

Barbara A. Gilchrest, Jean Krutmann (Eds.)

Skin Aging

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With 72 Figures and 24 Tables

 Springer

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dedicated to Claudia Billmann-Krutmann, M.D.

Foreword

A decade ago Barbara Gilchrest published a landmark volume titled *Photodamage* consisting of a mere 285 pages and somewhat more than a dozen chapters.

I wrote in the foreword that this field of study “was in its adolescence, a thriving enterprise, delivering new discoveries every month.”

The present volume by Gilchrest and Krutmann, titled *Skin Aging*, is a greatly expanded outgrowth of the original, which is at least double in size and with double the number of authors and chapters. It stands as a testimony to the enormous advances in knowledge that have occurred in ten years, not only with an avalanche of publications, but more profound insights made possible by molecular biology, genomics, and immunohistochemistry, among other rapidly developing disciplines. Indeed, photoaging owes its advances to its multidisciplinary structure.

This volume strikes a balance between the basic science of photobiology with an emphasis on photodamage and clinical interventions to combat and correct the destructive effects of solar radiation. One of the main themes is the prevention of photodamage, a timely focus, reflecting a shift in the traditional biomedical paradigm, which now exalts prevention over treatment. After all, treatment really means failure of prevention. Happily we can now claim that photoaging is not only not inevitable, but is entirely preventable by following a few simple rules. People who look much older than their chronologic age, previously termed premature aging, have simply failed to heed our advice out of ignorance or perversity!

This text is not only an invaluable reference source for a diverse readership of basic scientists, in academia and industry, but perhaps more importantly, a training manual for public health authorities and educators who seek to

inform a health conscious public about the best ways to prevent photoaging in our sun-worshipping culture, preserving an attractive, youthful appearance well into old age.

It is more than a hundred years since Unna from Germany and Dubreiulh from France explicitly described “farmers’ and sailors’ skin” which they correctly attributed to excessive exposure to sunlight.

Curiously these warnings fell on deaf ears for almost another 75 years until dermatologists, caring for an epidemic of aging persons concerned with a deterioration in appearance, which coincided with an epidemic of skin cancers, reignited the subject, fostering serious investigations into the basic biology of photoaging. The last 25 years of the 20th century witnessed an avalanche of publications, relating to all aspects of the subject, more than a thousand papers originating from all corners of the world.

Despite energetic campaigns by national dermatological organizations and constant exhortations by the lay press and mass media, we have largely failed to persuade the public to follow our advice. The proportion of older people showing the dreaded stigmata of wrinkles, blotches, sags, laxity and cancers has continued to grow, fueling a huge increase in the number of physicians practicing cosmetic surgery. This book is an invaluable resource for dermatosurgeons who would be well advised to know the basic science principles that underlie their specialty.

The epidemic of non-melanoma skin cancers, basal cell and squamous cell cancers, continues unabated. It is shocking that the annual incidence of these cancers is approximately equal to the incidence of all other forms of visceral cancers—lung, colon, and cervical—combined! It is estimated that 1 of 70 white Americans will experience a malignant melanoma in their life-

time, in which heedless exposure to solar radiation is the predominant etiologic agent.

People are living longer, on average 35 years more than in Unna's time. They also have more wealth and more leisure time for recreational activities and vacations under the sun. Dermatologists have initiated national campaigns to warn against the dangers of the fashionable belief that a deep tan makes one more attractive and happier. Whatever the supposed short-term social benefits, the ultimate long-term effect is the repulsive appearance of wrinkled facial skin, replete with bags and sags, blotchy dyspigmentations, tumorous growths, wrinkles, yellowing, poor texture, clogged pores, and dry-roughness, which certainly do not add to the quality of life of the elderly. Despite the warnings that there is no safe way to obtain a deep tan, tanning salons are thriving, increasing steadily, and amount to a multi-billion dollar business in the USA alone, with few regulations to limit the harm.

In the face of these foibles and follies, photobiologists continue to make surprising discoveries of the powerful capacity of solar radiation to damage unprotected skin. Even a single minimum erythema dose (1 MED) can damage the dermal matrix. One sunburn dose damages the matrix forever. The skin has a long memory!

In biblical Genesis we learn that God created light and declared it to be good, an unassailable truism in the case of visible light. The deity did not take into account ultraviolet light, which is of course invisible and should be called by its proper name, ultraviolet radiation, not ultraviolet light.

Like true missionaries, photobiologists have properly thundered against the multiple dangers of sunlight, but this zeal may need to be balanced against the known beneficial effects of sunlight, a subject not neglected in this volume. For example, sunlight stimulates the epidermis to synthesize pre-vitamin D₃, whose absence in the diet leads to osteoporosis and fractures, a major problem among the elderly. Sunlight clearly induces a feeling of euphoria and is extremely beneficial in moderating seasonal affective disorders.

Light can be harnessed by a variety of new technologies, subsumed under the general term of phototherapy, to treat effectively a number of chronic skin disorders such as acne, psoriasis

and even cutaneous cancers. These techniques employ a growing variety of ingenious ablative and non-ablative lasers at various wavelengths, frequencies and pulse durations to achieve desired benefits, sometimes abetted by photosensitizing drugs to generate oxidative free radicals to destroy tumors.

These salubrious developments are based solely on science, not empiricism as in the past. It is impossible to exaggerate the extent to which these novel phototherapeutic interventions have been brought to fruition based on the basic understanding of photobiologic principles, amply documented by the international authorities who have contributed to this comprehensive text.

Other developments which hover on the horizon open up novel which approaches for exploiting photobiologic principles to effectively treat a variety of unrelated chronic skin disorders, including potentially lethal ones such as T-cell lymphomas. One fascinating example of things to come relates to the repair of photodamaged DNA. The inability to remove or repair DNA damage induced by sunlight inevitably promotes tumor progression, culminating in a variety of cutaneous tumors, as strikingly illustrated in the devastating hereditary disorder xeroderma pigmentosum. This death-dealing disease results from the lack of specific repair enzymes that enable photodamaged DNA to persist throughout many cell replications, ending in carcinogenesis. The solution is to develop topical systems that can deliver these repair enzymes to the viable epidermis, penetrating the horny layer barrier without disrupting its structure. This remarkable feat has already been accomplished in preliminary studies, using liposomes loaded with repair enzymes.

Finally, a rapidly aging population has created an enormous need for so-called anti-aging remedies to correct the ravages of photodamaged skin. These include scores of oral supplements, hundreds of topicals containing every conceivable "active" ingredient—vitamins, hormones, minerals, macronutrients, free-radical scavengers, anti-oxidants, oriental herbs, ad infinitum.

This galaxy of offerings, all of them unregulated and with no requirement to substantiate claims of efficacy, are the modern equivalent of

snake oil, based mainly on advertising hype and unabashed huckstering.

In the face of this maniacal onslaught, aimed mostly at women, there are indeed topicals that possess scientifically verified anti-aging effects for correcting wrinkles, dyspigmentations, laxity, etc. Topical retinoids are the oldest and prominent among these credible pharmacological agents, while others are already in the pipeline.

It is the high duty of the photoaging fraternity to educate the public regarding these phantasmagorical, preposterous products, now a business worth 39 billion dollars annually, which is equivalent to the entire budget of the National Institutes of Health! This text does not duck its

responsibility to take up this controversial issue and to provide guidelines of what is credible and what is fakery.

In my coda to the forward of Gilchrest's volume ten years ago, I declared that the future of the specialty of photoaging was radiant (meaning bright). That future is now here. The specialty can now be also eulogized as brilliant (meaning distinguished, beyond compare).

Perhaps we are in reach of Ponce de Leon's dream of a fountain of youth, at least preserving the attractive appearance of youth into old age, based of course on science.

Albert M. Kligman, M.D., Ph.D.

Preface

Life expectancy has risen continuously in developed societies, yet the mystery of aging remains largely unresolved. As a consequence, the prevalence of mental and physical disability and diseases related to old age has increased steeply. To prevent this trend from continuing over the next decades and eventually destabilizing our health-care systems, we must find ways to promote successful, healthy aging. This requires (1) identification of aging mechanisms at a molecular level, (2) reduction of their impact over time on organs and organisms, (3) detection of individual genetic and environmental contributions of these aging mechanisms, and (4) development of diagnostic tools and specific strategies for prevention, regeneration, and compensation to delay unwanted age-associated changes.

Among all the organs, aging of the skin is of particular importance because it affects human health, it has a strong social impact due to its visibility, and it represents an ideal model organ for aging research because of its accessibility

and well-studied baseline cell–cell and cell–matrix interactions.

This monograph attempts to provide an up-to-date overview regarding all aspects of skin aging. It includes in-depth discussions of the molecular basis as well as concepts propagated for the diagnosis, treatment, and prevention of skin aging.

The explosion of knowledge in this field over even the past decade is remarkable. To capture the depth and breadth of this learning, we have recruited leading experts from multiple sub-disciplines. All authors are internationally recognized, and we are grateful for their excellent contributions. We hope that *Skin Aging* will serve you well as a state-of-the-art reference and will further stimulate your interest in this fascinating area.

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