THE ART OF SKIN HEALTH

RESTORATION AND REJUVENATION

SECOND EDITION

THE SCIENCE OF CLINICAL PRACTICE

ZEIN E. OBAGI, M.D.

CRC Press
Taylor & Francis Group

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To my most loving and supportive wife, Samar

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This comprehensive book represents the evolution of my philosophy of the science of skin health and clinical experience as a dermatologist for the past 35 years. It would not have been possible without the assistance, support, and contributions of a long list of many dedicated and talented individuals.

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Finally, much of the wisdom that I have gained was from my beloved mother who told me from an early age: "A blind person cannot see with his eyes, but he may acquire more knowledge better than a person who can see. Don't accept what you see as the ultimate that is etched in stone; open your mind to see and absorb."

PREFACE

> "The science of skin health must be taught in medical school. Physicians must know the difference between diseased skin and healthy skin to restore skin health."

This comprehensive book represents the entirety of my philosophy of healthy skin and clinical experience as a dermatologist for the past 35 years. This is the second edition of my original book (*Obagi Skin Health Restoration and Rejuvenation*, Springer-Verlag, 2000) and serves to describe my new way of thinking about the science behind skin health. The emphasis in this text is on skin, and it covers the science of restoring skin health, cellular function, and improving the skin's ability to tolerate procedures and surgery. The range of skin conditions addressed includes diseases of pigmentation (melasma, hypopigmentation, hyperpigmentation), textural disorders (scars, rhytides, large pores), aging, photodamage, inflammatory disorders, rosacea, and acne. The modern solutions described in this book are based on the latest scientific advances coupled with my 35 years of clinical experience. It is intended to provide the reader with a wealth of original theories and information on many issues encountered in day-to-day practice when dealing with skin. Any physician can follow these principles, both students and advanced skin care professionals, and they can be adapted to treat any patient.

Health and skin care occupy a prominent place within the mind of consumers. "Looking one's best" is an innate desire shared by all. The cry for youthful, disease-free, healthy skin has been heard, as can be seen in the dramatic expansion in skin care products currently available on the market. But sadly, such formulations often lack the support of research and science. Because of their ineffectiveness and lack of long-term improvement and sustainable results, customers are repeatedly left feeling disappointed and hopeless. These self-prescribed products are not part of a comprehensive program tailored to the patient's skin needs; their use is haphazard and lacks physician guidance.

Regrettably, patients seeking a clinician's advice are often misled. An increasing number of clinicians today make recommendations based on personal enticements and nonscientific marketing pitches. They may favor a "quick fix" for their patients because of time and economic benefits. As such, they are hasty to recommend any procedure that cuts, evaporates, resurfaces, plumps, and tightens the skin. They fail to address the skin itself—its quality, integrity, vitality, and, most important, suitability for a procedure.

Having begun my career in pathology, I was regularly exposed to diseased tissue. The way in which cells function, both individually and collectively,

became my principal focus. My mind was trained to think at a cellular level when addressing disease, an invaluable foundation that proved advantageous when I switched to dermatology. It soon became obvious that the generally accepted approach to treating skin was flawed. It is simply inadequate to treat a disease or its symptoms independently. Instead, the cells involved in the condition must be comprehensively and collectively addressed. The skin is not a wall that one can paint and superficially plaster; it is an organ that requires cellular activation and regulation to achieve health. It is therefore crucial that any practitioner dealing with skin—whether with incision, lasers, peels, injections, or other treatments—first respects and understands the skin's function at a cellular level in order to achieve the best possible results.

A baby's skin has always fascinated me. Microscopically, each cell is fulfilling its precise function, and this corresponds to its flawless appearance. As a physician, I wanted to offer this possibility to patients of all ages. And so, more than 35 years ago, my passion ignited, I set out to define the science underlying skin health. The fundamental principle driving my approach is that skin must be holistically restored at the cellular level. If the focus is limited to treating only the disease or its symptoms, the results will be limited and short lived.

Skin health and its science have many features that allow for a standardized method of treatment and superior overall patient outcome. Innovative products and protocols have been created in parallel, using the most novel scientific research and clinical experience. There are programs for diseased and nondiseased states, each relying on a systematic approach to holistically restore skin health.

Since my introduction of skin health science (which is the core of what this book is about), I have devoted my career to educating physicians all over the world on how to deal with skin from a different perspective. My goal has been to shift their focus away from the disease they intend to treat, which will help to calm down the symptoms and provide short-term remission, to focus mainly on the skin itself in order to bring it back to the state of optimal cellular activity and functions while treating disease. This approach will lead to better and longer lasting overall results. It is most gratifying to me to see that skin health science is currently being adapted by thousands of physicians worldwide and enabling them to obtain the best results in skin treatment and rejuvenation.

It is about time that as professionals dealing with skin, we set aside our differences on how to approach skin. We must adapt a unified approach that is proved to be the ideal one rather than follow the current individualistic, misguided, and narrow-minded approaches that focus solely on the surface of the skin and symptoms. We must address the science of skin health as the essential basis for treatment and intervention. This should be recognized as a science to be studied beginning in medical schools and residency programs, before learning about diseases of the skin. It will help to establish clear objectives when treating skin problems. It is no longer enough to say that a specific problem has been resolved, as many of us still believe. Wouldn't it be better to be able to say, "The main problem has been resolved, and skin health has been restored"?

Adapting skin health science should be the only valid approach to deal with skin because it is a comprehensive process that yields many benefits. The new definition of skin health that I have introduced will clarify the exact

meaning of skin health and eliminate the use of loosely described terminology that is often used to sell products that have nothing to do with skin health. Unfortunately, clinicians have become targets for promotion of certain products and devices, and few among us have the courage to refute some of the erroneous concepts that now dominate clinical practice. My hope is to challenge traditional procedure-oriented approaches to skin care and shift the emphasis back to skin health.

My new definition of skin health science will establish a well-rounded approach to restore and maintain skin health using fundamentals that can be adopted clinically and histologically through subjective and objective criteria, applicable to any skin type. The definition helps to establish a comprehensive diagnosis, to identify the objective of the treatment required, to allow the monitoring of treatment progress, and to accurately measure results on completion of the treatment.

Skin health science will also guide the physician through novel original principles, including

- Adapting Zein Obagi Skin Classification System as a guide in planning any treatment plan, selecting procedures, and determining the safe depth for any skin type
- Insuring that the proper topical agents are used for treatment by following Zein Obagi Skin Classification System
- Simplifying the proper selection of procedures by following Zein Obagi Skin Procedure Classification System based on the mechanism of action

Those of you who joined me years ago and are familiar with my original products, including Obagi NuDerm and the Obagi Blue Peel, will find this book more exciting than my first edition and easier to follow. I have maintained the original principles of skin health that I introduced 25 years ago, and the book contains many clinical concepts I used to develop Obagi NuDerm and the Obagi Blue Peel. However, my original principles have been expanded in this book, as evidenced by a selection of patients' photographs before and after using the original Obagi NuDerm, as well as patients' photographs before and after using the new ZO Medical system. The latter program was developed to include wider indications and applications when used purely for Skin Health Restoration, for maintaining skin health, and as a skin treatment. Those patients with no medical problems were given ZO skin health for prevention and daily skin care.

The three original principles of Skin Health Restoration include correction (improving the epidermis); stimulation (improving the dermis); and bleaching and blending (correcting pigmentation problems). Recently, I added a fourth principle, stabilization. This novel concept was created to address the need for prevention. It aims to maintain skin health by preventing diseases, changes in skin texture, and cellular dysfunction. When targeting any disease, the four principles should be employed, and the disease approached within the larger context of overall skin health. Using acne as an example, my treatment plan first involves correction, followed by specific acne agents, then stimulation, and finally bleaching and blending if discoloration exists. My objective here is to remedy the skin disease by thoroughly treating it within the entire skin unit. The rationale is that disease does not affect only a single spot on the face that can be seen or touched; rather, it influences all cells and layers, and one

must comprehensively treat every element to restore the skin to its optimal health. After the disease has been treated, the focus should shift to stabilization to maintain the results achieved.

The reader will notice that I address skin in a novel way. My style contrasts with the traditional, narrow approach to treating skin in which the focus is on the disease or its symptoms. This primitive method often yields limited improvement, frequent recurrences, and treatment failures. My approach is broader, yet still targets the core of the problem: the cells. The two primary objectives to my method are to restore skin health while treating the disease in parallel to achieve maximal results.

This book will provide key insights into achieving and optimizing patients' results. My extensive research and clinical experience on defining and refining the science of skin health has enabled me to provide a standard step-by-step approach to treating skin. I hope the text will prove to be an indispensable tool for practitioners dealing with skin in the following ways:

- Selecting a daily skin care program
- Providing treatment
- Rejuvenating skin
- Preventing skin problems
- Maintaining results
- Selecting the appropriate procedure based on the problem, the skin type, the mechanism of action, and the objective of such procedures
- Conditioning skin for procedures
- Managing skin after procedures

The practitioner will further learn that many currently used principles related to skin are either outdated or do not provide adequate information. This book will address these matters and set new standards for the following:

- Skin classification
- Topical agent classification
- Classification of procedures based on their mechanism of action
- Understanding and treating skin sensitivity and dryness
- Preventing and treating pigmentation disorders, aging, photodamage, and inflammatory diseases
- Selecting and performing the best procedure for a patient, from chemical peels to laser resurfacing

"Finis origine pendet"; the end depends on the beginning.

This book is intended for anyone who desires to deliver the safest, most comprehensive, current, and effective treatment results to their patients. Many of the principles I have put forth in this book are original. The ideas may challenge you and stimulate your own research, experimentation, and clinical studies. I encourage this; it is precisely what I have done and continue to do throughout my career in dermatology. I want the reader to see my principles as tools and to adapt them to create their own tour de force. Practitioners will develop their own preferences, and I encourage them to do so. But they must do so with a solid understanding of the skin's cellular function: the control of cells before and after procedures, the interaction between skin types, the safe procedure depth, and the skin's response to injury.

By being inventive, we progress as a species, in technology and in medicine. We must begin somewhere—and with imagination, inspiration, and hard work as key ingredients, it shall evolve. I often find comfort remembering that not too long ago our ancestors believed the world was flat. The pioneer who sought to change this view was ridiculed. Criticism and doubt will indeed follow whenever you seek to be inventive and change the established mindset. But we must never let this distract us from our patient's best interest.

As Aristotle said, "There is only one way to avoid criticism: do nothing, say nothing, and be nothing."

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Note: I have created this text for physicians and skin care professionals who want to learn about the products that we use in our clinics. Please contact ZO directly for more information about ZO Skin Health and ZO Medical protocols and standards of care.

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Note on Terminology: In this book, *ZO* refers to the products developed by Dr. Zein Obagi in conjunction with ZO Skin Health Inc. Neither has a business connection with Obagi Medical Products.

CHAPTER

1

A NEW PERSPECTIVE ON SKIN ANATOMY AND PHYSIOLOGY

Many textbooks are available on the structure and the physiology of the skin, and reading of these is recommended for a firm grounding in dermatological science. The purpose of this chapter is to connect the Skin Health Restoration program approach to the anatomical and physiological properties of the skin (Box 1.1).

The skin is the largest organ of the body, having a surface area of 1.8 m^2 and making up approximately 18% of body weight. It is readily available for inspection and can reveal health or disease. Functionally, the skin has many roles: thermal regulation, detection of sensation, immune responsiveness, energy storage, vitamin D production, and protection against environmental insults. During a lifetime, the skin undergoes numerous changes, including adapting to the change from a water to air environment at birth; adapting to hormonal influences at puberty; and, in females, adjusting to the effects of hormonal changes seen during menstruation and pregnancy and while taking contraceptive pills during the reproductive years. In addition, profound changes can occur during illness, trauma, and environmental exposures and throughout the aging process. Sun exposure, smoking, disease, scarring, and psychological factors can profoundly change the structure and appearance of the skin. Skin Health Restoration principles and treatments were developed to address many of these changes.

Some of the factors leading to deteriorative changes in the skin are controllable, whereas others, with our present state of knowledge, are not. This chapter examines the structure and function of the skin (Table 1.1), with an emphasis on defining the controllable factors of skin health. It also examines the physiological changes that accompany aging of the skin, both intrinsic biological aging and extrinsic photoaging that results from exposure to sunlight. Along the way, the chapter lays the scientific foundation on which the clinical treatments and procedures that follow are based.

Box 1.1

Skin health can be restored and maintained by directly targeting the different layers and cells of the skin involved in the processes of skin aging, dysfunction, and disease.

Table 1.1 Skin Functions and Activities

Function	*Activity*
Protection	Protect inner organs and maintain homeostasis
Barrier function	Prevent invasion of water, bacteria, irritants Prevent transepidermal water loss Build skin tolerance and reduce sensitivity Provide natural protection from ultraviolet radiation through melanin and keratin
Stability of body organs	Synthesize vitamin D Eliminate certain toxins
Immune system role	Carry out antigen processing and immune surveillance through Langerhans cells
Sensory recognition	Relay information to brain about external environment, mechanical stimulation
Temperature control	Conserve body heat through insulation, vascular constriction; cool the body through vasodilation, sweat evaporation
Sebum production	Reduce water loss, form acid mantle, discourage microbial growth

LAYERS AND COMPONENTS OF THE SKIN

SKIN STRUCTURES

The skin is stratified horizontally into three compartments—the epidermis, dermis, and subcutaneous layer—and is penetrated vertically by appendages such as hair follicles, sweat glands, and sebaceous glands (Figure 1.1). The outermost, thinnest layer, the epidermis, forms a barrier to the world (the barrier function), keeping out water, bacteria, toxins, ultraviolet light, and allergens in healthy skin. The epidermis also shows the genetic expression of skin color and reveals dryness, softness, or roughness. It can be clear or diseased, as is the case with acne, or have precancerous or cancerous lesions, pigmentation problems, psoriasis, rosacea, and a host of other conditions. Throughout the body, the epidermis is uniform in thickness, except for certain thickened areas, such as the palms and soles.

The dermis, composed of the papillary dermis and the thicker reticular dermis, lies below the epidermis. The papillary dermis contains thin, haphazardly arranged collagen fibers, abundant ground substance, and delicate elastic fibers, whereas the reticular dermis comprises thick collagen bundles and coarse elastic fibers. Upward projections of the dermis, the papillae, fit into the epidermal depressions, the rete ridges. This arrangement provides a greater interface between the epidermis and the dermis than would result from contact between two flat surfaces. A rich supply of blood vessels and

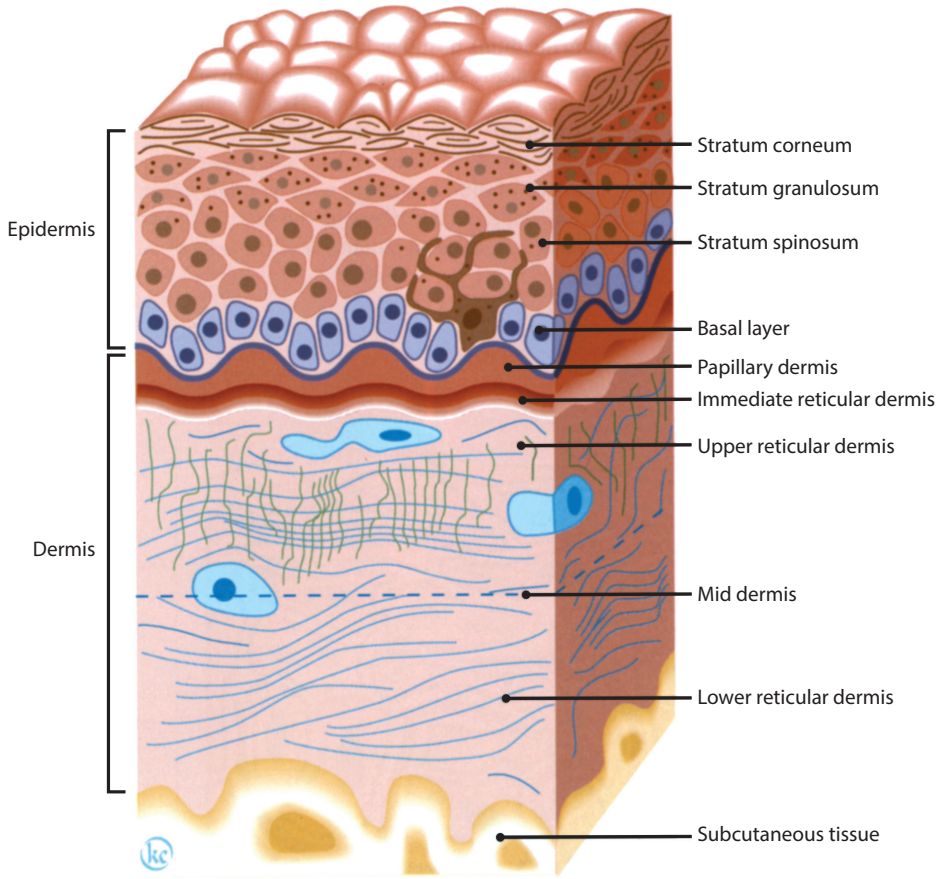

Figure 1.1 The layers of the skin (blood vessels omitted for clarity).

nerve endings can be found in the dermis. The deepest layer of the skin, the subcutaneous layer, is composed primarily of fatty tissue.

THE EPIDERMIS

Keratinocytes and the Keratinocyte Maturation Cycle

Four cell types are found in the epidermis: keratinocytes, melanocytes, Langerhans cells, and Merkel cells. Keratinocytes are the major cells of the epidermis. They originate at the basal layer, mature, lose their nucleus, and flatten as they move upward. At the uppermost level, they form a strong, flexible, dry surface known as the stratum corneum. This layer, composed of cells firmly attached to one another, continually loosens, detaches, and falls away in the natural process of exfoliation that takes 30 to 40 days in normally maturing skin. However, this transit time varies widely after mild injury or major trauma, in the presence of disease states like psoriasis, and throughout the aging process.

Keratinocytes are involved in a steady state of cell production and cell loss. The *keratinocyte maturation cycle* is the amount of time it takes for a keratinocyte to mature and transform into a corneocyte, reach the stratum corneum, and subsequently exfoliate from the surface of the epidermis. One of the main objectives of skin health, as discussed in this book, is restoration of a normal maturation cycle through skin conditioning. It usually takes 6 weeks of skin-conditioning treatment to complete one cycle, and more than one cycle may be required in some patients (Box 1.2). Some of the factors that participate in the regulation of the keratinocyte maturation cycle are the dermis, hormones,

vitamin A and its derivatives, epidermal growth factor, and cyclic nucleotides. Normal barrier function, in turn, increases skin tolerance. Skin barrier function, however, can be disrupted by overuse of moisturizers. The layers and cells of the epidermis are shown in Figure 1.2.

Melanocytes, Melanosomes, and Skin Pigmentation

Melanocytes are melanin-synthesizing cells that are found only in the basal layer where they are interspersed among the basal keratinocytes. Approximately every 10th cell of that single-cell layer is a melanocyte. Through its finger-like

Box 1.2

- **One of the main objectives of skin health is restoration of a normal maturation cycle through skin conditioning**
- **It usually takes 6 weeks of skin conditioning treatment to complete one keratinocyte maturation cycle.**

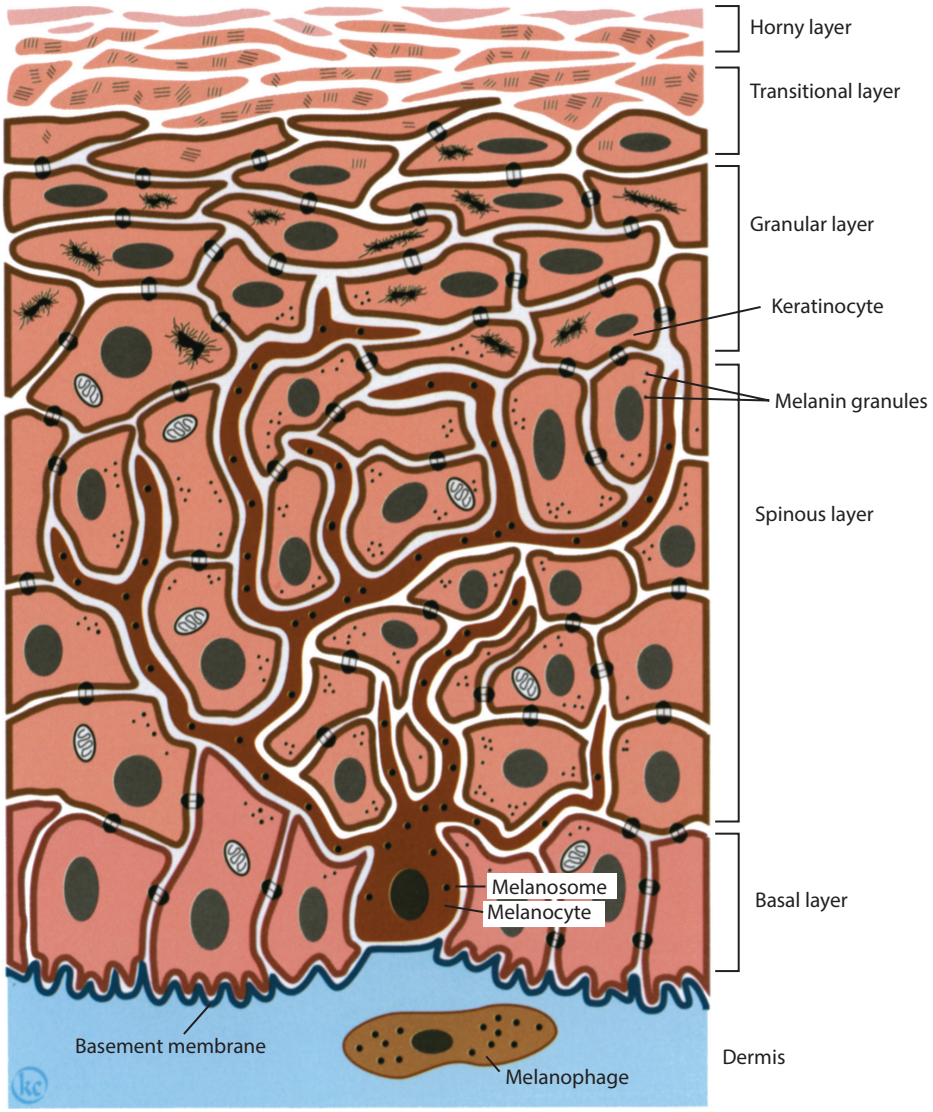

Figure 1.2 The layers and cells of the epidermis.

dendritic processes, each melanocyte is in contact with 30 to 40 keratinocytes. Inside the melanocyte, organelles known as melanosomes produce melanin pigment—the primary pigment of skin. These pigment granules migrate from the cytoplasm into the dendrites and are transferred from there into the surrounding keratinocytes, where they form a protective cap over the keratinocyte nucleus, protecting the nuclear DNA from the effects of ultraviolet (UV) radiation. Normal pigmentation of the skin depends on the efficient transfer of melanosomes to keratinocytes.

Variation in normal skin color, including that due to racial differences or the process of tanning, is not determined by the number or density of melanocytes but by the number, size, and distribution of melanosomes; the distribution of the pigment granules in the melanosomes; and the quantity of melanin produced. Melanosomes in darkly pigmented skin are large, single, and individually bound by a membrane. In lightly pigmented skin, melanosomes are smaller and clustered together in complexes enclosed by a membrane.

The main function of melanin is to protect DNA from UV light by acting as an antioxidant to reduce inflammation. Even melanin production in dark skin leads to the desirable tan, whereas in fair skin it leads to freckles, uneven color tone, and no tanning. The two types of melanin are eumelanin and pheomelanin. Eumelanin is stable, darkens when oxidized by UV light (produces a tan), and protects from UV light at a sun protection factor of 4 to 8. It is dominant in dark skin (skin types IV to VI on the Fitzpatrick scale). Pheomelanin, on the other hand, is unstable, provides little natural UV protection, and breaks down when exposed to UV light (causing DNA damage). Pheomelanin is present in all skin types (Fitzpatrick types I to VI) but is dominant in fair skin. It may be the causative factor in skin cancer in dark skin.

Melanin exists in the skin of animals and in many botanical and marine plants. Plant melanin should be included in skin care products, especially sunscreen, to offer extra protection from UV light, to protect skin melanocytes through an antioxidant effect, and to act as a shield to prevent penetration of UV light.

Tanning of the skin occurs in response to the UVA (320 to 380 nm) and UVB (290 to 320 nm) spectrums of solar radiation that reach the earth's surface. Within a few minutes of exposure to UVA, an immediate reaction occurs that then fades over 6 to 8 hours. During this time, preexisting melanin is photo-oxidized, resulting in an immediate pigment darkening, and melanocytes increase in size. A delayed reaction involving new pigment production becomes apparent only after 2 to 3 days of repeated exposure. This delayed reaction occurs in response to both UVA and UVB and involves an increase in the number of active melanocytes, enhanced melanosome production, and an increase in melanogenesis. The transfer of mature melanosomes from the melanocytes into keratinocytes increases, and keratinocyte proliferation increases. Changes also occur in the size and aggregation pattern of melanosomes, from smaller and grouped to larger and singly dispersed.

Skin can also darken in response to hormonal stimulation, such as with increased synthesis of melanocyte-stimulating hormone or adrenocorticotropic hormone, or during the poorly understood process of postinflammatory hyperpigmentation. Persons with lentigines (sun-induced dark spots) show increased numbers of melanocytes at the dermal-epidermal junction. Lentigines tend to be stable in color regardless of the length of exposure to UV light. These lesions

are believed to result from an increase in metabolically active melanocytes. Ephelides (freckles), on the other hand, are not due to an increase in melanocytes but represent areas of increased melanin synthesis. Freckles appear in childhood, and their pigmentation usually increases during the summer, indicating that melanocytes respond to UV light. Melasma, a very common patchy brown, tan, or blue-gray facial skin discoloration, is almost entirely seen in women in the reproductive years. It typically appears on the upper cheeks, upper lip, forehead, and chin. Melasma is thought to be the result of stimulation of melanocytes or pigment-producing cells by the female sex hormones estrogen and progesterone to produce more melanin pigments when the skin is exposed to sun. Women with a light brown skin type who are living in regions with intense sun exposure are particularly susceptible to developing this condition. Figure 1.3 shows a woman with melasma on the cheeks and forehead.

THE DERMIS

In contrast to the epidermis, the dermis is a layer of connective tissue 500 to 1,000 μm thick that is largely acellular. It is composed of a mucopolysaccharide gel held together by a fibrous matrix of primarily collagen fibers and about 5% elastin. The dermis lies beneath the epidermis and gives it structural support. It also provides nutrition and removes waste products. The dermis is subdivided into two layers: the more superficial papillary dermis and the deeper reticular dermis (see Figure 1.1). The papillary dermis is the most active dermal layer. It is constantly repairing damaged collagen and elastin tissue and producing collagen, elastin, and glycosaminoglycans. It contains a rich supply of blood vessels that penetrate from the deeper layers, as well as numerous nerve endings, thermoreceptors, and cryoreceptors.

Below the papillary dermis is the thicker, major layer of the dermis, the reticular dermis, which is densely packed with collagen and elastic fibers. Various cell types are also present, including mast cells, fibroblasts, macrophages, and dermal dendritic cells. The transition from papillary dermis to

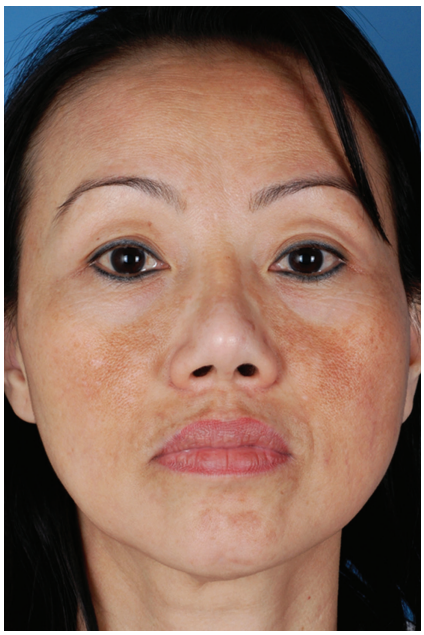

Figure 1.3 Asian patient with melasma on cheeks and forehead.

upper reticular dermis (called the *immediate reticular dermis,* or IRD) can be observed histologically. The IRD is the line where collagen fibers become thicker and more horizontal and elastic fibers become less distinct. Peels reaching the papillary dermis and the IRD lead to maximum skin tightening (Box 1.3). They are suitable for all skin types, and there is no risk for permanent effects, such as hypopigmentation skin thinning or textural changes. Complications such as keloids are rare. Healing is rapid, usually occurring in 8 to 10 days. Procedures below the IRD, such as those penetrating to the upper reticular dermis, can achieve skin leveling, but they have a higher incidence of color and texture changes and the possibility of keloids.

Collagen and Tensile Strength

Collagen is produced by fibroblast cells that lie among collagen fibers and makes up approximately 70% of the dry weight of the dermis. It has great tensile strength—a single fiber 1 mm in diameter can withstand a load of up to 20 kg (Box 1.4). It is insoluble because of chemically stabilizing intermolecular cross-linking. In young skin that has not been exposed to sun, mature collagen is cross-linked into collagen fibrils that come together into small groups of fibers, which are then organized into thin, wavy fiber bundles. The collagen fiber bundles are arranged in a mat-like orthogonal pattern, such that each layer is at right angles to the one above and the one below. These bundle formations are loosely arranged in the papillary dermis and become thicker in the deep dermis. Newly formed collagen fibrils become less soluble and more stable as they mature. Fully mature collagen fibers have a very low turnover rate compared with other body proteins.

In elderly persons, dermal collagen fibers become more heterogeneous, and the dermis becomes thinner. Reports on changes in the amount of collagen in unexposed human skin over time have been contradictory. It appears that the absolute amount of skin collagen decreases with age as skin becomes thinner, whereas the relative amount of collagen does not undergo significant change. Skin exposed to sunlight shows similar but more severe changes than normally aged skin, with less insoluble collagen than normal skin.

Box 1.3

Procedures for Skin Tightening

Peels reaching the papillary dermis and the immediate reticular dermis lead to maximum skin tightening.

Box 1.4

Collagen and Skin Tensile Strength

Collagen fibers provide the skin with its tensile strength, allowing the skin to serve as a protective organ against external trauma.

Elastic Fibers, Skin Elasticity, and Resilience

Elastic fibers are extracellular matrix protein complexes produced by fibroblasts, and they make up 2% to 4% of the total volume of the dermis. They form a network that is composed mostly of the protein elastin, which has unusual elasticity and tensile strength, and a small amount of microfibrils composed of a family of proteins. It is this network that maintains normal skin tension and provides extensibility. The integrity of the elastic fiber network in skin is very important because wrinkling, looseness, sagging, and other structural and mechanical changes in aging skin appear to be due to alterations in this network. In young skin, elastic fibers snap back quickly after stretching. Elastic fibers are continuously degraded and replaced by newly synthesized fibers in normal situations, but the turnover is slow.

The components of skin strength are shown in Box 1.5.

Extracellular Matrix and Hydration

The insoluble fibers of collagen and elastin are imbedded in the gel-like extracellular matrix of the dermis. This matrix is made up of noncollagenous glycoproteins and glycosaminoglycan-proteoglycan macromolecules. The glycoproteins facilitate cell adhesion, cell motility, and cell-matrix interactions, whereas the macromolecule complexes are important for hydration. Although the glycosaminoglycans are less than 1% of the dry weight of the skin, they are able to bind up to 1,000 times their own weight in water. Hyaluronic acid and dermatan sulfate are the major glycosaminoglycans in adult skin. As part of innate cutaneous aging, the content of hyaluronic acid diminishes with age; this may in part explain the reduced turgor of aged skin. Because of their high water-binding capacity, glycosaminoglycans allow some movement in dermal structures.

Fibroblasts and the Synthesis and Degradation of Connective Tissue

Fibroblasts, the "master" cells of the dermis, are responsible for synthesizing the connective tissue elements (the dermal-extracellular matrix) of the dermis, including collagen, elastic fibers, and the proteoglycan-glycosaminoglycan macromolecules. They are more numerous and larger in the papillary dermis than in the reticular dermis. Fibroblasts also control the turnover of connective tissue by secreting enzymes that degrade collagens (collagenases), elastin (elastases), and proteoglycans and glycosaminoglycans. With advancing age,

Box 1.5

Components of Skin Strength

Skin strength is the combination of:

- **Skin firmness: resistance to shearing forces, which is related to quantity and quality of *collagen***
- **Skin tightness: ability of skin to snap back after pulling or stretching, which is related to quantity and quality of *elastin*, especially in the papillary dermis**

fibroblasts become smaller and less active. In photodamaged skin, they are often hypertrophied.

Mast Cells and the Inflammatory Response

A second cell type of the dermis is the mast cell. These cells are found close to blood vessels, nerves, and appendages and are present in greater numbers in the subpapillary dermis. Mast cells are distinguished primarily by the presence of numerous, large cytoplasmic granules that contain histamine, enzymes, and other mediators. During an allergic reaction, mast cells bind to immunoglobulin E, and the granules discharge their contents as part of the inflammatory response.

THE SUBCUTANEOUS LAYER

The subcutaneous layer, composed of lobules of fatty tissue, functions as a buffer against blunt trauma and gives the skin its appealing full and plump appearance (Box 1.6). It also provides "gliding ability" to both the dermis and epidermis, which helps to make skin more flexible. Areas with abundant subcutaneous tissue heal better and have less severe scarring than areas with a very thin or no subcutaneous layer. This can explain why certain areas of the face, such as the upper lip, jawline, and neck, where the dermis is in contact with the underlying muscles with little or no fat in between, have an increased tendency for fibrosis and scarring after procedures. It is very important to avoid deep dermal penetration in these areas.

SEBACEOUS GLANDS

Sebaceous glands are found on all parts of the body except the palms and soles, but they are small and relatively inactive in hairless areas. They are formed from epidermally derived cells that bud out from the side of a hair follicle. The purpose of the sebaceous glands is to form oil, sebum, which lubricates and thus protects the hair and skin. The dominant pathological condition of the sebaceous glands is acne.

There are several misconceptions about sebum and aging. Skin aging involves changes to collagen and elastin and does not depend on the amount of sebum production or skin dryness. Thus, oily skin does not age at a slower rate. Dryness is in fact related to the loss of glycosaminoglycans and abnormal barrier function (Box 1.7). Sebum helps to keep the skin at a slightly acidic pH (between 6 and 7).

Box 1.6

Fatty Tissue

The subcutaneous layer, composed of lobules of fatty tissue, gives the skin its appealing full and plump appearance.

Box 1.7

Sebum and Skin Dryness

Dryness is related to the loss of glycosaminoglycans and abnormal barrier function, not to a decrease in sebum.

THE AGING PROCESS

In any discussion of skin aging, it is important to differentiate between biological aging (chronological aging) and photoaging that is a direct result of exposure to sunlight. Clinically, the appearance of photoaged skin is distinctly different from biologically aged, sun-protected skin (Table 1.2). The most visible signs of biological aging include laxity, paleness, smooth-to-fine wrinkling, deepening of expression lines, dryness, and general thinning. Bruising is more common, and healing is slower. In contrast, visibly photoaged skin is more yellowish in pigmentation with marked areas of hyperpigmentation, coarser and roughened in texture, more lax, and more deeply wrinkled. These differences are readily evident when comparing skin areas of elderly persons that are usually covered, and thus photoprotected, with areas that have not been photoprotected. As a general rule, individuals with biologically aged, photoprotected skin appear younger than individuals with photodamaged skin who are of the same chronological age. In biological aging, most skin functions are slowed, and there is atrophy of tissues, whereas in photoaging, there is an increase in irregular activity with hypertrophy of certain tissues. Although exposure to UV radiation is the most important extrinsic factor in skin aging, other external factors, such as environmental toxins and infectious agents, may also play a role. Figure 1.4 shows a patient with skin atrophy, laxity, and wrinkles (intrinsic aging). Figure 1.5 shows a patient with classical signs of photodamage.

BIOLOGICAL AGING

Biological aging is characterized by a decrease in functional capacity and increased susceptibility to certain diseases and environmental insults. The

Table 1.2 Clinical Appearance of Biologically Aged and Photoaged Skin

Biologically Aged Skin	*Photoaged Skin*
Lax	Leathery
Deepened expression lines	Dry
Dry	Nodular and hypertrophied
Overall thinning	Yellow Telangiectasia Deep wrinkles Accentuated skin furrows Sags and bags Variety of benign, premalignant, and malignant neoplasms

most pronounced changes in biologically aged skin occur within the epidermis, affecting primarily the basal cell layer. The aging process takes place within all organs of the body and can be seen visibly in the skin. Skin aging is influenced by several factors, including genetics, environmental exposure, hormonal changes, and metabolic processes. Together, these factors lead to cumulative alterations of skin structure, function, and appearance. The functioning of the central nervous, immune, endocrine, and cardiovascular systems, as well as of the skin, is also impaired with age. Chronologically aged skin is thin, relatively flattened, dry, and unblemished, with some loss of elasticity and age-related loss of architectural regularity. General atrophy of the extracellular matrix is reflected by a decrease in the number of fibroblasts. Reduced levels of collagen and elastin, with impaired organization, are primarily due to decreased protein synthesis affecting types I and III collagen in the dermis, with an increased breakdown of extracellular matrix proteins. Oxidative stress is considered of primary importance in driving the aging process. The original

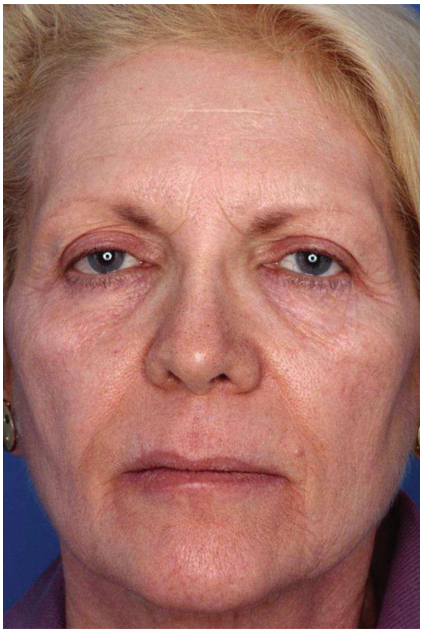

Figure 1.4 Patient with intrinsic aging. Notice skin atrophy, laxity, and wrinkles.

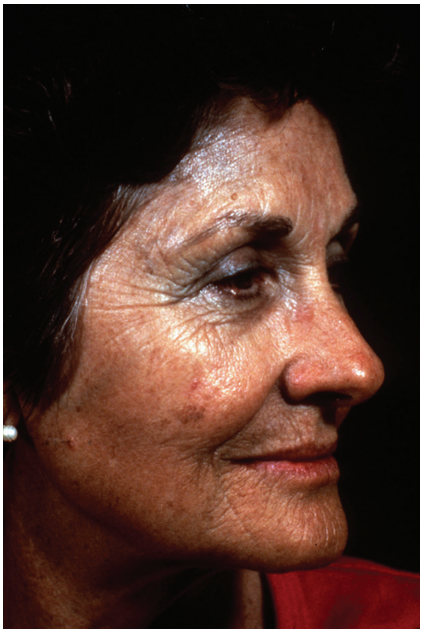

Figure 1.5 Patient with classical signs of photodamage (extrinsic aging).

free radical theory of aging purported that the molecular basis of aging was derived from a lifetime accumulation of oxidative damage to cells resulting from excess reactive oxygen species (ROS) produced as a consequence of aerobic metabolism. Although the skin possesses extremely efficient antioxidant activities, ROS levels rise, and antioxidant activities decline during aging.

A flattening of the dermal-epidermal interface is one of the more profound structural changes that occur with age. Because of this and the other aged-related structural and morphological changes that occur at both the tissue and cellular levels, normal skin functions progressively deteriorate, and skin becomes more susceptible to the development of various benign and malignant diseases. Hereditary factors, hormone levels, and various metabolic substances modulate the structural and physiological changes inherent in the aging process. Skin barrier functioning, permeability, thermoregulatory mechanisms, response to injury, sensory perception, metabolism, and immune function are all altered as we age. Several theories have been proposed over the years to explain the changes that occur, but it is likely that multiple pathways are involved. Alterations occurring during biological aging are shown in Box 1.8.

Changes to the Epidermis

With age, corneocytes become bigger and adhere less to one another, the rete pegs of the epidermis disappear, and, along with a decrease in the number and size of dermal papillae, the lower surface loses its undulating contour. As a result, the epidermis flattens and has less surface contact with the dermis (with less nutrient and waste transfer). In this way, the skin becomes less resistant to shearing forces and more vulnerable to insult, leading to an increased risk for epidermal peeling. Although this flattening of the dermal-epidermal junction may give the appearance that the epidermis thins substantially with age, the actual thickness of the epidermis decreases only 20% over the human lifespan. It is the dermal layer that thins markedly during the biological aging process. Along with the various structural changes that occur, there is a progressive decline in active melanocytes. In addition, keratinocytes change shape, becoming shorter and fatter.

Changes in Histology of the Dermis and the Appearance of the Skin following Biological Aging

Alterations in the dermal structural network of elastic fibers, collagen, proteins, and glycosaminoglycans lead to changes in the resilience and strength of aging skin. One of the most prominent changes occurring in biological

Box 1.8

Alterations during Biological Aging

Skin barrier functioning, permeability, thermoregulatory mechanisms, response to injury, sensory perception, metabolism, and immune function are all altered as we age.

aging is the decrease and increasingly abnormal structure of the elastic fibers, which may cause skin laxity and the loss of resiliency after stretching. Loss of elastic microfibrils and the appearance of cavities are also highly characteristic of biological aging. Collagen is a tougher, more stable material and does not show the well-defined aging changes that are seen with elastic fibers. However, there is less collagen per surface area in aging skin, and it is less dense and stiffer, probably owing to progressive cross-linking. Also, the fibers of collagen appear thickened and stain differently. The three-dimensional meshwork of collagen becomes distorted from many years of mechanical stress and, in this way, contributes to the laxity, sagging, and wrinkling of older skin.

One of the marked differences between the sexes is that men have a thicker dermis than women across all age groups. Similarly, collagen density is greater in men than women, although the rate of collagen loss is similar in both sexes. These differences may explain why facial skin of women appears to show greater deterioration with age.

Additional age-related dermal changes affect fibroblasts, which become smaller and show decreased metabolic activity and a decreased proliferation rate. The concentrations of glycosaminoglycans—an important factor in the water-holding capacity of the dermis—are stable until about 40 years of age and then fall continuously. This decrease of glycosaminoglycans that is observed in later years may be due to decreased synthesis and might have explained the dry and wrinkled appearance of aged skin. However, biological aging does not appear to alter the water structure significantly.

Other Changes

With age, lipid content of the skin decreases, and lipid composition changes. And, although the fat content of the subcutaneous layer is greater in women than in men, the distribution of subcutaneous fat changes and the volume decreases in both sexes as they age. Androgen-dependent production of sebum by the sebaceous glands begins to decrease in postmenopausal women and declines steadily thereafter. The clinical consequences are a 40% to 50% decrease in sebum output, which may account for the prevalence of dry skin in older women. Excessive use of soaps and cosmetics and actinic damage may be even more important. In men, the output of sebum does not begin to decline until about their early 70s. The secretions of sweat glands are also diminished. Table 1.3 shows skin changes in biological aging.

Table 1.3 Skin Changes in Biological Aging

Skin Component	*Histological Change*	*Clinical Change*
Elastic fibers	• Decreased amount • Abnormal structure	• Skin laxity • Loss of resiliency
Collagen	• Less per surface area • Less dense and stiffer • Three-dimensional meshwork becomes distorted	• Laxity • Sagging • Wrinkling
Glycosaminoglycans	Decreased synthesis	• Dryness • Wrinkling
Subcutaneous fat	Decreased volume	• Loss of full and plump skin appearance

PHOTOAGING

Ongoing photoaging results in marked changes to both the epidermal and dermal layers that are distinct from those observed with biological aging (see Table 1.2). Photoaging of the skin is broadly characterized by hypertrophy. Sebaceous glands become enlarged, and neoplastic growths are frequent. In marked contrast to biologically aging skin, the dermis of photodamaged aging skin thickens, and small blood vessels become dilated and deranged. The microvasculature collapses, showing only a few dilated, thickened, tortuous vessels. In addition, the number of hair follicles is reduced, and hair thinning is more prominent than in biologically aged skin. Figure 1.4 shows a patient with photoaging and fine wrinkles.

Epidermal Damage

Excessive sun exposure causes significant changes in the epidermis. Melanocytes increase, enlarge, and become more branched. Keratinocytes may become vacuolated and necrotic or show variation in size, shape, and staining properties. The thickness of the photodamaged epidermis is variable, with alternating areas of atrophy and hyperplasia. It is thought that atrophy may result from depletion of cells from the basal layer, whereas areas of hyperplasia may reflect compensatory overgrowth of UV-damaged tissue.

Not surprisingly, many of these morphological changes are associated with clinical changes in the appearance of the skin. Melanocyte hyperplasia causes irregular pigmentation interspersed with more severely damaged areas in which melanocytes are depleted or unable to transfer pigment to keratinocytes. Hyperplastic melanocytes that produce great amounts of pigment give rise to solar lentigines. Also known as liver spots, solar lentigines are benign lesions that occur on photodamaged skin. Most lightly pigmented persons develop solar lentigines on sun-exposed hands, wrists, arms, neck, and face in middle age. Injury to basal keratinocytes results in a scaly stratum corneum and actinic keratoses.

Dermal Damage

Many of the visible signs of deterioration in photoaged skin reflect major structural changes in the dermis. The dominant change to the dermis is hyperplasia of the elastic tissue, ending in complete disorganization. Compared with biologically aged skin, new apparently abnormal elastin accumulates, whereas elastin degradation is slowed. The degree of elastosis correlates with the amount of sun exposure. Histologically, large quantities of thickened, tangled, disorganized, and degraded elastic fibers are seen, and with extreme damage, an amorphous mass of what once was elastic tissue is present. In sun-protected skin, elastosis this extensive is never seen, even in people of advanced age.

Together with hyperplasia of the elastic tissue, collagen fibers become fragmented, thickened, and more soluble in sun-damaged skin, whereas glycosaminoglycans increase. Collagen is degraded as a result of the upregulation of collagen-degrading enzymes that occurs in response to UVB radiation. In contrast, mature collagen appears to become more stable and resistant to enzymatic degradation with biological age.

Box 1.9

Maintaining Proper Skin Functioning

Despite the effects of aging, it is theoretically possible to keep the skin functioning properly throughout life so that it overcomes damage from the environment and remains in a healthy state.

MAINTAINING SKIN HEALTH AND FUNCTION THROUGHOUT LIFE

Facial skin is remarkable for its ability to reveal health or disease of the skin, as well as that of the other organs of the body. Genetics, environmental exposure, hormonal changes, and metabolic processes, alone or together, lead to changes in skin structure, function, tolerance, and appearance. Moisturizers, so popular in over-the-counter products, cannot slow the progress of these intricate and inter-related changes. In fact, moisturizers slow down the rate of natural exfoliation, causing decreased skin tolerance, dullness, dryness, and actual moisturizer addiction. Yet consumers continue to purchase moisturizers in the hope that "this one will be different." For profound beneficial clinical changes, skin must be treated on the cellular level with agents that target different layers and cells of the skin. The restoration and maintenance of skin health should be based on many of the anatomical and physiological properties of the skin reviewed in this chapter. This volume presents the advances in Skin Health Restoration that allow the maintenance of skin health and function throughout life. The principles of skin health are defined and described, skin-conditioning processes are presented, and simple, standardized programs are explained. It is time to end patients' moisturizer addiction and give them the solutions that lead to fundamental and lasting changes. Box 1.9 discusses a view on maintaining proper skin functioning throughout life.

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CHAPTER

2

PRINCIPLES AND OBJECTIVES OF SKIN HEALTH RESTORATION

A LIFETIME OF HEALTHY SKIN

This chapter presents the original principles and objectives of the Skin Health Restoration program that were developed over the past 30 years. These comprehensive solutions defy the traditional narrow focus on skin *disease* and aim to provide truly healthy skin for the lifetime of any individual, regardless of age, sex, race, or skin condition. Current dermatology training, published literature, and clinical practice focus mostly on the treatment of skin disease and do not address overall skin health. This situation gives rise to a number of questions, including the following: 1) If a patient has no active skin *disease,* is his or her skin healthy? 2) Is skin health restored when a skin disease has been treated and cleared? 3) Is it advisable to wait for a disease to appear, or should we intervene to prevent its appearance? 4) Is maintenance of skin integrity and function not as important as resolving a disease or performing a procedure to improve the appearance of skin? Our answers to these questions may reveal deficiencies in the current mainstream attitude toward skin health.

HEALTHY SKIN: DEFINITION AND MODEL

Skin health does not have a widely accepted definition or model—it means different things to different people throughout the world. Healthy skin is frequently described as beautiful, flawless, glowing, and young, but these terms are imprecise and reflect subjective and nonquantifiable characteristics. The definition of skin health introduced in 1983 and expanded in 2008 provides specific, easily recognized physiological, histological, and clinical characteristics. Specifically, healthy skin is smooth, even in color tone, firm and tight, well hydrated, tolerant to external factors, contour rich, and free

Box 2.1

Skin Health Defined

- **Smooth**
- **Even in color**
- **Firm and tight**
- **Well hydrated**
- **Tolerant**
- **Contour rich**
- **Free of active disease**

from underlying disease (Box 2.1). Skin treatments must correct any abnormalities in skin health that deviate from this definition so that the skin attains desirable attributes.

The definition of healthy skin has many applications. The first is in establishing a comprehensive patient diagnosis by listing the common characteristics of healthy skin and then determining which of these are lacking in the skin of the patient being evaluated (Table 2.1). The practitioner must then create a treatment plan that corrects any abnormalities (based on the definition) by treating the patient's skin disease. The definition also improves the physician's ability to monitor the progress of a topical product regimen aimed at Skin Health Restoration and for judging treatment results and success rates. Figure 2.1 highlights characteristics of a baby's skin, which illustrate the goals for achieving success in any comprehensive topical Skin Health Restoration treatment regimen. Table 2.2 delineates each of the main characteristics of healthy skin as seen in a baby and identifies the etiology behind each of these characteristics.

SKIN PHASES OVER A LIFETIME

Most of us begin life with healthy, unflawed skin. However, environmental/external and internal factors, hereditary factors, and the natural,

Table 2.1 Definition of Skin Health: Attribute Presence versus Absence

Attribute Present (Optimized Skin Health)	*Attribute Absence (Sub-Optimal Skin Health)*
Smooth	Rough
Evenly colored	Dyschromic
Firm	Weak (little to no resistance to shearing force)
Tight	Lax
Hydrated	Dry
Tolerant	Intolerant
Contour rich	Hollow, sunken
Free of underlying disease(s)	Underlying disease present

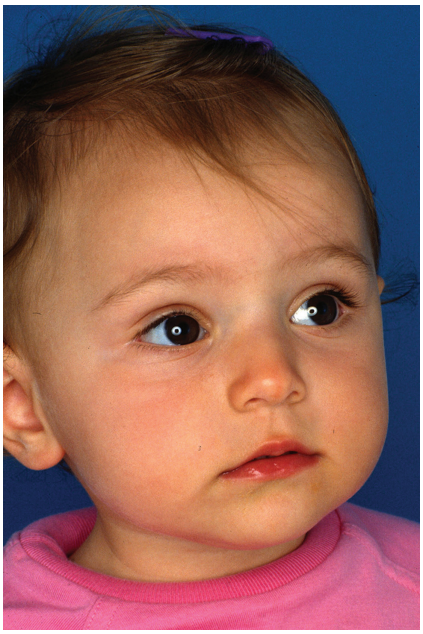

Figure 2.1 Healthy skin. This 1-year-old girl has skin that embodies each major skin health attribute.

Table 2.2 Factors Underlying Skin Health Characteristics

Characteristic	*Factors*
Smooth	Soft, compact stratum corneum and minimal basket-weaving (histology) Continuous epidermal cell renewal and repair owing to balanced and regulated keratinocyte maturation cycles (KMCs). (Each cycle is approximately 6 weeks; KMCs are described later in this chapter.)
Firm	Abundant, optimally functioning collagen
Tight	Abundant, optimally functioning collagen and elastin
Evenly colored	Properly functioning melanocytes
Well hydrated	Abundance of glycosaminoglycans (thus, no need for external moisturization)
Intact barrier function	Smooth stratum corneum with little to no basket-weaving. Multiple layers of corneocytes that are bound well together Overlying stratum granulosum and stratum lucidum below the numerous layers of well-defined, pink keratinocytes arising from the basal layer
Heals rapidly and properly	Effective renewal of keratinocytes Good circulation
Contour rich	Optimal volume of collagen, elastin, and subcutaneous tissue
Free of clinically active disease	Normal skin histology

chronological changes associated with aging proceed to undo what was ours at birth. With the passage of time, activities promoting skin health decrease, and a deterioration of skin quality begins. The skin is not diseased, but intrinsic aging and photoaging have caused anatomical, physiological, and clinical changes. These range from a sensation of dryness and the appearance of dull, weathered skin, to the appearance of wrinkling, jowling, laxity, hypertrophy, and easy bruising. Although these changes (phases) may not be clinically detectable at an early stage, they are occurring and will become detectable at a later age. It may be surprising to learn that skin reaches a relatively inactive phase at age 30, with decreased cellular function and the appearance of wrinkles. The phases skin passes through in a lifetime are shown in Box 2.2; they are divided into one of the following three categories: a healthy (optimally active) phase, an altered (deteriorated) phase, and an inactive phase. Some of the most common causes of skin deterioration may be controllable, whereas others are not (Table 2.3). Of note, many of the individual factors leading to skin deterioration have inflammation as an underlying cause.

SIGNIFICANT FACTORS IN ACHIEVING SKIN HEALTH

The skin health definition presented previously described the external characteristics of healthy skin, whereas the baby skin model specified the

Box 2.2

Skin Phases over a Lifetime

HEALTHY (OPTIMALLY ACTIVE) SKIN PHASE

- From birth to age 9 or 10 years
- Embodies the definition of optimal skin health
- Optimized epidermal and dermal cellular function and continuous, regular cell renewal and repair (normal KMC*)
- No sebum production
- No chronic inflammation
- No dryness or sensitivity

ALTERED (DETERIORATED) SKIN PHASE

- From age 10 to 30 years
- Begins to diverge from the main characteristics that define optimal skin health
- Irregular cellular functions, including impaired epidermal cell renewal (abnormal KMC*)
- Impaired skin barrier function
- Sebum produced at varying levels
- Chronic inflammation
- Textural irregularities
- Enlarged pores, dyschromia, atrophy, sebaceous gland hyperplasia, and a "dull" appearance
- Skin disease may be present or beginning to appear

INACTIVE SKIN PHASE

- Begins at age 30 years
- Progressively greater deviation from the characteristics that define optimal skin health (compared with the previous two phases)
- Irregular epidermal cellular function (abnormalities in KMCs*)
- Weakened, impaired barrier function
- Chronic inflammation
- Advanced textural changes and irregularity
- Conspicuous signs of extrinsic and intrinsic aging (e.g., hypertrophy, atrophy)
- Laxity and wrinkles (due to damaged existing collagen and elastin in combination with an overall decrease in the production of collagen and elastin)
- Increased likelihood of concurrent skin disease

*The keratinocyte maturation cycle (KMC) is described later in this chapter.

Table 2.3 Common Causes of Skin Deterioration

Controllable	*Uncontrollable*
Excess sebum production (abnormality of pilosebaceous units)	Genetic factors and skin type
Dysfunctional melanocytes	Intrinsic and chronological aging changes
Sun exposure	Abnormalities in the skin caused by an underlying, incurable, systemic disease (including immunological disorders); many of these can have an unpredictable course*
Unhealthy diet (e.g., high glycemic index and/or excessive hormonal exposure through the consumption of nonorganic dairy products), lifestyle, unsuitable topically applied products	
Medications (some systemic medications have effects on the skin)	
Complications of surgical and nonsurgical rejuvenation procedures	
Exposure to irritants and allergens	
Prolonged use of certain medical and nonmedical topical agents (i.e., topical steroid–induced skin atrophy)	
Chronic inflammation	

*Some chronic, incurable, systemic disorders and their associated skin inflammation (e.g., lupus erythematosus) can be controlled with medications; however, regardless of periods of control with medications, many are associated with an unpredictable course.

physiological, histological, and clinical characteristics of such skin. The next step was to determine the factors and processes that negatively influence skin health so that treatment programs could be created to help restore it. Investigations and clinical experience have revealed that the areas of most concern in skin health include the following: the integrity of the skin barrier function, duration of the KMC, and presence of chronic inflammation (Box 2.3).

SKIN BARRIER FUNCTION

It would be hard to overstate the importance of an intact barrier function in skin health. As a physical, chemical, and immunological barrier, it prevents penetration of harmful substances and excessive transepidermal water loss. We do not currently know all of the intricate mechanisms of the barrier function, but we do know that the barrier function can be repaired by following the ZO Skin Health Restoration principles using topical regimens.

Box 2.3

Factors Responsible for Skin Health

- **Skin barrier function**
- **Keratinocyte maturation cycle (KMC)**
- **Chronic inflammation**

The barrier function acts as a protective skin envelope consisting of 1) a matrix of water, lipids, and proteins that surrounds keratinocytes and corneocytes and 2) stratum corneum cells (corneocytes), which are keratinocytes that have completed their differentiation process, having lost their nuclei and cytoplasmic organelles. As new corneocytes appear, the older cells are shed through desquamation. The normal/healthy barrier function relies on a 40-day cycle of epidermal renewal (the KMC); this entails the production of new cells through mitosis within the basal cell layer, which subsequently mature to become corneocytes. Corneocytes are arranged in multiple layers, enveloped by the natural matrix of water, lipids, and proteins. These two components need to be in balance and work together to maintain the integrity of the barrier function. Disturbances of either component result in a compromised barrier function.

Moisturizers, which contain approximately the same components (water, lipids, and proteins) as the skin's natural elements, impair the skin's barrier function. Specifically, when a moisturizer is applied to the skin surface, cells on the surface detect a large amount of moisture and send a message to the body to stop delivering water to the skin (essentially, a feedback loop). To clarify, externally applied moisturizers alter the balance of water, lipids, and proteins in the skin, which leads to a compromised barrier function and to an acquired skin sensitivity.

Externally applied moisturizers are also detrimental in that they interfere with the natural exfoliation and desquamation of corneocytes (dead keratinocytes). Under normal circumstances, the KMC regulates natural skin exfoliation in a proper manner. But when moisturizers are applied, corneocytes within the stratum corneum do not exfoliate in the usual fashion but accumulate on the surface instead. This accumulation sends a message to the basal cell layer to terminate mitosis and slow down or end the creation of new keratinocytes. With repeated application of moisturizers, new epidermal cells stop being created in the basal cell layer. Subsequently, with repeated application of moisturizers, the epidermis thins, the barrier function is compromised, and skin becomes more sensitive. Box 2.4 shows barrier function activities.

Box 2.4

Barrier Function Activities

- **Transmission of messages from superficial to deeper layers of the skin, which is intended to elicit appropriate responses following exposure to external stimuli**
- **Maintenance of proper natural epidermal hydration (e.g., minimization of transepidermal water loss)**
- **Enhancement of epidermal renewal and repair, which is responsible for building and maintaining skin tolerance**

THE KERATINOCYTE MATURATION CYCLE

As briefly mentioned previously, the skin's normal barrier function depends on a 40-day cycle of epidermal renewal, the KMC. This cycle is the foundation of Skin Health Restoration because without adequate epidermal exfoliation and subsequent replacement with fresh, active cells, skin health is compromised. A properly regulated KMC is essential for the production of skin that is naturally hydrated and tolerant of detrimental external stimuli. In this text, the term KMC is synonymous with the process of natural skin exfoliation because each can be measured in time. The term KMC describes the amount of time it takes for a keratinocyte to mature and transform into a corneocyte, reach the stratum corneum, and subsequently exfoliate from the surface of the epidermis (Figure 2.2). This normal 40-day cycle is shortened in certain diseases such as psoriasis, malignant tumors, and verruca. The cycle can be lengthened as a result of intrinsic aging, photoaging, and the use of moisturizers and topical corticosteroids. The main objective of Skin Health Restoration regimens is to restore normal maturation cycles, which restores optimal skin barrier functions. Normal barrier function, in turn, increases skin tolerance. Skin should have developed a good level of tolerance before undergoing any rejuvenation procedure.

Benefits of Regulating the Keratinocyte Maturation Cycle

Completion of two to three KMCs while using Skin Health Restoration principles and certain topical agents will establish sufficient skin tolerance and produce a number of clinical benefits (Box 2.5). The stratum corneum becomes smooth, soft, and compact, with a minimal basket-weave pattern. Mitosis in the basal layer, as well as within adnexal structures, proceeds at an optimal rate, producing a population of healthy keratinocytes and a thicker epidermis. Bacterial flora are reduced, and comedones and enlarged pores decrease in size and number. The skin becomes properly hydrated and does not need externally applied moisturizers. With restoration of the skin's barrier function, the skin's tolerance to cosmetics, dermatological treatments, and other external or environmental factors increases, and the pigmentary system is effectively controlled.

In general, one to two maturation cycles produce a good level of tolerance; three maturation cycles (5 months) are needed to renew most of the epidermis. Renewal of the epidermis entails repairing damaged DNA, producing and maintaining adequate amounts of soft keratin, fully restoring hydration, and regulating natural skin exfoliation. With an aggressive Skin Health Restoration program, tolerance (to the initial expected amount of erythema,

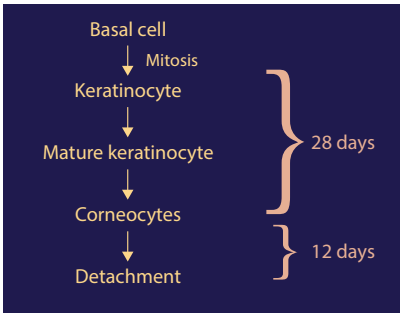

Figure 2.2 The keratin maturation cycle (KMC) describes the amount of time it takes for a keratinocyte to fully mature as it rises upward from the basal cell layer and is eventually shed from the surface of the epidermis. Specifically, the KMC describes the transformation of keratinocytes to corneocytes as they reach the stratum corneum, continue to rise upward from the basal cell layer, and ultimately exfoliate from the surface of the epidermis.