many aspects, but in general, it is defined as the gradual physical, psychological, and social changes in persons that lead to increased risk of weakness, disease, and ultimately death [59].

3.2. Population Aging around the World

The United Nations department of economic and social affairs announced on 20 February 2023, that "population aging is a defining global trend of our time" [60]. Where Asia is at the forefront of this trend with Hong Kong, South Korea, and Japan predicted to have the highest share of people aged 65 and older by 2050 [60] (see Figure 6).

3.3. Aging Related-Disorders

From a more biological perspective, aging is the progressive physiological changes in an organism that lead to senescence [40,61–63]. Or, in other words, a decline of biological functions and the lack of an organism's ability to maintain homeostasis and adapt to various stressors (such as age-related disorders of the body's organs/systems/tissues/cells involved in the operational aspects of metabolism/defense and unregulated growth like cancer) [40,61–63]. The nine hallmarks of aging have been reviewed elsewhere [40,61–63] that cover (1) gene variability, (2) shortening of telomers, (3) epigenetic factors, (4) protein instability or weakening of large molecules, (5) lack of detecting nutrient and metabolic communications, (6) cellular apoptosis, (7) fatigue/collapse of stem cells, (8) mitochondrial trauma/abnormality/impairment, and (9) breakdown of signaling between cells [40,61–63]. However, other investigators have proposed that the major cause of aging and age-related disorders is due to oxidative stress at the molecular level [62].

Figure 6. The World's Oldest Populations. Only includes countries/territories with a popula- tion of more than 1 million people. Source: United Nations Population Division [60]. Adapted with permission.

3.4. Aging and the Global Burden of Cancer Attributable to Lifestyle Risk Factors

Cancer is the second leading cause of death worldwide, and exposure to risk factors plays an important role in the burden of many cancer types [64,65]. Also, it is well es- tablished that cancer is more common as people age [64]. To gain a perspective on the magnitude and importance of lifestyle factors a recent study published in the Lancet 2022 analyzed 369 causes of death and disability along with 87 risk factors from 204 coun- tries and territories on the global burden of cancer. In 2019, the top risk factors were
(1) smoking (vaping), (2) alcohol use, (3) high body-mass index, (4) unsafe sex, (5) high fasting plasma glucose levels, (6) ambient particulate matter pollution, (7) occupational exposure to asbestos, (8) dietary intake low in whole grains, (9) dietary intake low in milk, (10) second-hand smoke, and (11) dietary intake low in fruits [65]. Remarkably, overall, 44 % of the cancer deaths were due to modifiable risk factors where behavioral and dietary/metabolic risk factors had the highest rates (that accounted for the most cancer deaths), while exposure to pollution represented moderate rates of cancer deaths [65].

In 2011, Alegria-Torres et al. published a landmark review on epigenetics and lifestyle, which predicted and supports the 2022 Lancet study on the global burden of cancer [66]. Notably, Alegria-Torres outlined environmental and lifestyle factors such as diet/nutrition, behavior (physical activity, sleep, working habits, stress, etc.), and smoking (vaping), and alcohol consumption that affects human health [66].

4. Factors of Lifestyle Health

Different Types of Lifestyle Health

Different lifestyle aspects leading to healthy outcomes have been reported from mul- tiple perspectives. Kassis et al. (2023), reported how aging impacts five key biological functions (immune, digestive, nervous, musculoskeletal, and cardiovascular) with pre- ventive strategies that focused on dietary intake, physical activity, and sleep quality [67]. Loef et al. (2023), found in a 30-year study that predictors of healthy aging suggested that

long-term cardio- and metabolic parameters such as overweight and cholesterol levels were the most significant factors in predicting healthy physiological aging [68]. In 2019, Bosnes et al. examined lifestyle predictors of positive aging in a 20-year prospective study that found among the midlife variables (smoking, physical activity, alcohol consumption, obesity, and social support) that non-smoking and social support were the most significant predictors of successful aging [69]. When modification of lifestyles was studied in older age (40–80 years) individuals, Katz and Sakaniwa et al. found that adopting healthy lifestyles was correlated with lifetime benefits among subjects even with major co-morbidities (e.g., cardiovascular disorders, cancer, diabetes, and kidney disease) [70,71]. Furthermore, Wahl et al. reported in humans the intake of the Mediterranean, Finnish, and Okinawan diets were associated with improved age-related health variables and suggested that neurodegen- erative disease including dementia could be ameliorated [72]. Finally, Buettner and Skemp, in 2016, reported the discovery of 5 places around the world where people consistently live over 100 years old [73]. The common factors among the 5 locations among the world's centenarians include: (1) movement, (2) purpose in life, (3) managing stressors in life, (4) controlled decreased volume of dietary intake of plant-based foods, and (5) belonging to and interacting within a social community with strong relationships [73].

5. Four Factors of Lifestyle Health

5.1. Factor 1: Lifestyle Health—Nutrition, Diet and Skin Health

The purpose of this section and later sections is not to present comprehensive coverage on various aspects of lifestyle/habits and factors, but to summarize the recent progress reported in the scientific literature and how this applies to skin health and anti-aging.

5.2. Nutrition-Diet Lifestyle Benefits

Eating is directly associated with health. Good nutrition is essential to keeping current and future generations healthy across the lifespan [74]. A healthy diet helps children grow and develop properly and reduces their risk of chronic diseases. Adults who consume a healthy diet live longer and have a lower risk of disorders and certain cancers [30]. Additionally, healthy eating can help people with chronic diseases manage these conditions and avoid complications [59]. In other words, nutrition plays a key role in lifestyle habits and practices that impact virtually every chronic disease [4], and there is strong evidence for the role of nutrition in cardiovascular disease, diabetes, obesity, and certain cancers, among many other disorders [5,66]. For example, in 2022, La Vignera and Basile presented a report entitled "Diet and prostate health: an underrated tool?", which described how dietary changes can notably impact prostate health and improve the benefit of traditional medical care (as reviewed by Stewart and Lephart, 2023) [75].

While diet has become a focus to enhance human health, the attention on what types of diets yield the best outcomes is paramount from the perspective of consumers. The "Mediterranean or Eastern" diets versus a "Western diet" have gained popularity to increase the general health status and well-being and address many diseases and disorders [8,66,76–80] (Figure 7). For example, the Mediterranean diet is one of the most widely described and evaluated dietary patterns in the scientific literature with validated health benefits [8,76,77,79,80]. It is characterized by high intakes of vegetables, legumes, fruits, nuts, whole grains, fish, some olive oil, moderate intake of red wine, where most proteins and fats are derived from vegetable sources with low intake of red meat, potatoes, processed meat, refined carbohydrates, and sweets [77,79,80]. Additionally, the Eastern (Asian) diet has high intake of plant-based foods (source of protein from vegetables like bean sprouts, spinach, eggplant, bok choy, cabbage, kale, snow peas, leeks, and mush- rooms). Fruits and legumes, grapes, melons, cherries, dates, mangoes, etc.; steamed or stir-fried produce along with nuts, seeds, beans (soy, mung), lentils, tofu, or tempeh, plus rice and whole grains. Moderate intake of fish (dependent upon country's coastline), dairy, eggs, and poultry. Very low intake of meat, processed meat, refined carbohydrates, and sweets [8,76,77]. Conversely, the Western diet, prevalent in high-income countries, contains

refined carbohydrates, red meat, processed meats, fats/lipids/cholesterol, which increase sympathetic nervous system, oxidative stress, and inflammation and low intake of fruits and vegetables [75–77] (Figure 7). Additionally, a traditional Eastern European diet (in Rus- sia, Poland, and the Czech Republic) may contribute to poor health status, particularly for the high cardiovascular disease rates reported by Stefler et al. in 2021 [81]. Notably, Europe and Central Asian (from the Caspian Sea in the west to Western China and Mongolia) are regions, where cardiovascular disease is responsible for more than half of all deaths across this area due to poor diets and daily habits (smoking) [82].

Figure 7. Comparison Among Mediterranean, Western and Eastern (Asian) Diets. Adapted with permission from Stewart, K.L.; Lephart, E.D. Overview of BPH: Symptom relief with dietary polyphe- nols, vitamins, and phytochemicals by nutraceutical supplements with implications to the prostate microbiome. *Internat. J. Mole. Sci.* 2023, 24, 5486. https://doi.org/10.3390/ijms24065486 [75].

5.3. Nutrition, Diet and Skin Health

A reasonable balanced diet provides the nutritional components to delay aging, prolong life and enhance the QOL [4,8,34]. This narrative overview for this section demonstrates that a healthy diet is one of the most important factors to achieving healthy skin [8,34,76,83]. Certain nutrients, vitamins, minerals and other compounds/molecules and factors will be described herein, previous journal reports have presented more detailed information elsewhere as cited.

Various nutritional elements such as water, protein, trace elements (iron, iodine, zinc, copper, selenium, etc.), vitamins (A, B complex, C, D, and E) other dietary, daily habits and lifestyle heath choices are known to impact skin health.

For example, does dietary fluid intake affect skin hydration? The answer is basic and complex due to the nature and importance of water in the human body for normal physiological function, maintaining body volume (intracellular and extracellular), ther- moregulation, and acting as a lubricant and shock absorbent [84,85]. It is also important in the character/composition of the avascular epidermis [2,22]. Drinking enough water is important to your overall health and to your skin (most individuals do not drink 8 to 10 glasses of water per day); however, it's not clear whether drinking extra water affects skin hydration in healthy people [86]. Your skin is also affected by your diet, lifestyle, environment, and skin care routine [84]. However, in the case of the elderly or in obesity, dry skin is a common complaint [84]. Higher water intake in a regular dietary routine might positively impact skin physiology especially for its hydration and biomechanical properties, particularly in individuals with lower daily water consumption [84].

What about dietary protein intake? Protein is a critical nutrient for human growth, development, maintenance, and repair of body tissues/cells, which perform a large array of functions (as enzymes, structural components, transport/signaling, hormones, proper fluid, and acid-base balance, immune, and DNA replication) [87]. It is no surprise that protein intake is essential for healthy skin, particularly the two amino acids, i.e., lysine and proline that support collagen composition [88,89]. Notably, collagen is the most abundant protein in the body [88]. Protein deficiency in developed countries is rare, however, low-protein diets are associated with poor wound-healing and other skin problems, especially with aging [34]. Finally, oral intake of collagen supplements has been reported to enhance skin, nail, and hair health [88,90–92].

Vitamins in both topical and oral forms play a key role in many dermatological conditions [89,93]. Vitamin deficiencies can occur. Deficiencies of water-soluble vitamins, such as most B vitamins and vitamin C, may develop after weeks to months of under- nutrition, while deficiencies of fat-soluble vitamins, such as vitamins A, D, E and B12, can take up to a year to develop due to the body storage capacity for these nutrients [89,93]. Numerous reports suggest that oral supplementation of various vitamins can enhance general skin health and treat dermatological disorders [89,93–95]. In general, vitamins can have anti-aging effects such as [88,89,93–95], antioxidant, anti-inflammatory, hydration, skin barrier, turgor/tone/radiant, and repair/wound healing properties that are beneficial for skin health.

In fact, feeding the skin is a new trend in food and cosmetic treatments, where beauty is no longer dissociated from well-being, and where consumers consider nutrition as an important pillar in skin health. This is especially the case when ingredients/products contain food extracts or natural plant sources having nutricosmetic and/or nutraceutical benefits. [35,50,94,95].

Lifestyle health routines of dietary intake of plant-derived compounds such as carotenoids (astaxanthin, lutein, zeaxanthin, lycopene), chlorophyll, and polyphenols (resveratrol, flavonoids, isoflavonoids, green tea, etc.) have been shown to benefit skin health in a variety of ways [50,88,94,95] such as decreasing fine lines/wrinkles, dullness and roughness while enhancing healing, hydration, pigmentation, and radiance [36,50,88,94–101]. The mechanisms by which plant-derived compounds enhance skin health include: anti-aging (sirtuin activa- tion), protection against UV damage, direct antioxidant actions and/or stimulation of nuclear factor erythroid 2-related factor (Nrf2) that is the master regulator for antioxidant responses, anti-inflammatory [by blocking nuclear factor-kB (NFkappB) and activator protein 1 (AP1), interleukins and oxidative stress], stimulation of collagen, elastin, tissue-inhibitor of matrix metalloproteinase(s) (TIMPs) and superoxide dismutase (SOD), blocking androgen hormone action and enhancing skin parameters (hydration, smoothness, radiance, pore size, firmness, and frown lines/wrinkles) [2,8,23,35,36,38,43,47,49,76,79,83,95–103].

Interestingly, chlorophyll, the most abundant plant pigment responsible for giving plants their green color, also blocks assaults to DNA from carcinogens, and chlorophyllin is a water-soluble derivative of chlorophyll [102]. Finally, chlorophyll also plays a role in regenerating Co-enzyme Q 10 (CoQ10) [102], where CoQ10 as an oxidant has been shown to: (a) reduce the production of free radicals, (b) be involved in the regeneration of vitamin E, (c) reduce keratinocyte DNA damage, (d) reduce UVA-induced MMP produc- tion from fibroblasts, (e) enhance collagen and elastin expression, inhibit IL-1alpha, IL-6 production, and melanin synthesis, and (f) inhibit MMPs and regulate the sulfide oxidation pathway [88].

Probiotics are active microorganisms that have beneficial effects on the host by altering the microbiota composition of a specific portion of the host's flora [104]. Numerous studies have found a close relationship between the skin microbiome and skin health benefits along with the gut-skin axis, where the gut microbiome can influence the skin via various chemical messengers including hormone and immune signaling [23,104,105]. Several skin- related topics (acne, antioxidant activity, atopic dermatitis, barrier function, enzymatic regulation of the extracellular matrix, moisturization, photo-aging, pigmentation, rosacea,

TEWL, suppression of pathogens, and UV protection, etc.) have been covered in diverse reviews on topical and oral probiotics in skin health [104–109]. Therefore, it is beyond the scope of this narrative overview to describe this topic further.

Diet lifestyle factors such as the role of whole-food, plant-based (WFPB) diet on skin health parameters was reported by Solway et al. in 2020 [102]. This WFPB diet was defined as "eating plant foods in their whole, unprocessed form, such as vegetables, fruits, beans, lentils, nuts, seeds, whole grains, and small amounts of healthy fats. It did not include animal products, such as red meat, poultry, fish, dairy, eggs or processed foods or sweets" [102]. Their findings showed that a WFPB diet maximized the antioxidant potential by providing the essential vitamins (A, C, and E) to help combat oxidative stress, advanced glycation end products (AGEs) and methylglyoxal [110–113], which resulted in lengthening telomeres that contributed to healthier, younger-looking skin [102]. The findings by Solway et al. are supported by numerous other scientific reports that have examined different aspects of diet/lifestyle health and skin parameters [3,34,42,83,95,108,114–117].

From a clinical perspective, there are some reports that investigated the role of lifestyle and nutrition (especially vitamins, minerals, and dietary supplementation) on dermatologi- cal conditions such as photo-aging, psoriasis, acne vulgaris, atopic dermatitis, rosacea, and hidradenitis suppurativa, etc. [118–121].

5.4. Lifestyle/Daily Habits- Negative Impact on Skin Health [AGEs, Alcohol, Smoking, High Fat, Body Mass Index (BMI)]

Advanced glycation end products (AGEs) are well studied toxins, where glycation is a non-enzymatic chemical process that involves the formation of a covalent bond between a sugar molecule (e.g., glucose or fructose) and a protein or lipid [110–112]. This differs from physiologic glycation that is under enzymatic control [102]. AGEs can accumulate within tissues/organs to disrupt structures and function, but in the skin, it causes alterations in col- lagen, elastin, vitronectin and laminin structures, delayed wound healing and declination of skin strength and flexibility [114,115]. Remarkably, external factors such UV irradiation, cigarette smoking, poor dietary choices (Western diets), alcohol, obesity, and cooking meth- ods can increase the rate or abundance of AGEs, whereas whole-food plant-based (WFPD), Mediterranean or Eastern diets contain the least number of AGEs [102,122–124].

Alcohol consumption (two drinks per day) and smoking have damaging influences on skin health [115,116,125]. Alcohol's two major effects on skin: (a) dehydration (diuretic water loss along with decline in vitamins and minerals) and (b) inflammation (increased oxidative stress along with peripheral vasodilation), which can impair quality of sleep, skin cell turnover and alter carotenoid concentrations to lessen antioxidant defense [115,116,125]. The are zero health benefits associated with smoking [125,126]. Smoking's detrimental influence on skin is dependent upon history and level of use, which causes severe signs of aging (loss of skin tone/turgor and appearance of lines/wrinkles) [125]. Even in individuals with the shortest smoking history, facial and perceived age was advanced compared to their chronological age, especially in the facial region around the mouth and eyes [125]. Unfortunately, smoking and vaping have similar harmful influences on skin health [126], and a growing body of research has found that e-cigarettes (vaping), like regular cigarettes, results in serious respiratory disorders especially in youth and young adults [127].

Astonishingly, Gunn et al., in 2016, conducted a twin study entitled "Mortality is Written on the Face", where nurses rated the perceived age of each twin from photographs and selected which twin had survived the other twin. The conclusions of study sug- gested that facial cues are the most important in linking perceived age and survival [128]. Notably, for women there is a strong link between estrogen levels with aging, attractive- ness, facial appearance, and coloration, which are negatively influenced by alcohol and smoking [39,129,130].

High fat dietary intake and obesity (body mass index; BMI $\geq$ 30) have been linked in reference to lifestyle health, an extensive range of chronic diseases, including dermal disorders [83,131–134]. In brief, obesity is now considered to be a global epidemic and

is increasing in prevalence (by 2035 more than 50% of the world's population will be obese) [132,133]. In general, the effect of a high-fat diet results in aging of the skin by inflammatory damage [83]. Almost 60–70 percent of obese patients present with a variety of skin disorders, such as eczema, psoriasis, atopic dermatitis, infections, poor wound healing, and other skin malignancies like melanoma [134,135]. Specifically, obesity is one of the important casual factors of many inflammatory diseases [136,137]. In the skin, functional changes in adipocytes, lymphatic vessels and epidermal keratinocytes are involved in obesity-induced exacerbation of skin inflammation [135–137]. Particularly, skin barrier health is directly related to the changes that occur in the composition and function of dermal immune cells that decline with aging [138,139]. Therefore, the profound impact of increased fat deposition and obesity on cutaneous immunology and its role in the pathophysiology of various chronic inflammatory dermatological conditions is without question [134–139]. However, semaglutide, a glucagon-like peptide 1 (GLP-1) receptor agonist, approved for the treatment of type 2 diabetes mellitus (T2DM) and more recently utilized for weight loss in overweight/obese individuals, has been shown to be highly effective against severe psoriasis in T2DM patients [140,141]. Thus, the importance of lifestyle health factors that may ameliorate the harmful influences of obesity and overweight conditions warrants further research and development of aids and treatments not only for the range of chronic diseases but to improve skin health [134].

Finally, all nutrients, dietary supplement ingredients or daily habits covered in the section above are summarized in Table 1 that display the various influences on the skin along with the cited reference(s).

Table 1. Summary of Key Nutrients/Vitamins/Dietary Intake and Other Factors Influencing Skin Aging.

Nutrient/Diet/Habit	Influence on Skin Health	Reference
Water	skin hydration-biomechanics	[2,22,84,85]
Proteins	support/repair, extracellular matrix (collagen/elastin)	[88,90–92]
	Trace Elements	
Copper	extracellular matrix/angiogenesis	[89,94,95]
Iron	wound healing/antioxidant capacity	[89,94,95]
Selenium	keratinocyte function/antioxidant function	[88]
Zinc	/development-keratinocytes	[88]
	Vitamins and Other Compounds	
A	aging, improves wrinkles, stimulates dermis	[89,93–95]
B-Complex (below)		[88,89,94,95]
B1 (thiamine)	hydration/anti-inflammatory	
B2 (riboflavin)	skin tone/radiant balance	
B3 (niacinamide)	keratin/barrier function	
B5 (pantothenic acid)	hydration/wound healing/anti-inflammatory	
B6 (pyridoxine)	anti-inflammatory/skin balance	
B7 (biotin)	if deficiency-improves skin, hair/nails	
B9 (folate)	skin support/tone/turgor	
B12 (cobalamin)	collagen/hydration, anti-inflammatory, deficiency-hyperpigmentation	
C	antioxidant/boost collagen/hydration	[89,93–95]
D	anti-inflammatory, skin protectant	[89,93–95]
E	antioxidant, anti-aging, improves wrinkles	[89,93–95]

Table 1. *Cont.*

Nutrient/Diet/Habit	Influence on Skin Health	Reference
	Dietary Intake/Supplementation	
Coenzyme Q 10 (CoQ10)	antioxidant (↓ oxidative stress), enhance vitamin E	[88]
Collagen peptides	boost collagen and elasticity (skin, hair, nails)	[88,90–92]
Carotenoids	antioxidant, increases collagen, elastin,	
Astaxanthin, Lutein	reduces appearance of wrinkles by inhibiting	
Zeaxanthin, Lycopene	oxidative stress and MMPs	[88,97–101]
Chlorophyll	antioxidant/anticancer	[102]
Polyphenols	antioxidant, anti-inflammatory, boost collagen and	
Resveratrol, Flavonoids,	elastin, TIMP, SOD, Nrf2, inhibits oxidative stress,	
Isoflavonoids, Green Tea, etc.	NFkappKB, Matrix Metalloproteinases (MMPs)	[8,36,50,75,96,98–101]
Probiotics	reduces oxidative stress and photoaging	[104–106]
	Daily Habits/Negative Impact	
Advanced Glycation	toxins causing skin damage	
End Products (AGEs)	skin inflammation/stiffening	[114,115]
Alcohol	dehydration/inflammation decrease skin barrier	[115,116,125]
Smoking (vaping)	damage skin/skin aging many negative influences	[125,126]
High Fat	skin inflammation/damage/infections	[83,134–137]
Increased BMI (Obesity)	skin inflammation/damage/infections	[83,134–137]

6. Factor 2: Lifestyle Health—Rest, Relax, Recover (RRR) and Manage Stressors

Another important lifestyle health factor is rest, and the most important aspect of rest is sleep, which is essential for health and well-being [142–144]. Sleep is a fundamental physiological need to which humans devote approximately one-third of their lives. Sleep duration and quality of the sleep cycle determine health outcomes, because without this critical rest interval the body's cells/tissues/organs, etc. and functions are adversely affected [142–144].

Each sleep cycle begins with non-REM sleep (for memory consolidation), while REM sleep is critical for processing sensory impressions and each cycle lasts between 70–100 min with an average of four to six cycles per night [142,143]. The sleep interval in healthy people decreases with aging, where newborns need 14–17 h of sleep per day, while adults sleep 7–9 h [142,143]. Less than 7 h of sleep is associated with poor health and decreased well-being [142–144].

For example, the function of sleep has many components which include: (a) reduction in energy consumption, body temperature, blood sugar, helps to control body weight and strengthens your heart, (b) immune cell production, restores defense mechanisms, decreases inflammation/stress and repairs cells/tissues, (c) removal of toxins from the brain (produced by cellular respiration) by increased blood flow to this organ, and increases memory consolidation/formation, (d) boosting mechanical/hormonal balance, executive functions, performing tasks on vigilance, motor speed, and post-exercise recovery [142–144].

It is estimated between 37 to 43 percent of the general population have sleep problems that contribute to a variety of mental and physical health disorders [142,144,145]. One of the potential integrative treatments for sleep disturbance is lifestyle health interventions because the encouragement is to make small changes in one's routine that can have a large impact long-term for many disorders including skin health [1,33,142,145].

What are the factors that enhance sleep disturbance or improve the quality of sleep? First, a general list of factors that can impact sleep quality include a) diet (fats, protein, and carbohydrates), while caffeine, low vitamin D levels, alcohol, nicotine, enhanced

calorie intake and obesity impair sleep quality [142,145–157]. Whereas a balanced diet with adequate vitamin intake and regular physical activity provides weight loss, enhanced melatonin levels, memory consolidation and improved quality of sleep [142,145–157] (Table 2). Assuredly, there are many other factors that influence sleep, but such coverage would be beyond the scope of this overview.

Table 2. Factors Influencing Sleep Quality.

	Factors Improving Sleep Quality	**Factors Deteriorating Sleep Quality**	**References**
Diet			
	Balanced diet	Intake of inflammatory foods (sugar, alcohol, etc.)	[146,147]
Carbohydrates		Low-carb diet and High-carb diet (>70% energy)	[146,147]
Fats	Polyunsaturated Fatty Acids (PUFA)	Saturated Fatty Acids	[146,148]
	(omega-3 > than omega-6 fatty acids)	Trans Fats	[146,148]
Proteins	Appropriate intake of proteins	Too Low Protein or Too High Protein Intake;	
		Red Meats and Processed Meats	[146,149]
Other Factors:			
		Caffeine (chocolate, coffee, tea, energy drinks)	[146,150]
	Adequate Vitamin D Levels	Low Vitamin D Levels	[151]
		Alcohol (beer, wine, etc.)	[152,153]
		Nicotine (cigarettes, chewing gum, e-cigarettes)	[154,155]
	Regular Physical Exercise	Lack of exercise or obesity	[156,157]

6.1. Sleep and Skin Health

Sleep is vital for health and healing because it has a bidirectional impact: poor sleep increases the risk of disease and illness as well as the converse, disease, illness, and other factors disrupt sleep [158]. The concept of lifestyle health where diet and exercise are beneficial, however, when individuals are fatigued and not mentally focused this lifestyle plan is unlikely to succeed. Sleep is vital in regulating skin physiology such as the skin surface pH, TEWL, blood flow and skin temperature [158,159]. For example, in reference to skin health a clinical study of post-menopausal women showed that those who slept less than five hours per day had higher TEWL loss, decreased skin barrier function and longer recovery after UV-induced erythema [159]. Even after a single night of disrupted sleep, periocular areas are known to show dark circles giving a tired appearance [160]. Sleep impairment is associated with chronic inflammatory skin conditions such as atopic dermatitis, eczema, psoriasis, rosacea [161–165]. In this regard, sleep deprivation is known to increase cortisol levels that suppress the immune response along with impairment of T cell function and antigen presentation that result in increased infections. Additionally, sleep loss has been shown to increase proinflammatory cytokines that further increase inflammatory skin disorders like psoriasis and eczema [163]. Finally, isotretinoin, a drug widely used in dermatology to treat acne, had been found to cause sleep disturbances [163].

6.2. Skin Health and Circadian Factors

Organisms have conserved over millennium an internal rhythm that helps them an- ticipate (to changes in radiation, temperature, and food availability) and adapt to daily changes in the environment [166]. Light synchronizes this internal circadian clock, when photons processed by the retina send neural information to a part of the brain called the suprachiasmatic nucleus (SCN) in the anterior hypothalamus [165]. Other factors (food intake, exercise, temperature, aging, trauma/injury, etc.) also affect “clocks” in peripheral tissues, including the skin [166–168]. The communications between the central SCN clock and the skin clock(s) coordinate various functions (i.e., homeostasis, proliferation/repair,

immune and stress responses) [166–168], Notably, the circadian skin clock(s) in the epider- mis, dermis and hypodermis can be altered/disrupted by sunburn (UV-induced erythema), aging, infections, hydration, inflammatory dermal disorders, food intake, sleep, and in- jury/wound healing [166–172]. The biological rhythms in the skin and skin clock genes have been reviewed in detail elsewhere [166,168–170]. However, the fluctuation in human skin characteristics as they cycle through the day and night (as regulated by skin clock genes) is shown in Figure 8. For example, in the epidermis, cellular proliferation in ker- atinocytes is 30-fold higher at night than at noon (12 PM) and epidermal stem cells show a similar pattern and have a higher rate of proliferation at night versus day [169]. Also, the circadian rhythms via modulation associated with skin clock genes altered aquaporin 3 (AQP3) expression impacting skin hydration [167]. Interestingly, it was shown that UV ex- posure, aging, and low temperature resulted in increased TEWL, while vitamin C, collagen and probiotics increased ceramide production and improved skin hydration [167]. Finally, understanding the role of circadian clock genes in the skin will provide new insights to the pathogenesis of skin disorders and novel aids and treatment, especially via lifestyle health approaches.

Figure 8. The fluctuation of human skin characteristics as they cycle from day to night in a circadian pattern [170]. Adapted with permission from, Pernodet, N.; Pelle, E. *Chronobiology of the Skin, Skin Circadian Rhythm and Clock Genes: A New Approach to Slowing Down the Aging Process*, 9th ed.; Chemical Publishing. Los Angeles, CA, USA, 2015, Volume 2.

6.3. Skin Health and Exposome Factors (Stressors)

Miranda A. Farage from Procter and Gamble reported in 2008 that 50 to almost 70% of women reported skin sensitivity worldwide [173]. Later in 2013, Farage et al. confirmed their earlier findings, but also recognized that psychosocial influences, as well as biological and environmental factors contribute to skin sensitivity [174]. The first published reports on air pollution and skin aging appeared in the Journal of Investigative Dermatology in 2010 [175,176]. Both reports suggested that air pollution exposure was significantly correlated with extrinsic skin aging, particularly to pigment spots on the face and hands and, to a lesser extent, for wrinkles [175,176]. However, more recently a much broader perceptive of skin aging includes the concept of the exposome. For example, the exposome can be defined as the measure of all the exposures of an individual in a lifetime and how those exposures relate to health. An individual's exposure begins before birth and includes insults from environmental and occupational sources, etc. Understanding how exposures from our environment, diet, lifestyle, etc. interact with our own unique characteristics such as genetics, physiology, and epigenetics impact our health is how the exposome will be articulated [177]. Thus, exposome factors that lead to stressed skin (via oxidative stress

mechanisms) can be defined as any disturbance to skin homeostasis from environmental (meteorological factors like temperature, humidity, etc.), photo-aging, water/air pollution (external and household), tobacco use (smoking and/or vaping) and internal exposure like (unhealthy diets, hormonal variations/changes with menopause), lack of sleep, psychoso- cial or cultural stresses [2,14,116,178–180]. In general, exposome stress factors can influence six key skin functions, namely the skin barrier, pigmentation, defenses (antioxidant, im- mune cell mechanisms, microbial and microbiome maintenance), structure (extracellular matrix components), neuroendocrine and thermoregulatory functions [179,180]. The physi- cal signs of stressed skin include dry skin, fine/moderate lines/wrinkles, oily skin, sensitive skin, pruritus, erythema, pale/dull skin, edema, and inflammatory skin conditions such as acne, atopic dermatitis, pigmentation disorders, rosacea, and skin infections [178–180]. Parreson et al., in 2021, suggested how to avoid exposome factors/stressor by: (a) getting adequate sun protection (sunscreen, sun avoidance, and protective clothing, (b) adopting a healthy lifestyle (eating a balanced diet, sleeping well, acquiring and using personal stress management skills and utilize psychosocial interventions for obtaining and exchanging ideas), and (c) enhancing the skin's physical barrier and defenses against exposome factors with topical and oral antioxidants, antipollution products, probiotics, moisturizers and other personal care products [180].

Finally, in this regard, the emerging strategies for photoprotection (using sunscreens) [181,182], lifestyle health interventions [2,14,116,158,183] and the use of bioactive textiles to enhance the skin's microbiota [184], along with the effects of spaceflight's influence on human skin [185] have been reported.

7. Factor 3: Lifestyle Health—Physical Exercise and Skin Health

Regular moderate to intense exercise levels have long been known for its active role in improving physical fitness, sustained health and is widely accepted as a preventive and therapeutic strategy for many chronic and age-related diseases [186,187]. It has been proposed that exercise sustains health by: (a) helping to control body weight, (b) enhancing circadian rhythms, (c) promoting repair/regeneration, (d) protecting the integrity of barriers (from organelles to cells/tissues and organs), (e) benefiting turnover and recycling of cells/tissues, (f) providing cardiovascular and immune protection, (g) improving resilience,
(h) boosting energy, (i) improving mood, (j) providing better sleep and (k) maintaining the body's homeostatic balance of functional systems [186,187]. The concept and topic of the health benefits of exercise is easy to follow and understand, especially since the mitochondria with each cell in the body produces the energy needed [via the synthesis of adenosine triphosphate (ATP)] to carry out cellular respiration and the functions/thousands of biochemical reactions each second of life [188]. Each cell in the human body uses about 10–15 million molecules of ATP every second [188].

In dermatology, exercise has positive influences on: (a) skin aging, (b) skin cancer,
(c) psoriasis, (d) venous ulcers, (e) androgenetic alopecia, and (f) skin moisturizing and hydration [189,190]. In brief, the known skin benefits of regular physical exercise include:
(a) improving blood flow to nourish cells and remove toxins from the skin, (b) pre- venting the signs of aging by boosting collagen, elasticity, tone/turgor, the skin barrier,
(c) inhibiting the anti-inflammatory actions of oxidative stress and MMPs, (d) decreas- ing stress by increasing dermal resilience, and (e) maintaining improved overall skin well-being [189–191]. However, it must be pointed out that individuals with inflammatory skin disorders (i.e., acne, atopic dermatitis, eczema, psoriasis, rosacea, etc.) should seek medical guidance before starting an exercise program, plus everyone should be cautious and wear protective clothing and limit their sun exposure [192].

8. Factor 4: Lifestyle Skin Health—Social/Community and Skin Health

Within the framework of lifestyle health, social interactions and/or isolation play important roles in determining an individual's well-being because chronic and age-related disorders/diseases are linked to the lack of social contact with meaningful in person

activities [193,194]. Social isolation is well known and common in older groups, but the increased isolation among younger adults is due to greater social media use [194].

In a recent study by Cudjoe et al., in 2022, found that social isolation in older adults is associated with higher levels of (the inflammatory biomarkers) interleukin-6 (IL-6) and C-reactive protein (CRP) that suggested a link between social isolation and morbid- ity/mortality [195]. Kottner et al., in 2023, showed that isolation in older individuals displayed skin changes (thinning of the epidermis, flattening of the dermal-epidermal junction, decreases in the fat layer (hypodermis) and collagen and elastin fibers in the dermis [196], which indicated that clinical practice guidelines to promote skin health in older people might be improved [196].

One factor associated with social isolation might be a negative body image that is com- mon in men and women (usually associated with an increase in BMI and/or decreased skin health-lack of dermal elasticity and the appearance of wrinkles) [197]. However, physical activity and exercise, yoga, massage, dance therapy and body awareness therapy represent alternative methods to address negative body image issues, especially in women [197,198].

Social isolation was the norm during the COVID-19 pandemic. This isolation resulted in cutaneous changes in the general public, patients, and health care workers [198–200]. In general, there was an increase in atopic dermatitis, psoriasis, rosacea plus many other skin inflammatory diseases [199–201]. However, much of the increase was due to allergic dermatitis induced by hypersensitivity to personal protective equipment (PPE; masks, goggles, face shields, gloves, heat stress, etc.) [199,200]. Conversely, one study during the COVID-19 pandemic examined the connections between the neurological, neuroen- docrine, and immune systems that triggered dermatoses influenced by factors such as stress, fear, negative thoughts, and anxiety, which resulted in skin inflammatory outbreaks not attributed to PPE use [201]. This suggested that a psychological component potentially linked to social isolation was the main cause, which was greater than only among those infected with COVID-19 [201]. This last study opens a perspective of how our environment interacts with human health and the interlinking of humans socially with each as well as through ecosystems like the microbiome, including that of the skin. [202].

Finally, it is well established that social relationships provide a clear link to improved health and well-being [193,194,203], including dermal health [196,201]. Just as the review of combined data for a variety of outcomes found that social media interventions that aim to increase physical activity and well-being were effective [204], this approach might be an application for improved skin health in the future.

9. Conclusions

Lifestyle health has been recognized as an evidence-based innovation that defines how daily habits and practices impact both the prevention and treatment of disease and provides an important adjunctive component to overall health [21]. Specifically, an approach with small changes over time can have a dramatic impact on the health and well-being of individuals not only, in general, but also can be applied to skin health. This narrative overview presented four lifestyle health factors to maintain and improve skin health. Lifestyle health factor 1: nutrition—diet and skin health; factor 2: rest (sleep) and skin health; factor 3: movement/physical exercise and skin health, and factor 4: social and community associations and skin health (see Figure 9).

Lifestyle change is often a gradual process involving multiple forward efforts and some setbacks, but this paradigm is a routine/program rather than an event. Finally, there are many ways to enhance skin health (especially with aging), if people alter their perspective and feelings about making changes based on short duration interventions with healthy goals in mind [2,5,9,11,17,38,49,50,79,96,116,205].

Figure 9. Summary of Enhancing Skin Anti-Aging Through Healthy Lifestyle Factors.

dead skin and decrease the chance of hangnails forming. Nails are easier to cut after soaking; be sure to cut them straight across to avoid ingrown nails, and keep them short for safety. If ingrown nails develop, see your primary care provider or podiatrist.

- Lubricate dry skin with moisturizing creams or ointments (such as Eucerin or Aquaphor). Use care in applying creams over bony areas, since they may soften the skin and promote skin breakdown.
- Soiled skin can break down easily. Urine and stool have irritants in them and should be cleaned up immediately to prevent weakening and breakdown of the skin surface.
- Avoid using talc powders, as they may support yeast growth. They can also "cake up" and keep moisture in, causing skin breakdown.
- Calluses may form on your feet and hands.These can be removed by soaking frequently in warm water and toweling briskly to remove dead skin. You can use moisturizing creams to help soften calluses. Note that calluses may indicate an area of excess friction or pressure.
- Finger and toe nails require special care. Soak them and rub gently with a towel to remove

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What is Healthy Skin?

Your skin is much more than an outer surface for the world to see. It protects you from bacteria, dirt and other foreign objects and the ultraviolet rays of the sun, and contains the nerve endings that let you know if something is hot or cold, soft or hard, sharp or dull.Your skin also plays an important role in regulating your body's fluids and temperature.

Below the smooth, hairy outer skin, or epidermis, that we see every day is a thick, strong and elastic layer of tissue known as the dermis.The dermis is richly supplied with blood vessels, sweat and oil glands, and nerve endings.

Healthy skin is smooth, with no breaks in the surface. It is warm (not hot or red) and neither dry and flaky nor moist and wrinkled. Healthy skin is a mirror of a healthy body.

How to Take Care of Your Skin

Nutrition:

To keep your skin healthy, eat a well-balanced diet that includes plenty of protein foods, fruits and vegetables (fresh if possible) and liquids. If you are having a skin problem, such as a pressure sore or a healing surgical incision, you should increase your intake of protein (lean meats, dairy foods and le- gumes), carbohydrates (breads, cereals), vitamins A, C and E, and zinc. Extra iron may be needed if you are anemic (see "Anemia" paragraph, right).

Circulation:

The skin is served by a large number of blood ves- sels, and adequate circulation is needed to maintain skin health.You can help ensure a healthy blood sup- ply by considering the following suggestions:

- **Smoking** — DON'T! Nicotine in cigarettes causes blood vessels to get small (constrict) and prevents blood, oxygen and nutrients from flowing to the body tissues.
- **Edema**, or swelling caused by fluid collecting in the tissues, usually occurs in a part of the body that is not moved frequently and is below the level of the heart (i.e., the feet, legs and hands). Skin over areas of edema becomes thin and pale and injures easily because of poor circulation. Edema can be prevented by elevating your legs and hands frequently, performing regular Range of Motion (ROM) exercises and wearing com- pressive stockings.

- **Anemia** (a decrease in red blood cells). Oxy- gen is essential for skin health, and is carried by red blood cells. A decrease in their number means less oxygen gets to the skin, which means that skin cells may become unhealthy or even die. Anemia should be evaluated and treated by your health care provider.

- **Vascular Disease**, or a narrowing of the blood vessels, can be caused by diabetes, smoking, high blood pressure or elevated cholesterol. The result is decreased blood flow to the skin. Work closely with your health care provider to man- age conditions that can lead to vascular disease and cause skin problems.

Tips for Maintaining Good

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The intimate relationship between dermal demand of nutrients and adequate supply from the blood circulation seems to have been understudied. In fact, the title of this book can be read in two ways; balanced nutrition is necessary for maintaining healthy skin, and there are nutritive aspects to restore healthy conditions after a disease state has developed. Skin care has an important metabolic and nutritive component. Maintenance and restoration are integral processes in skin health.

It is satisfying to see that the two editors, Professors Jean Krutmann from Düsseldorf, Germany, and Phillippe Humbert from Besancon, France, have been able to compile the pertinent aspects by attracting contributions from the world leaders in this subject area. Three major sections make up the treatise: Nutrition and Skin, and its scientific basis; Functional Food, addressing botanicals and other micronutrients as well as probiotics and; thirdly, Aspects of Clinical Dermatology, culminating in the topic of beauty from inside.

The need for scientifically sound information on this subject area is particularly urgent, since the general public is being supplied with suggestions from the news media and, increasingly, from the Internet with material which is not always based on sufficient scientific evidence. The present treatise will also be good for delineating the problems and limitations in current knowledge. The authors, the editors, and the publisher can be congratulated to a timely opus!

Duesseldorf, Germany — Helmut Sies

The relationship between nutrition and skin has become a “hot” topic that is exciting researchers and clinicians worldwide. New insights into the effects of orally applied, biologically active molecules on skin functions have stimulated a continuously growing interest in the development of nutritional supplements and, most importantly, functional food products to benefit human skin. This monograph attempts to provide an up-to-date overview regarding all aspects of nutrition and skin. It includes in-depth, critical discussions of the molecular basis as well as current concepts propagated for nutrition-based cosmetic, preventive, and therapeutic dermatological strategies. The explosion of knowledge in this field over even the last few years is remarkable with consequences for practicing dermatologists, patients, cosmetic and nutritional industry, and consumers in general. To capture the depth and breadth of this learning, we have recruited leading experts from multiple subdisciplines. All authors are internationally recognized, and we are very grateful for their excellent contributions. We hope that this book will serve you as a state-of-the-art reference and will further stimulate your interest in this fascinating area.

Duesseldorf, Germany — Jean Krutmann
Besançon, France — Philippe Humbert
March 2010

Core Messages

- Abnormal nutrition causes cutaneous changes that are either due to insufficient food supply; i.e., inadequate intake of nutrients, vitamins, and minerals, or to excess calory intake.
- In countries with inadequate food supply, protein-energy malnutrition (*marasmus*, *kwashiorkor*) is common and children ≤ 5 years are at highest risk. In 2001, approximately 50% of childhood deaths were indirectly or directly attributable to inadequate nutrition.
- In countries with adequate food supply, the most common nutritional abnormalities are obesity due to excess food consumption, and malnutrition due to psychological (anorexia nervosa, bulimia) or medical conditions (metabolic disease, chronic illness, hospitalization), affecting both children and adults.
- Skin changes provide important clues for lack or overabundance of individual nutritional components and can help clinicians to correctly detect, diagnose, and consequently treat nutritional disease, which can be confirmed by laboratory testing.
- While the importance of individual components for normal function of the skin is undisputed, there are many compensatory mechanisms in place. Nutritional disease is rarely the result of the deficiency of a single nutrient.
- While substitution of deficient nutritional components usually results in rapid resolution of symptoms, toxic effects of overload have become more common with the increasing popularity of dietary supplementation. This is particularly common with lipophilic vitamins (A, D, E, and K) because they accumulate in the tissue.

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1.1 Nutritional Deficiencies

1.1.1 Marasmus and Kwashiorkor

Nutritional deficiencies can be exogenous or endogenous. The primary exogenous reason is insufficient intake of nutrients. Endogenous etiologies include intestinal or metabolic disease that interferes with the absorption and delivery of nutrients to the cellular machinery (e.g., intestinal malabsorption, gastrointestinal and metabolic disease, infections, cancer) (Table 1.1). With prolonged nutritional deficiencies, energy storage is exhausted and energy supply lags behind. Because of their increased nutritional needs during the growth phase, children ≤ 5-years old are particularly susceptible to the developmental and physiologic consequences of poor nutrition.

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Table 1.1 Causes of nutritional deficiency

Exogenous (inadequate food intake)	Endogenous (inadequate food absorption/metabolization)
Poverty	Intestinal malabsorption
Old age	Gastrointestinal disease
Alcoholism	Metabolic disease
Psychiatric disorders	Chronic systemic disease
Diets (e.g., "fad diets," "allergy diets")	Cancer
Child neglect	Recurrent infections
	AIDS (inadequate intake, e.g., due to candida esophagitis)

Table 1.2 Differential diagnosis of hyperkeratotic papules on the extremities due to nutritional deficiency

Vitamin A deficiency (phrynoderma)
Vitamin C deficiency
Essential fatty acid deficiency

Marasmus is due to insufficient (although balanced) nutritional quantities. Marasmus is not only due to decreased overall caloric supply, but also results from a deficit in essential nutritional components (e.g., vitamins, essential amino acids, minerals). Therefore, the cutaneous changes of marasmus are multifold. Aside from a decrease in the subcutaneous fat, the dermal and epidermal layers are thinned which gives the skin an aged appearance. In addition, there is dryness of the skin, sometimes to the degree of ichthyosis-like scaling. Vitamin A and C deficiency result in follicular hyperkeratosis (see below, Table 1.2). Because of anemia and vasoconstriction, the skin color is pale, while in sun-exposed areas there is spotty hyperpigmentation. The hair is dry, loses color ("premature graying"), and hair loss (telogen effluvium) is common. The growth of the nails is delayed, and the nail plates may show longitudinal ridging. Marasmus is corrected by carefully restoring protein-calorie intake and by supplementation of vitamins, essential fatty acids, and zinc according to their respective blood levels.

Kwashiorkor occurs if normal carbohydrate consumption is coupled with insufficient protein intake; i.e., chronic malabsorption such as in cystic fibrosis. It is most common in infants in third world countries as soon as their mothers discontinue breast feeding. Kwashiorkor can also occur in children receiving a calorie-rich diet that is poor in proteins of animal origin [4]. These children show the cutaneous changes of marasmus (see above), and in addition develop diffuse edema due to hypoalbuminea, and increased vulnerability of the skin (e.g., to mechanical trauma), which results in erosions and blisters in areas of friction. A further characteristic of kwashiorkor is a reddish-brown scaly dermatitis ("flaky paint"), and dusky erythematous plaques with a waxy appearance in pressure-exposed areas (diaper area, over bony prominences) with a thickened, pigmented stratum corneum on histology. Depigmentation of the skin can be observed (predominantly in the perioral area and on the lower legs). Moreover, depigmentation of the hair to a reddish color is often observed. Correction of kwashiorkor must be undertaken carefully; electrolyte imbalances need to be taken into account, combined with supplementation of vitamins, essential fatty acids, and zinc as above.

In both marasmus and kwashiorkor, individual hair shafts show pigmented areas alternating with depigmented areas ("signe de la bandera" or "flag sign"), reflecting intermittent periods of food availability. In fact, because of overlapping features, a clear distinction between marasmus and kwashiorkor can not always be made with certainty. In these cases, the term *protein-calorie malnutrition* is used instead. Generally, chronic nutritional deficiencies increase the susceptibility to opportunistic infections by causing a secondary immune deficiency. Particularly problematic are mixed infections of the skin with fusiform bacteria and spirochetae (e.g., bacterium fusiforme, spirochäta refringens) causing necrotizing ulcerative gingivitis, noma, or cancrum oris which can be life-threatening. In adults, similar treatment-recalcitrant ulcerations occur on the lower legs following insect bites.

Most commonly, malnutrition is due to inadequate food availability, but it is also seen in individuals with medical conditions, particularly in hospitalized patients, which often can simply be ascribed to poor logistics (negligence of nutritional needs in patients waiting for a complex diagnostic workup). Other reasons are individuals voluntarily subjecting themselves to unusual diets and individuals with excessive alcohol consumption [3]. *Anorexia nervosa* and *bulimia* are psychiatric disturbances that lead to physical disturbances. Cutaneous changes associated with these disorders are manifold including dry skin, pruritus, patchy hyperpigmentation, freckles, lanugo hair, brittle terminal hair and nails, and paronychia. Russell's sign refers

to callus formation on the hand used to elicit vomiting, which is another diagnostic clue. Early recognition is desirable, because the mortality is much lower with early intervention.

1.1.2 Essential Fatty Acid Deficiency

Malnutrition is a common cause of essential fatty acid (e.g., linoleic, linolenic, and arachidonic acid) deficiency. Patients present with diffuse eczematous skin changes that can be pruritic and preferentially affect the periorificial areas. With long-standing essential fatty acid deficiency, there can also be depigmentation and alopecia (telogen effluvium). In children, there is growth failure. Essential fatty acid deficiency is associated with impaired wound healing, capillary fragility, abnormal liver, and kidney function, and neurologic damage. The differential diagnosis includes zinc deficiency (see below), and necrolytic migratory erythema. Plasma levels of linoleic, linolenic, and arachidonic acids are decreased. In contrast, palmitoleic and oleic acids are increased, and there is abnormal presence of 5,8,11-icosatrienoic acid in plasma. Therapeutic fatty acid supplementation is effective.

1.1.3 Vitamin Deficiencies

Vitamins are cofactors in metabolism; nutritional vitamin deficiency results in metabolic disturbances. In Western societies, this is mostly due to impaired intestinal absorption (e.g., in inflammatory bowel disease, inherited metabolic disease, parenteral nutrition, following surgery), or due to alcoholism. Because the deficiency usually involves multiple vitamins, it is often difficult to determine the relative role of individual vitamins [1].

Vitamin A deficiency causes ichthyosis-like skin changes with generalized fine scaling and a thickening of the outermost skin layer, the stratum corneum ("phryonoderm"), which is particularly pronounced in the follicular openings, causing follicular hyperkeratosis [2]. This is often associated with effluvium and fragility of the hair. One of the earliest signs of vitamin A deficiency, however, is impaired night vision and the inability to see in bright light. Metaplasia of the conjunctival epithelium in vitamin A deficiency has been called keratoconjunctivitis sicca (Bitot macules), which can progress to keratomalacia, permanent scarring and blindness. Finally, vitamin A deficiency is associated with an increased incidence of epidermal neoplasias (anticarcinogenic activity of vitamin A). The differential diagnosis of vitamin A deficiency includes lichen pilaris, ichthyosis vulgaris, Darier disease, and other vitamin deficiencies (see biotin, vitamin C deficiency below). Extracutaneous manifestations include growth failure and mental retardation. For diagnosis plasma retinol levels are measured. Vitamin A supplementation resolves ophthalmologic symptoms within days and cutaneous changes within weeks.

Vitamin B1 (thiamin) is involved in carbohydrate metabolism, and B1 deficiency is known as *beriberi*. It is seen with gastrointestinal disease, a diet restricted to polished rice, alcoholism, pregnancy, lactation, and diabetes mellitus. Mucocutaneous changes include edema and glossitis with glossodynia. Predominant are neurologic symptoms including peripheral neuropathy, confabulation (Korsakoff's syndrome), and encephalopathy (Wernicke). Low urinary aneurin excretion is used as a diagnostic test. Supplementation is effective.

Vitamin B2 (riboflavin) can be due to a poor diet, but can also be caused by medications that impair its absorption (galactoflavin, phenothiazines, tricyclic antidepressants). Cutaneous changes that indicate vitamin B2 deficiency include seborrheic dermatitis-like scaling on the face (nasolabial folds), head, and genitocrural region. In addition, these patients present with cheilitis, perleche, pallor, and atrophy of the tongue

Table 1.3 Differential diagnosis of cheilitis due to nutritional deficiency

Zinc deficiency – genetic – acquired
Biotin deficiency
Vitamin B2 deficiency*
Vitamin B6 deficiency
Vitamin B12 deficiency*
Folic Acid deficiency
Zinc deficiency*
Iron deficiency*

* in association with angular involvement (perleche)

(Table 1.3). Ophthalmologic involvement includes blepharitis, conjunctivitis, and corneal vascularization. Vitamin B2 is a cofactor of flavin mononucleotide (FMN) and flavin adenine dinucleotide (FAD), which are involved in many redox reactions. On blood testing patients show a normochromic anemia. Decreased erythrocyte glutathione reductase activity confirms the diagnosis. The differential diagnosis includes seborrheic dermatitis and zinc deficiency. In mild cases, the recommended treatment is riboflavin 3–10mg daily per mouth, in refractory cases 2 mg daily via the intravenous route.

Vitamin B3 (niacin) deficiency causes pellagra. Pellagra is characterized by a triad consisting of changes in skin, nervous system, and the gastrointestinal tract ("3D's": dermatitis, dementia, diarrhea). An early symptom is diarrhea. At later stages, patients report increased UV sensitivity (face, sun-exposed distal upper extremities) and sun-burn-like pruritic or burning erythematous macules, and occasionally blisters (Table 1.4). The facial rash at times resembles the butter fly rush of lupus erythematodes, but is always associated with other components of the triad. Quite characteristic is the sparing of the forehead as well as eczema of the neck and upper chest that can resemble a necklace (Casal's necklace) (Fig. 1.1). Here the skin is erythematous to brown (or black), scaly. Sometimes there is an eczema craquele-like appearance with fissures and occasionally there are crusts. These lesions are common on the dorsal hands (Fig. 1.2), and can also be found on the feet and in the genitocrural region. Glossitis and stomatitis can also be present. Neurologic symptoms include peripheral polyneuropathy, encephalopathy, and depression. The differential diagnosis includes contact eczema, photo-induced dermatitis, and porphyria cutanea tarda. Pellagra is a clinical diagnosis, there are no laboratory markers. Niacin is a component of nicotinamide-adenine-dinucleotide (NAD) catalyzing redox reactions. A frequent setting for niacin deficiency is a niacin-deficient diet, which has occurred with the introduction of corn as a major food that only contains bound niacin that cannot be used by the human body. This is exemplified by endemic pellagra in geographic areas with predominant corn consumption, e.g., in South America. Aggravating factors include alcoholism, long-standing antibiotic therapy, isoniazid, 5-fluoruracil, inflammatory bowel disease, abnormalities of tryptophan metabolism (carcinoid), and Hartnup disease (see below). As with the other vitamin deficiencies, vitamin B3 supplementation will resolve the symptoms, but exogenous niacin can release histamine causing urticaria and worsening of preexistent asthma. Niacinamide is the preferred choice for supplementation, because it avoids these adverse effects.

Table 1.4 Differential diagnosis of photosensitive eruptions due to nutritional deficiency

Vitamin B3 deficiency (pellagra)
Hartnup disease

Vitamin B6 (pyridoxine) deficiency is usually accompanied by other deficiencies and is associated with seborrhoic dermatitis-like skin changes in periorificial distribution (eyes, nose, mouth) as well as cheilitis and glossitis. Pyridoxine is a cofactor of enzymes involved in amino acid metabolism (e.g., transaminases, synthetases, hydroxylases) and the metabolization of linoleic acid into arachidonic acid. Associations have been described with drugs such as isoniazid, penicillamine, hydralazine hydrochloride, oral contraceptives, phenelzine sulfate, cycloserine, and with uremia and liver cirrhosis. Diagnosis is made bymeasuringpyridoxineserumlevels.Supplementation is effective.

Lack of *vitamin B12* (cyanocobalamin), because of decreased intrinsic factor, is known for causing pernicious anemia, but can rarely also be due to strict vegetarian diet. Aside from its hematologic consequences (megaloblastic anemia), occasionally vitamin B12 deficiency also is associated with atrophic glossitis, angular cheilitis, mucositis, and symmetric acral (dorsal fingers and toes) and flexural hyperpigmentation. Poliosis, vitiligo, and alopecia areata occur with increased frequency. The differential diagnosis for the hyperpigmentation includes Addison's disease. Intramuscular supplementation is effective (1 mg per month), resolving symptoms within 2–12 weeks.

Folic acid deficiency has similar mucocutaneous changes to vitamin B12 deficiency including hyperpigmentation and glossitis, but cheilitis and mucosal erosions have also been described. Decreased serum folate is diagnostic; oral supplementation is effective.

Vitamin C deficiency is the cause of scurvy. In the past, this was common among sailors and other people without access to fresh fruits and vegetables for extended periods of time. Although vitamin C deficiency has become much less common today, it is still encountered in the setting of urban poverty where it preferentially affects the very young and the aged (exacerbated by general malnutrition, mental incapacity, alcoholism). It is also seen with fad diets. Cutaneous changes of vitamin C deficiency include follicular hyperkeratosis on the extensor surfaces of the extremities, which characteristically show perifollicular hemorrhage (Fig. 1.3). The propensity for hemorrhage is due to fragile blood vessels, which is particularly pronounced in newborns and infants that present with petechia (over mechanical pressure points) and intestinal as well as urinary tract bleeding. In children, subperiosteal hemorrhage with radiographic alterations and pseudoparalysis has been described. Adults with long-standing vitamin C deficiency report impaired wound healing, bleeding gums, gingivitis, gingival hypertrophy, and loss of teeth. General symptoms of scurvy include fatigue, muscle weakness, myalgia, arthralgia, diarrhea, and anemia. The onset is approximately 1–3 months after onset of insufficient vitamin C intake. Long-standing, severe vitamin C depletion can result in diffuse edema, oligura, anemia, dyspnea, and neuropathy. Supplementation with vitamin C is usually successful, if the deficiency is recognized early enough. Left untreated, the condition can lead to death. Low vitamin C serum levels are diagnostic. The recommended dose for vitamin C supplementation in individuals with deficiency varies between 100–1,000 mg of ascorbic acid per day. Infants should be treated with 50 mg of ascorbic acid up to four times per day.

Fig. 1.3 Scurvy: follicular hyperkeratoses with perifollicular hemorrhage

Vitamin D deficiency is not associated with cutaneous changes (it primarily causes bone disease; i.e., rachitis in children and osteomalacia in adults). Vitamin D deficiency has also been associated with higher susceptibility to infections; i.e., tuberculosis.

Vitamin E deficiency is not associated with cutaneous changes (it primarily causes neurologic abnormalities).

Biotin (vitamin H) deficiency causes an exfoliative dermatitis on acral skin, cheilitis, and/or periorificial dermatitis. If occurring in newborns, the disease may present with erythroderma and alopecia. The most common extracutaneous feature is enteritis. Other extracutaneous findings include metabolic acidosis, developmental delay, hearing loss, paraesthesias, seizures, and conjunctivitis. Biotin deficiency is associated with impaired cellular immunity, there is a predisposition for infections; i.e., candida dermatitis. Biotin is a cofactor of carboxylases (biotinidase, holocarboxylase). Decreased serum biotin levels can be acquired or genetic. The differential diagnosis includes essential fatty acid deficiency. Hyperamonemia and organic aciduria are used for screening; the definitive diagnosis is established by assaying carboxylase synthetase activity in fibroblasts. Supplementation is effective.

Vitamin K deficiency, in severe cases, can lead to hemorrhage of the skin and mucous membranes. Clinical hemorrhage together with a prolonged prothrombin time leads to the diagnosis. This is seen in newborns or in later life in individuals with malabsorption, cystic fibrosis, liver disease, and drugs (warfarin, salicylates, cephalosporins). Treatment consists of parenteral vitamin K (1 mg newborns, 2 mg children, 5–10 mg adults).

1.1.4 Trace Element Deficiencies

Zinc deficiency is known for the classic triad of dermatitis, alopecia, and diarrhea. However, only 20% of patients present with all three components of the triad at a given time. Zinc deficiency can be hereditary or acquired. H*ereditary zinc deficiency (acrodermatitis enteropathica)* is an autosomal recessive intestinal abnormality of zinc absorption due to a mutation in a zinc transport protein. Human milk contains a zinc transport protein that is much less abundant in cow's milk. Therefore, infants typically develop cutaneous changes days to weeks after being switched to bottle feeding (cow milk). Following intestinal absorption, zinc is bound to albumin. Whereas 99% of body zinc is intracellular, zinc storage is poor (total body zinc 2–3 g) and depletion occurs rapidly; i.e., within a month (zinc deficiency = <70mg/dl). Patients initially present with a perioral erosive dermatitis and perleche that progresses to involve the entire face, scalp, acral sites, and the diaper area. This can be accompanied by ulcerations of the oral mucous membranes and glossitis. The periorificial distribution is helpful in making the diagnosis. Palmar erythema, sometimes with anular or collarette-like scaling, may be present. If the dermatitis is accompanied by alopecia (telegon effluvium) and/or photophobia, zinc deficiency needs to be considered. Conversely, telogen effluvium alone without accompanying skin changes cannot be ascribed to zinc deficiency. Other differential diagnoses of zinc deficiency include seborrheic dermatitis or other eczematous eruptions. At times, patients present with persistent cutaneous infections, e.g., candida dermatitis, paronychia, as well as with onychodystrophy, blepharitis, and conjunctivitis. There is an immunodeficiency, preferentially due to functional impairment of T cells. Before the advent of zinc supplementation, affected individuals, primarily newborns and infants, would die from infections. The predominant extracutaneous symptom is diarrhea with electrolyte imbalance of variable degree. Long-standing zinc deficiency also leads to delayed wound healing, growth retardation, anorexia, anemia, hypogonadism, and altered mental status. Individuals with zinc deficiency are frequently infertile. If they conceive, infants may show malformations.

The cutaneous changes of *acquired zinc deficiency* are similar, but usually milder than those of hereditary deficiency. Because of its relatively mild symptoms, acquired zinc deficiency may be underdiagnosed. It can develop relatively quickly with an unbalanced diet (exclusive high fiber content interferes with absorption), parenteral nutrition lacking sufficient zinc supplementation, malabsorption (including cystic fibrosis), or abnormal intestinal loss of zinc. Chronic diarrhea is a common cause and can lead to a vicious cycle where diarrhea compromises zinc absorption and zinc deficiency in turn causes diarrhea. Other dis- ease associations include chronic renal failure, malignancy, drugs, alcoholism, HIV infection, and pregnancy (Table 1.5). Zinc is a critical component of many enzymes. An important consequence of zinc deficiency is poor incorporation of essential fatty acids into eicosanoids. Skin histology shows a "pallor" of the upper epidermis. In more pronounced cases, there may be vacuolar degeneration of the upper epidermis,

Table 1.5 Causes of acquired zinc deficiency

Poor Intestinal Zinc Absorption	Malabsorption
	Chronic liver and pancreatic disease
	Other gastrointestinal disease
	Alcoholism
	Unbalanced diet (e.g., exclusive high fiber)
	Parenteral nutrition lacking zinc supplementation
Increased Zinc Excretion	Liver cirrhosis
	Renal disease
	Diabetes mellitus
	Dialysis
Increased Catabolism	Cancer
	Chronic recurrent infections, AIDS
	Trauma, burns
Decreased Serum Albumin	Nephrotic syndrome
	Liver cirrhosis

Table 1.6 Differential diagnosis of periorificial dermatitis due to nutritional deficiency

Zinc deficiency – genetic – acquired
Essential fatty acid deficiency
Biotin deficiency
Vitamin B2 deficiency
Vitamin B6 deficiency
Glucagonoma syndrome
Pseudoglucagonoma syndrome

epidermal hyperplasia, and hyperkeratosis. In later stages, there is epidermal atrophy with flattening of the rete ridges and dermal fibrosis. The differential diagnosis of zinc deficiency (see Table 1.6) includes abnormal amino acid absorption, biotin deficiency, essential fatty acid deficiency, and the glucagonoma syndrome ("necrolytic migratory erythema"), all of which may show similar histologic changes. Serum zinc levels are measured for diagnosis. Because alkaline phosphatase is zinc-dependent, it can serve as an additional surrogate marker. Supplementation of zinc can be achieved by the oral or intravenous routes (1–2 mg/kg/day in the acquired, 3 mg/kg/day in the hereditary form).

Iron deficiency is associated with pallor of the skin, dry/scaly skin, perleche, glossitis, dull, shaggy hair, in the case of long-standing deficiency with telogen effluvium and coilonychia [5]. Blood smears typically show microcytic, hypochromic anemia. Serum iron is decreased, being tightly regulated between intestinal absorption, protein-bound transport (transferrin), and intracellular storage (ferritin). Supplementation is effective.

Copper deficiency (*Menkes Syndrome, Kinky hair Syndrome, Steely hair disease*) is due to X-chromosomal recessive mutations in the Cu(2+)-transporting ATPase (ATP7A). Patients present with saggy and hypopigmented skin, there are follicular hyperkeratoses, and the hair is sparse, hypopigmented, and brittle (pili torti, monilethrix, occasionally trichorrhexis nodosa). In addition patients lack eyebrows and lashes. Extracutaneous changes include neurodegenerative changes. At birth and for the first few months, infants appear normal, but subsequently develop hypotonia, seizures, and failure to thrive resulting in death by 2–3 years of age. Another feature is tortuous, elongated arteries due to immature elastin fibers. Copper is a component of enzymes important for elastin, collagen, and melanin synthesis, e.g., lysyl hydroxylase, tyrosinase, etc. Total body copper content is 80 mg, 90% of which is associated with ceruloplasmin, the remainder with other plasma proteins, mainly albumin. Due to fluctuations, serum copper and ceruloplasmin are unreliable predictors in the neonatal period. However, because the lack of copper impairs the function of enzymes of catecholamine synthesis and metabolism, there is a distinctive increase in the dihydroxyphenylacetic acid to dihydroxyphenolglycol ratio that is of diagnostic value. Despite the defective transport protein, intramuscular copper injections can be effective if commenced within days after birth, particularly in individuals with residual ATP7A activity.

Selenium deficiency presents with a whitish discoloration of the nails and effluvium. It has been reported in patients receiving parenteral nutrition. Extracutaneous features include cardiomyopathy, muscle pain, and weakness. Because selenium is essential for glutathione peroxidase, low activity of this enzyme and low plasma selenium are diagnostic. Supplementation is effective (2 mg/kg/day).

1.2 Excess Nutrition

1.2.1 Obesity

In Western societies excess nutrition has become a significant problem (Table 1.7). Overweight (body mass index 25–29.9) and obese (body mass index ≥ 30) individuals have an increased general morbidity, predominantly from metabolic and cardiovascular disease. There are several characteristic skin changes that are more common in overweight individuals, and can be used as markers for individuals at risk for internal disease. In overweight and obese individuals, pseudoacanthosis nigricans is an indicator for insulin resistance and metabolic syndrome. The skin folds of obese individuals are subject to increased friction, they are commonly hyperpigmented (inner thighs, submammary region) and carry skin tags (achrocordon). The enlarged surface between the folds creates a niche for microbial growth, which is further exacerbated by sweating. Over time, this commonly leads to intertiginous eczema, secondary overgrowth of bacteria, erythrasma, dermatophyte, and yeast infections. Other skin findings associated with obesity include hyperhidrosis, striae distensae, stasis dermatitis, venous hypertension, and leg ulcers.

1.2.2 Hypervitaminoses

With the increased popularity of vitamin supplementation, excess vitamin intake has become more common (often triggered by aggressive advertisements promoting the vitamin's beneficial effects). Because lipophilic vitamins (A, D, E, K) can accumulate in tissue, these are more prone to having toxic effects. Syndromes due to excess hydrophilic vitamins are not as well described.

Table 1.7 Causes of excess nutrition

Exogenous (excess food intake)	Endogenous (abnormal metabolism)
Social	
Depression	Genetic
Anxiety	
Iatrogenic	

Several meta-analyses have failed to demonstrate sustained beneficial effects of vitamins A, B6, B12, C, E, and beta-carotene on carcinogenesis and cardiovascular disease.

Hypervitaminosis A develops with excess supply of vitamin A. Today, this is seen with long-term vita- min (over)supplementation. The skin findings of hypervitaminosis A include pruritus, generalized scaling, dry mucous membranes, alopecia (telogen effluvium), cephalea, nausea, increased serum transaminases, and lipids. Hyperostoses similar to those seen with retinoid medication have been described. Hypervitaminosis A is also characterized by an orange-yellowish skin tint. In contrast to generalized jaundice from hyperbilirubnemia, there is sparing of the sclera, eyelids, ears, and axillary folds. The same pattern of skin discoloration is seen with excessive beta-carotene consumption (the natural provitamin of vitamin A contained in carrots, red palm oil, etc.) which is used for self-tanning. The skin color is particularly evident in the palms and soles (depends on the thickness of the epithelium; i.e., mucous mem- branes are less affected). This is quite common in children and vegetarians, it is sometimes also seen with renal disease, diabetes mellitus, and thyroid dis- ease (myxedema) due to a decreased ability to convert beta-carotene into vitamin A in these diseases. Serum carotenoid levels are increased. Patients should be educated about the limitations of photoprotection by beta-carotenes (cf. Chap. 6).

Historically, hypervitaminosis A was seen in inuit populations who consumed polar bear liver that contains excessive amounts of vitamin A causing hypervitaminosis A. Therefore, inuits have learned to be very careful about eating polar bear liver while hunting.

Hypervitaminosis C develops after long-standing dietary intake of vitamin C which then interferes with vitamin B12 metabolism and bears the symptoms of its deficiency (see above). The combination of vitamin C with estrogen medication can lead to kidney (oxalat) stones.

Hypervitaminosis D, e.g., in patients with renal disease supplemented with vitamin D, can result in anorexia, cephalea, vomiting, diarrhea, hypercalcemia, and calcium deposition in the skin (*calcinosis cutis*).

Hypervitaminosis E is rare and only manifests after very high vitamin E consumption, causing gastrointestinal upset, cephalea, and icterus in premature neonates.

1.2.3 Trace Element Deposition

Dietary *zinc* supplementation can be toxic if overdosed causing nausea, vomiting, upper intestinal hemorrhage, vertigo, and neutropenia. In these cases, serum zinc levels are markedly increased. Therefore, monitoring of serum zinc levels and blood counts are warranted with long-standing zinc supplementation.

Because normally 95% of nutritional iron is not absorbed (mucosa block), *iron overload* is usually due to an inherited abnormality in iron absorption (primary hemochromatosis) or to parenteral iron overload (secondary hemochromatosis). Iron is deposited in many tissues including liver, heart, and skin. Diffuse bronze-color hyperpigmentation of the skin with a predilection of sun-exposed areas can facilitate the early diagnosis of hemochromatosis. The hyperpigmentation not only derives from cutaneous iron deposits, but also from an induction of melanogenesis. Other cutaneous changes include ichthyosis-like scaling, alopecia, and coilonychia. Organ involvement consists of the classic triad of diabetes mellitus, cardiomyopathy, and liver cirrhosis (which in turn has the characteristic cutaneous findings of palmar erythema, teleangiectasia, etc.). Therapy consists of deferroxamine and bloodletting.

High content of either *lead* or *mercury* in food is associated with a bluish-gray discoloration of the gums.

Aluminum intoxication can cause porphyria-like bullous skin changes.

Arsenic is well known as a skin carcinogen that increases the incidence of Bowen disease and basal cell carcinoma. The nails show whitish lines (Mees lines). Extracutaneous consequences of arsenic ingestion are lung cancer, vomiting, diarrhea, hepatic/renal damage, as well as peripheral neuropathy.

Argyrosis is the term for cutaneous deposition of silver metal. In cases of chronic silver consumption, the skin has a diffuse grayish color with a predilection of sun-exposed areas, but also involving the sclerae, mucous membranes, and finger nails (typically toe nails are not affected). Silver deposits can be visualized by dark field or electron microscopy. No therapy is available. Argyrosis has become rare since many of the silver-containing medications (e.g., for the treatment of rheumatoid arthritis) have been discontinued.

Chrysiasis, the deposition of gold in the skin, is similar to argyrosis. Only the color of gold deposits is somewhat different; i.e., diffuse bluish-gray. In contrast to argyrosis, the mucous membranes are typically not affected in chrysiasis. Other cutaneous changes associated with gold intake are maculopapular, vesiculobullous, and urticarial eruptions, occasionally also an erythema multiforma-like rash. Gold-containing medications (e.g., for the treatment of rheumatoid arthritis) have become rare.

1.3 Abnormalities of Amino Acid Metabolism

Hartnup disease is an autosomal recessive disorder of intestinal and renal amino acid transport presenting with amino aciduria. Patients show a sun-burn-like photosensitive eruption reminiscent of pellagra, sometimes blistering, onset is at <13 years. Post-inflammatory hypopigmentation is a common residual. The differential diagnosis of the skin changes includes pellagra and lupus erythematodes. The primary extracutaneous feature is intermittent ataxia, sometimes also nystagmus and tremor. A high-protein diet or oral nicotinamide supplementation have been reported to be beneficial (nicotinamide is photoprotective, cf. Chap. 11.).

Phenylketonuria is an autosomal recessive abnormality of phenylalanine metabolism; i.e., lack of downstream metabolic product tyrosine and accumulation of phenylalanine. Paucity of tyrosine results in diffuse hypopigmention of the skin and hair of affected individuals ("blond and blue eyed"). Other cutaneous changes include eczematous (early onset atopic dermatitis, but also unspecific dermatitis) and scleroderma-like skin lesions. Phenylalanine accumulation is toxic for the brain and causes mental retardation, developmental delay, microcephaly, seizures, and behavioral and psychiatric problems. Urinary screening for phenylalanine accumulation has been widely established for approximately 40 years. Strictly speaking this is not a nutritional disease, but it is the prototype of an inherited condition that can be cured by dietary restriction of phenylalanine together with supplementation of tyrosine and other amino acids. Incompliant adults experience recurrences of the dermatologic manifestations. Individuals resuming the diet may show darkening of their hair.

Tyrosinemia is a rare autosomal recessive disorder of tyrosine metabolism with accumulation of tyrosine

metabolites in the liver, kidneys, and central nervous system. Tyrosinemia type II (Richner-Hanhart syndrome, oculocutaneous tyrosinemia) is characterized by photophobia, corneal ulcerations with onset during the first year of life (the latter can be misinterpreted as herpes keratitis). A painful focal palmoplantar keratoderma occurs during early childhood or may be delayed until adolescence. Although again not a nutritional disease in the strict sense, a diet restricted in tyrosine and phenylalanine will clear the keratitis, keratoderma, and will ameliorate or prevent cognitive impairment.

Arginine-Succininc Acid disease is due to mutations in the gene encoding for arginine succinase and manifests with fragile hair (trichorhexis nodosa) and neurologic symptoms.

Alkaptonuria is an autosomal recessive defect of the enzyme homogentisic acid (or alkapton) oxidase. Cutaneous changes include a grayish-blue discoloration of the ears and the axillae (ochronosis). There can also be arthritis and darkening of the urine (due to oxydation).

Eosinophilia-Myalgia-Syndrome stands for a scleroderma-like disorder with woody induration of the distal extremities that historically was observed in individuals who consumed large quantities of contaminated L-tryptophan.

1.4 Nutrition, Skin Physiology, and Skin Pathology

In this chapter, the characteristic skin findings that are reproducibly associated with either lack or abundance of individual nutrients, vitamins, or trace elements are described. These observations allow us to deduce the importance of individual nutritional components for skin physiology. The substitution of deficient components rapidly reversesas associated skin changes. In contrest the prophylactic supplementation of nutrients to enhance skin physiology has yielded disappointing results. The available studies not only fail to consistently prove beneficial effects of vitamin supplementation on skin physiology, but meta-analyses even indicate an increased risk for cardiovascular disease with high doses of vitamins B6, B12, C, and E. Thus, to date it is still controversial if prophylactic vitamin supplementation can have sustained beneficial effects. One possible explanation is that the metabolism of cutaneous tissues, in particular the epidermis, is remarkably autonomous; i.e., many metabolic reactions in the epidermis occur independent from the rest of the body. Furthermore, while several of the vitamins mentioned above are potential oxygen radical scavengers, systemic delivery is unlikely to achieve a sufficient concentration in the epidermis to effectively prevent free radical formation.

Similarly complex is the evidence for nutritional supplementation effects on skin pathology. For example, there is a decade-long discussion about the dietary factors that may elicit or exacerbate acne vulgaris, but suggestive data has not been replicated. Approximately 10% of children with severe atopic dermatitis experience flares upon food allergen exposure. However, diagnostic testing and recommendations for avoidance of individual food ingredients should regularly be reevaluated (retested), because of the risk of developing nutritional deficiency due to unnecessary food restriction. Thus, the goal of testing is to identify food that is tolerated in order to reduce the risk for nutritional deficiency. Current evidence does not support a major role for maternal dietary restrictions during pregnancy or lactation for infants with atopic disease. However, there is moderate evidence from meta-analyses that prophylactic (but not therapeutic) use of dietary probiotics may be beneficial for atopic dermatitis; these findings warrant replication. For treating psoriasis, the supplementation of omega-3-fatty acids has been proposed to have beneficial effects by modulating eicosanoid metabolism, but again the replication of the data is not sufficient. Finally, not only psoriasis, but also leg ulcers have been shown to be associated with nutritional deficiencies. Yet, it remains to be established if poor nutrition is a direct cause or merely an associated bystander of these skin pathologies.

References

Core Messages

- Skin aging is caused by
  (i) UV radiation,
  (ii) Infrared radiation,
  (iii) tobacco smoke and
  (iv) traffic related particulate matter
- Damage to macromolecules such as mtDNA and proteins in dermal fibroblasts drives chronic skin aging

2.1 Introduction

For decades it has been appreciated that aging is the consequence of both genetic and environmental influences. Genetic factors are evident, e.g., in the >100-fold variation among species in the rate of aging; and recent studies of fruit flies, worms, and even mice have identified specific longevity genes whose modification can greatly alter lifespan [22]. Conversely, a role for environmental factors can be deduced both from epidemiologic and laboratory-based experimental data. Such influences include ionizing radiation, severe physical and psychological stress, overeating versus caloric restriction, and in the case of skin ultraviolet irradiation.

In this regard, skin is no exception as skin aging results from intrinsic (genetic, endocrinologic) and extrinsic (environmental) factors. In this chapter I will focus on extrinsic skin aging for the following reasons: (a) The overall topic of this chapter is functional food for skin or, in other words, manipulation of skin aging by nutrition-based strategies; (b) It has already been shown for topical approaches (sunscreens, cosmeceuticals, etc.) that extrinsic skin aging can be effectively manipulated. (iii) And thus, nutrition-based anti-skin-aging strategies will be most effective if they are directed against extrinsic skin aging.

Extrinsic and intrinsic skin aging can be clearly distinguished at a clinical, histological, and molecular level. The two most prominent clinical signs of extrinsic skin aging are the formation of coarse wrinkles and an increase in the number of pigment spots (Fig. 2.1). Interestingly, ethnic differences exist, because, e.g., Caucasian women develop earlier and more severe skin wrinkling whereas Japanese women show more lentigines at a younger age. Among all environmental factors, solar ultraviolet (UV) radiation is most important for extrinsic skin aging, a process accordingly also termed photoaging.

Within recent years substantial progress has been made in elucidating the underlying molecular mechanisms. From these studies it is now clear that both UVB (290–320 nm) and UVA (320–400 nm) radiation contribute to photoaging. UV-induced alterations at the level of the dermis are best studied and appear to

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Fig. 2.1 Coarse wrinkle (**a**) and pigment spot (**b**) formation in extrinsic skin aging

be largely responsible for the phenotype of photoaged skin. It is also generally agreed that UVB acts prefer- entially on the epidermis where it not only damages DNA in keratinocytes and melanocytes but also causes the production of soluble factors including proteolytic enzymes which then in a second step affect the der- mis; in contrast UVA radiation penetrates far more

deeply on average and hence exerts direct effects on both the epidermal and the dermal compartments (Fig. 2.1). UVA is also 10–100 times more abundant in sunlight than UVB, depending on the season and time of day. It has therefore been proposed that, although UVA photons are individually far less bio- logically active than UVB photons, UVA radiation

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The role of diet in maintaining healthy skin

Abstract

Introduction: Skin is of crucial importance in the human system. There are numerous factors that affect its appearance and function. Various skin conditions and fast aging are manifestation of certain disturbances.

Aim: To give information to dermatologists and nutritionists about the role of the diet in maintaining healthy skin and the usage of knowledge in everyday practice and working with patients, a detailed analysis of available literature is performed on the impact and mechanisms of various food ingredients on the role and appearance of skin. The data will be useful to the readers of this text.

Data: The data on the nutrients that affect healthy skin are obtained: The quality, health and beauty of the skin are affected by various vitamins, minerals, proteins, as well as by other nutrients. Some foods make skin shiny and healthy, but there is also bad diet for skin, as well as foods with harmful effects, depending on skin type.

Discussion: It is of crutial importance to protect skin from negative factors. In order to provide for normal functioning of the skin it is necessary to incorporate various foods of animal or plant origin, taking in consideration skin type as well.

Conclusion: It is clear why full attention should be paid to skin, its health, functions and appearance. Adequate diet is of crutial importance, with appropriate use of vitamins, minerals, proteins and other nutrients paying attention to possible benefitial effects of certain foods, adjusted to the skin type. This should be applied in everyday practice in working with patients.

Keywords: diet & skin, vitamins, minerals, nutrients, skin type

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Introduction

Skin is the organ of crucial importance due to its numerous functions: barrier function, mechanical, immune, sensory, endocrine, thermoregulatory, vitamin D synthesis. It is involved in the respiration; it affects social and sexual communication.[1,2] It is of crucial importance how skin appears to be, what depends on its texture, colour, surface, elasticity, sweating, sebum, scent. This primarily affects personal feeling as well as the reactions of other people. Factors that affect skin appearance and its function are numerous First of all, exposure to strong ultraviolet radiation should be avoided as well as smoking and staying in space filled with cigarette smoke[3,4] and also stress should be avoided. That is because free radicals are released as they destroy molecules and damage skin tissue, what brings about the loss of water and collagen deterioration as well as faster skin aging. The consequences are skin redness and dryness, loss of elasticity and wrinkling. There are opinions that genetics affects aging in only 20%. Other factors make for 80%: sun exposure, smoking, especially diet, which is most important.

Adequate and balanced diet, comprised of variety of foods is extremely important. Skin mirrors processes in the whole system, so that many skin disorders and rapid aging are manifestations of certain disturbances, like lack of nutrients, vitamins and minerals. To keep your skin healthy, eat a well-balanced diet that includes plenty of protein foods, fruits and vegetables (fresh if possible) and liquids. If we “feed” skin from the inside, we can’t make a mistake. Also, physical activity plays an important part.

In the aim to give information to dermatologists and nutritionists about the role of the diet in maintaining healthy skin and the usage of knowledge in everyday practice and working with patients, a detailed analysis of available literature is performed on the impact and mechanisms of various foods ingredients on the role and appearance of skin with beneficial effects, and what foods should be avoided, what diet is compatible with the particular skin type. The data will be useful to the readers of this text.

The data on the nutrients that affect healthy skin are obtained: The quality, health and beauty of the skin are affected by various vitamins (vitamin C, E, A, K, D and B complex), minerals (selenium, copper, zinc, proteins, as well as other nutrients. There is also alpha liposoic acid, dymetilaminoethanol (DMAE), hyaluronic acid, essential fatty acids. Sufficient intake of liquids is necessary with balanced healthy diet.

Vitamins

Vitamin C

Due to the sun exposure, free radicals are released, which damage collagen and elastin, fibers that sustain skin structure and make it firm and tight. The consequences are wrinkling, stains, pre-cancers and other signs of aging.[5] Vitamin C is a potent antioxidant,[6,7] which affects free radicals and diminishes their negative effects. Strengthening the immune system, it improves acne inflammation. Many other studies have found that vitamin C can increase collagen production, protect against damage from UVA and UVB rays, correct

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pigmentation problems, and improve inflammatory skin conditions.[8] Vitamin C is found in citrus fruits (lemons, oranges, and grapefruit) and in other fruits (strawberries), vegetables (peppers, broccoli, cabbage, cauliflower.[9] Supplements of 500 to 1000mg can be taken daily. Topical application can reduce the sun exposure effects.

Vitamin E

Vitamin E is considered to be the most important lipido-soluble antioxidant in tissues.[10] Vitamin E is also a potent antioxidant in reduction of sun exposure damage and carcinogenic damage.[11,12] If used together with vitamin A, there is lower risk of basocellular carcinoma for 70%. It also reduces wrinkling. Vitamin E can be found in vegetable oils, nuts, seeds, olives, spinach. Supplementation of 400IU daily is recommended, with caution because of possible hemmorrhaging.

Vitamin A

Vitamin A is necessary for skin tissue regeneration. In its absence, skin becomes dry, rough and peeling. Sufficient vitamin A intake is provided through diet, so that there is no need for supplementation. Topically applied, it reduces wrinkles and skin lines - it is used as anti- aging substance. It can be found in fruits and vegetables in the form of beta-carroten, which is metabolized in vitamin A in the system.

Vitamin K

It is very important for stopping hemorrhaging. It affects less bruising and dark circles around eyes.

Vitamin B complex

From this group, the most important one for skin is biotin (B7) which is the skin, nales and hair foundation. If there is lack of this vitamin, skin inflammation followed by itching and peeling, with possible hair loss may occur. It can be found in bananas, eggs and rice. Niacin (B3) maintains skin moisturized and has anti-inflammatory effects. It can be synthesized in the system, and it occurs in many foods (meat, fish, milk, leafy vegetables, cereals, legumes). Panthoteic acid (B5) has positive effects on damaged and dry skin. It can be found in milk, yeast, liver and kidneys, seeds, broccoli.

Minerals that improve the skin appearance and its quality

Selenium

Selenium protects skin from the sun exposure damage and plays a key role in elastin development, which is important for the skin structure. It can be found in sea food, whole wheat, nuts, eggs, garlic.

Copper

Copper and zink enable elastin development. The lack of copper is rarely registered. Oral intake or in the form of cremes lower fat production. It is efficient in acne treatment and in prevention of the appearance of the new ones. It is found in poultry, red meat, and oysters.

Zinc

Zinc is an important trace mineral that aids repair of damaged tissue and heals wounds. Another important application of zink includes protecting skin from the sun's harmful ultraviolet rays. Food

sources high in zink include: oysters, pecans, poultry, pumpkin seeds, ginger, legumes, sea food, mushrooms and whole grains.

Alpha-lipoic acids

They are strong antioxidants, protecting cells from damage that free radicals cause- free radical neutralizer,[13] while also slow down the skin aging process. They can be used as supplements or in the form of cream. DMAE also has effects like an antioxidant. It enables cell membrane stabilization, soothing the sun exposure damage as well as pollution provoked damage. It also prevents lipofuscin creation, the pigment responsible for the creation of dark areas on the skin. It is used as the addition for mesotherapy as well as in creams.

Hyaluronic acid

This is a component of every living organism and an intercellular substance, which lubricates joints as well as it, affects cells as a type of glue, holding them together and making skin smooth and full. Hyaluronic acid is powerful antioxidant within the skin that prevents wrinkle-producing free radical damage of the skin as well as maintain the normal level of hydration within the skin.[14] I is not present in natural diet, so that it is supplemented locally (hyaluron fillers, creams).

Essential fatty acids

Omega-3 fatty acids and omega-6 fatty acids are a valuable nutrient for the skin.[15] They play two major roles in the body: provide appropriate structure, flexibility and functioning of cell membranes and are essential for the synthesis of intracellular lipids in stratum corneum. Being the precursor of eicosanoids (prostoglandins, leukotrienes, thromboxynes), they also have regulatory properties.[16] They are very important in the fat production which makes for a natural skin barrier. In case they are lacking, skin becomes dry and easily inflamed, due to the presence of other irritating fats produced in skin.[17] Omega-3 fatty acids also have anti-inflammatory properties, aiding acne and face redness reduction. Diet provides sufficient intake (wheat, poultry, oils, pastry), while omega-3 fatty acids (which are abundant in cold water fish - salmon, mackerel, sardines) have to be supplemented in the form of fish oil. They make skin looks younger and smoother. With balanced diet and occasional multi- vitamin supplementation, sufficient intake of liquids and skin care are necessary.

Foods that make skin shiny and healthy[18]

i. Carrots (beta carotene - vitamin A)
ii. Green tea (anti-oxidants- lower stress, good sleep)
iii. Citrus fruits (Vitamin C)
iv. Berries
v. Tomato (antioxidant)
vi. Almonds, walnuts (healthy fats - energy for exercise and functioning of the system)
vii. Unsweetened yoghurt (good for teeth, bones better digestion)
viii. Cheese (prevention of gums and cavity problems- oral bacteria)
ix. Vegetables (minerals, vitamins, fibers, low calories - reduced bloating, shiny young appearing skin)
x. Sweet potato (antioxidant)

xi. Red or yellow bell peppers
xii. Dark chocolate
xiii. Algae and other sea food (detoxication, cell building)
xiv. Red oranges, cherries, blueberries (dark fruits affect collagen)
xv. Meat, dairy products, egg yolk) (vitamin A)
xvi. Sea shells, sardines, sunflower seeds (essential fatty acids)
xvii. Salmon (essential fatty acids)
xviii. Avocado, mango (antioxidants- vitamin E)
xix. Legumes (biotin)

Bad diet for skin

a. Sugar (promotes inflammation risk and rapid skin aging)
b. Spicy hot food (promotes face redness with obvious capillary)
c. Caffeine (possible dehydration, but also anti-inflammatory effect)
d. Chocolate and fatty foods (sugar and saturated trans fats)
e. Alcohol (excessive drinking - free radicals, diuretic)
f. Processed foods (lack of micronutrients and excess of preservatives - emulators, colors, taste enhancers, aromas)
g. Fatty and fast foods and hydrogenised oils (lack of vitamins and minerals, high level of preservatives)
h. Salt (water retention, bloating)
i. Starch (white flour products)

Stress can also have a negative impact on skin; higher oil production can block and inflame skin pores, what is the base for bacteria development. Inflammation can be promoted due to high cortisol exposure. Smoking destroys skin. Only 5 cigarettes a day deprive cells of the necessary oxygen, while one cigarette lowers vitamin C for 25mg. Women smokers need double vitamin C dose in comparison to non-smokers.

Skin types and skin care

Depending on how oily the skin is, how serious the water retention is, as well as on skin sensitivity, there are 5 basic skin types. Although it mainly has to do with genetics, some other factors influence skin characteristics, for example: hormones, birth control pills, as well as diet.[19]

Basic skin types

i. Normal skin (smooth, consistent complexion, without obvious lipid traces, does not demand special care)
ii. Oily skin (the entire face). Causes: malnutrition, hereditary factors, hormones, stress, wrong care
iii. Dry skin (not enough sebum or moisture. Causes: genetics, weather conditions, inappropriate care and hygiene)
iv. Mixed skin (fat in certain areas)
v. Sensitive skin (easily irritated, prone to redness and inflammation).

Appropriate care

a. Normal skin: regular hydration and avoidance of fatty products

b. **Oily skin:** with right hygiene and application of adequate local products for skin care, attention should be paid to diet: avoidance of carbohydrates and sweets)

c. **Dry skin:** with appropriate care diet rich in essential fatty acids is recommended (Diet that makes your skin shiny), vitamins A, D, E, zinc.[20] Avoid dehydrating foods (coffee, fizzy drinks) and foods that are digested slowly (fried and smoked meats, processed meats)

d. Mixed skin is most widely spread and demands special care

e. **Sensitive skin:** determine the cause of sensitivity and try to treat it.

Discussion

It is necessary to pay attention to skin health in order to realize its numerous functions that as an organ of human system it is processed. Skin is the barrier to the environment (it protects the body against mechanical stimuli, various negative substances, microorganisms, radiation), it is important for maintaining homeostasis (it regulates the loss of liquids and body temperature), it has an important in the immune system and pain and temperature sensations, its appearance is important for the psychological state. It is of crutial importance to protect skin from negative factors like ultraviolet radiation, various chemicals, tobacco smoke, infections, as well as make available all the necessary nutrients in the diet, and appropriate care. In order to provide for normal functioning of the skin it is necessary to incorporate various foods of animal or plant origin,[18] which contain vitamins, minerals, proteins, essential fatty acids,[5–17] taking in consideration the type skin as well.

Conclusion

It is clear why full attention should be paid to skin, its health, functions and appearance. That is the reason why all the relevant facts should be known. Adequate diet is of crucial importance, with appropriate use of vitamins, minerals, proteins and other nutrients paying attention to possible beneficial and also harmful effects of certain foods, adjusted to the skin type. Adequate diet not only enables proper functioning, but also offers possibility of better communication and self image. We should be making effort to have healthy and beautiful skin. “When combined with a good diet, right dietary supplements can help keep your skin not only appear healthy, but also years younger”. This should be applied in everyday practice in working with patients.