
1 Introduction: Perspectives and Prospects

Albert Kligman

In the five years since the first edition was published, advances in our knowledge of the nature of dry skin and its treatment have been nothing short of stunning. An enormous amount of new information has been produced by an international confederation of investigators from diverse disciplines, encompassing dermatologists, biochemists, molecular biologists, geneticists, anatomists, physiologists, pharmacologists, immunologists, and even psychologists.

More than 350 scientific papers on dry skin have been published in the last five years. Dry skin is a popular topic in scores of women's magazines giving rise to a thriving industry whose annual sales in the United States alone are about 40 billion dollars, equal to the budget of the National Institutes of Health. More than 90% of women apply moisturizers to their face and hands every day for most of their lives. Nonetheless, authors of dermatology give short shrift to the subject, relegating it to a minor condition among the panoply of dermatologic disorders. Academicians frequently take the position that dry skin disorders are trivial, banal problems, amounting to nothing more than cosmetic nuisances that are disagreeable but not important to health and well-being. This disparaging assessment is simply wrong, stemming from neglect of the subject in the training of medical professionals. Dry skin, especially as the population ages, is becoming ever more serious and worthy of more attention by biomedical professionals. For example, few doctors are aware that the dry, fragile, cracked skin of the hospitalized, immobilized elderly is an early warning sign of impending pressure ulcers which are enormously distressful to patients and an enormous burden on the health care system, worsening steadily as the population continues to age. Moreover, dry, rough, fissured skin is a sure sign of advanced malnutrition, presaging death and disease among the elderly with limited access to the healthcare system. My informal inquiries among diabetologists reveal that few are aware that dry, cracked, fragile skin, which is easily torn, is exceedingly common in insulin dependent patients, presaging dreaded infections of the foot, which may necessitate amputation. Few physicians are sufficiently informed to know which moisturizers among hundreds are most efficacious for treatment and prevention of dry skin syndromes. Treatment is often left to nurses who use whatever moisturizers are available in the supply closets.

Likewise, my experience shows that general practitioners are in no better position than their patients regarding selection of the most effective moisturizers for treating the common everyday dry skin disorders, such as winter xerosis. It should be emphasized that the prevalence of dry skin among the elderly in northern climates approaches 100%. Leaving aside appearance, rough feel, and various discomforts, the most important sensorial component of xerosis is persistent itching which can ruin the quality of life.

It should be appreciated that the generic term "dry skin" denotes a diverse family of conditions ranging from relatively benign disorders such as winter xerosis to devastating, life threatening

hereditary ichthyotic states. Dry skin is not a diagnosis any more than the term “rash” to describe inflammatory disorders. A variety of pathologies precede the development of the different varieties of dry skin. Proper classification and an understanding of the pathogenesis of dry skin disorders is the key to proper treatment. This is no easy task.

The commonest way to treat dry skin is through the use of “moisturizers.” So, what in fact is a moisturizer and what is dry skin? In my 1978 paper that described the regression method for assessing the efficacy of moisturizers, I professed an operational definition, which has received general acceptance.¹ “A moisturizer is a topical product, which is effective in relieving the signs and symptoms of dry skin.” This definition was intended to be useful rather than definitive since very little was known about the anatomy, physiology, and biochemistry of dry skin syndromes. We now know that this definition was an oversimplification of what has turned out to be an exceedingly complex problem, which still continues to puzzle us. Happily, basic research has brought us a great deal of light where formerly dark clouds hovered over nearly every aspect of the subject.

Pierard was not merely being mischievous when he asked “is dry skin really dry” suggesting that, as is often the case in scientific inquiry, the obvious conceals more than it reveals.²

The manifestations of dry skin are expressed clinically in the form of scales, a result of faulty desquamation in which corneocytes are shed in clusters rather than as single cells. This immediately directs attention to the outermost portion of the stratum corneum where shedding takes place. However, this focus on surface scaling is misleading and misguided. Merely spraying water on the surface or applying any kind of oil, swells and hydrates the corneocytes so that they do not reflect and scatter light, filling up the empty spaces between loose scales, which immediately obliterate the signs of dry skin. As I earlier noted, even one day of unseemly warm, wet weather in Philadelphia will completely eliminate the appearance of dry skin. Obviously, the underlying pathologic factors leading to scaling are still present. Grading the efficacy of moisturizers based on the visible reduction of scales yields spurious results. To the naked eye every moisturizer works well, enabling hundreds of marginal products to compete in the market place. Sometimes harmful ones are touted as the most effective.

It is now recognized that scaling is simply a common pathway of a variety of disorders related to abnormal epidermal differentiation and cornification. The underlying pathologies however may be very different involving a variety of causal mechanisms. As a result, we are now obliged to look at the dry skin problem at a much deeper layer, using new sophisticated methods to characterize the abnormalities of epidermal differentiation, a tightly regulated process that can go awry from a variety of endogenous and exogenous causes. Methods are now at hand to characterize and quantify abnormal mechanisms.³

Dermatology in general has been the beneficiary, usually unacknowledged, of the great advances in our understanding of the biologic significance of the stratum corneum in health and disease. Until recently, the stratum corneum was depicted as having one function, namely acting as a “barrier” to the inward and outward diffusion of endogenous and exogenous substances. The term “barrier,” short-hand for the stratum corneum, was always thought of as a passive inert structure, dead as a door nail, little more than a plastic wrapping, comparable to Saran Wrap (my description). Largely owing to the energetic and creative researches of Peter Elias and his academic group in San Francisco, we now understand that the stratum corneum is very much alive metabolically and has a surprising number of functions in maintaining the physiologic stability and homeostasis of normal skin.⁴ One of these is worth citing: the stratum corneum is a very lively signaling or semiotic device, rapidly responding to mechanical and chemical stresses and insults inaugurating a series of events aimed at repair and restoration to a normal status. Environmental changes, especially dry, cold weather bring forth a variety of adaptive responses to prevent dehydration.⁵ Other functions of the stratum corneum include: (1) a reservoir for various endogenous metabolites, cytokines, and enzymes, (2) a depot for topical drugs such as corticosteroids and anesthetic agents, (3) source of antimicrobials (defensins and carthelcidins).⁵ The important contributions of many other scientists located in industry and academia are well-represented in this text.

Homage is also due to the basic investigations of Anthony Rawlings and his coworkers of Unilever regarding the principles of formulating moisturizers and their mechanisms of action right down to the molecular level, again emphasizing the multiplicity of events that have to be synchronized to produce a normal stratum corneum.⁶

The modern period began with Irwin Blank at Harvard who at mid-century laid down the foundation for all future work.⁷ He placed a piece of dried callus in various hydrophilic oils, basic ingredients of all moisturizers. The callus remained hard and brittle even after months. Brief immersion in water immediately made the callus soft and elastic. After exposure to soaps, the callus could no longer absorb as much water and became less soft and elastic. These beautifully simple experiments shaped the ways moisturizers were to be formulated thereafter.

Special honors are also due to S. Jacobi, who like Irwin Blank was not a clinician but a Ph.D. scientist. He discovered the famous “natural moisturizing factor,” made up of low molecular weight, water-soluble substances, dominantly amino acids, which are chiefly responsible for the ability of the stratum corneum to absorb water and to hold onto it in the face of a hostile dry environment.⁸ He went on to show that an extract of the natural moisturizing factor could ameliorate dry skin.

Incidentally, the first important clinical paper on dry skin was written by Louis Duhring, the first professor of dermatology of the University of Pennsylvania School of Medicine, under the interesting title of “pruritus hiemalis,” otherwise known as winter xerosis.⁹ He found that in susceptible persons cold, dry winter weather in Philadelphia invariably caused reoccurrence of winter xerosis. I cite this informative and eminently readable paper because Duhring emphasized certain features of dry skin that receive little attention, namely purely subjective sensorial symptoms, notably itching (hence the term pruritus in his title) and also other discomforts such as stinging and tightness. Intractable itching is a maddening sensation, antagonistic to sleep, leading to compulsive scratching, which in turn causes further damage to the skin, inaugurating the well-known itch-scratch cycle. We now know that scratching and other forces that disrupt the horny layer initiate the release of a cascade of epidermal proinflammatory cytokines and chemokines, which perpetuate the pathologic process. Scratching not only increases permeability to damaging substances but also promotes colonization and infection by pathogenic microbes such as *S. aureus* and hemolytic streptococci, which in older, immunocompromised persons may go unnoticed in the absence of fever and evaporation but which nonetheless cause malaise and fatigue.

It cannot be said too often that even the ordinary forms of dry skin are not trivial problems about which members of the health profession should be better informed. The chapters in this volume convey all the information which clinicians might want to know.

The marketplace for new and better moisturizers is being driven by a new breed of consumer, mainly women, who are better educated, more demanding, more critical, with more disposable income to boot. We already see the effects in the availability of a plenitude of supra-moisturizers which are designed to accomplish a great deal more than keeping the skin soft, smooth, and moist.

Multiple ingredients are being added to the moisturizer matrix to produce the universal formulation that covers all needs, an impossibility of course. Toward this ideal we already find offerings of products that include sunscreens, antioxidants, vitamins, minerals, phytoestrogens, bioflavonoids, inflammation inhibitors, hormones, enzymes, and everything else. Of course, the claims for many of these products are enormously exaggerated, unsubstantiated, untested, often fictional, aimed only to increase sales in a frenetic, competitive, unregulated marketplace, catering to a credulous susceptible public looking for the newest and the best. I know of one French mega-moisturizer which has 83 “active” ingredients, including 6 sunscreens, 5 free-radical scavengers, 7 macro and micro-minerals, 5 vitamins (including some that have no chemical existence), 9 emollients, 3 hormones, and a vast assortment of ancient Chinese and Indian herbs which have a special appeal to the Green Movement who seem to believe that “naturals” are safer and superior to synthetics. Needless to say, major manufacturers of skin care products who have long been in business in Europe, Japan, and the United States eschew these pseudoscientific concoctions. The notion of multifunctional products is basically sound and the compositions are scientifically certified.

Progress toward the creation of the complete “ideal” moisturizer is already in evidence. New delivery systems give promise of enhanced efficacy, based on liposomes, niosomes, transferosomes, methods of bypassing the horny layer barrier by physical means (electroporation, sound waves, etc.). Standing on the wings is the fantastic possibility of nanotechnology, in which the tiniest solid particles of oils and emollients can be directly delivered to the visible epidermis. Along with these creative stirrings are entirely new approaches to enhance effectiveness. Elias’ group has proposed the use of physiologic lipids, analogous to those comprising the bilaminar membrane of the intercellular spaces of the horny layer, which give the horny layer its barrier properties.¹⁰ These are actually prodrugs that incorporate into the lamellar bodies of the epidermis to be subsequently extruded by exocytosis into the newly forming stratum corneum, at and just above the granular layer.¹¹ In a similar vein, Rawlings’ group has proposed what he calls lipid modulation as a way to make moisturizers more effective.¹¹ The idea here is to incorporate ceramide-dominant lipids in moisturizers to correct for their absence or lack in virtually all dry skin disorders.

Japanese scientists are also experimenting with these so-called “skin-identical lipids” to enhance efficacy.

This second edition covers the problem of dry skin in a comprehensive, complete, systematic way, incorporating the voluminous amount of new knowledge that has so recently been acquired. All the major players in this consistently enlarging field are represented here along with many other contributors who are enriching our knowledge of the subject.

This new volume is certain to become a standard reference text for a varied readership with different interests who will be able to locate within this expanded new text the specific information being sought.

The editors themselves are major players in this field who with a wealth of personal experimental experience, have produced a one of a kind volume that merits great praise as a scholarly practical treatise for those who want a reference source that includes everything that is worth knowing about the subject of dry skin and its treatment.

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