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A CME-CERTIFIED SUPPLEMENT TO

Seminars in Cutaneous Medicine and Surgery

Editors

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**STRATUM CORNEUM
SKIN BARRIER
MAINTENANCE
AND RESTORATION:
EVIDENCE-BASED
APPROACH TO
CLEANSING AND OTHER
SKIN CARE PRACTICES**

Guest Editors

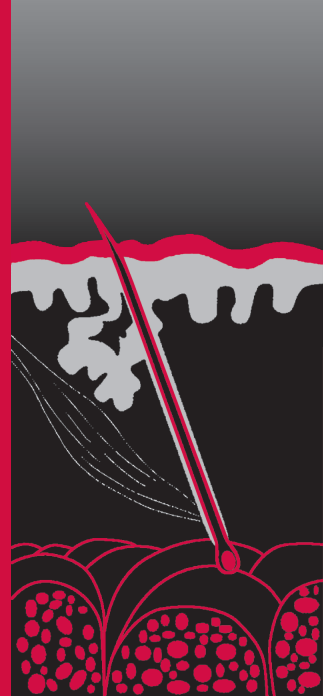
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Stratum Corneum Skin Barrier Maintenance and Restoration: Evidence-Based Approach to Cleansing and Other Skin Care Practices

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Educational Needs

It has long been recognized and appreciated that the stratum corneum plays a vital role in maintaining proper skin hydration and preventing excess transepidermal water loss. However, more recent research has delved into the complex interactions among the three principal active constituents of the stratum corneum (ceramides, fatty acids, and cholesterol). For skin barrier function to be healthy—or for the health of the skin barrier to be restored—an optimum amount and balance of these active constituents must be present.

In addition, over the past decade several key compounds in the stratum corneum have been identified and their roles in maintaining the integrity and optimum function of the human skin barrier have been well characterized. These include natural moisturizing factor, filaggrin, and aquaporin-3.

Against this background of recent findings, research over the past 5 years also has led to a new understanding of when, how, and with what skin should be cleansed in a variety of clinical circumstances and what ingredients in basic skin care products should be avoided to prevent further dysfunction of the stratum corneum.

Clinicians and their patients will benefit from an update regarding the basic scientific research advances on the physiology and function of the skin barrier, an overview of what is currently known about tolerance and toxicity of ingredients commonly used in skin-cleansing agents, and up-to-date, evidence-based expert recommendations for clinicians to consider as they guide patients and parents/caregiving partners of pediatric patients in the principles, techniques, and agents of skin care.

Learning Objectives

After participating in this continuing medical educational activity, clinicians should be able to:

- Adapt patient care practices to reflect the current understanding about the stratum corneum structure and the role of skin cleanser and moisturizer ingredients.
- Discuss the factors that adversely affect skin barrier structure and function, including medical conditions (for example, atopic dermatitis and allergic contact dermatitis) and environmental challenges (such as exposure to allergens and the use of harsh detergents for skin cleansing).
- Determine from skin cleanser product labels which ones contain ingredients that help maintain the normal integrity and function of the skin barrier and help heal injured skin by promoting and supporting barrier function.
- Incorporate into clinical practice evidence-based recommendations for skin-cleansing regimens and cleansing agents suitable to specific dermatologic conditions in pediatric and adult patients.
- Evaluate the results of studies now in progress examining the safety, efficacy, and mechanisms of action of botanical ingredients in skin care products.
- Demonstrate improved ability to instruct patients and parents or caregivers on cleansing techniques and agents that will help maintain or restore the skin barrier and avoid complications such as skin infections, irritation, and inflammation.

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Target Audience

This educational activity is intended for dermatologists, pediatricians, family physicians, nurses, nurse practitioners, physician assistants, and other health care practitioners who treat diseases of the skin in children and adults.

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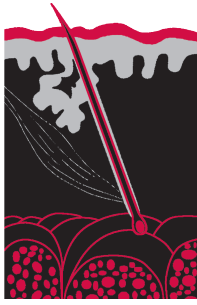
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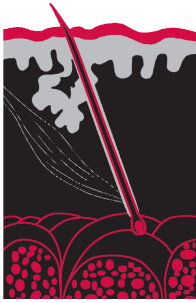


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Seminars in Cutaneous Medicine and Surgery presents well-rounded and authoritative discussions of important clinical areas, especially those undergoing rapid change in the specialty. Each issue, under the direction of the Editors and Guest Editors selected because of their expertise in the subject area, includes the most current information on the diagnosis and management of specific disorders of the skin, as well as the application of the latest scientific findings to patient care.



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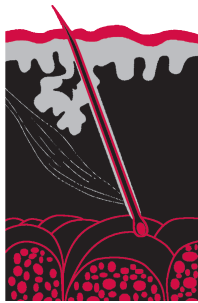


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Seminars in Cutaneous Medicine and Surgery

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VOLUME 32
NUMBER 2S

Seminars in Cutaneous Medicine and Surgery

STRATUM CORNEUM SKIN BARRIER MAINTENANCE AND RESTORATION: EVIDENCE-BASED APPROACH TO CLEANSING AND OTHER SKIN CARE PRACTICES

S15 Routine Skin Care As Prophylaxis and Treatment

Joseph F. Fowler, Jr, Chair

S16 Understanding Skin Barrier Differences: A Demographic, Cultural, and Medical Diversity Viewpoint

*Lawrence F. Eichenfield, Peter M. Elias, Joseph F. Fowler, Jr,
Paul Horowitz, and Renee P. McLeod*

S21 Update on the Structure and Function of the Skin Barrier: Atopic Dermatitis as an Exemplar of Clinical Implications

*Peter M. Elias, Lawrence F. Eichenfield, Joseph F. Fowler, Jr,
Paul Horowitz, and Renee P. McLeod*

S25 The Chemistry of Skin Cleansers: An Overview for Clinicians

*Joseph F. Fowler, Jr, Lawrence F. Eichenfield, Peter M. Elias,
Paul Horowitz, and Renee P. McLeod*

S28 A Lifetime of Well Skin Care: Practical Recommendations for Clinicians and Patients

*Renee P. McLeod, Peter M. Elias, Lawrence F. Eichenfield,
Joseph F. Fowler, Jr, and Paul Horowitz*

S30 Stratum Corneum Skin Barrier Maintenance and Restoration: Evidence-Based Approach to Cleansing and Other Skin Care Practices

*Paul Horowitz, Renee P. McLeod, Lawrence F. Eichenfield,
Joseph F. Fowler, Jr, and Peter M. Elias*



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Routine Skin Care As Prophylaxis and Treatment

Beginning in the mid-1960s, researchers in dermatology began publishing the results of studies on transepidermal water loss (TEWL). Subsequent research gradually revealed the dynamic relationship between the healthy function of skin, proper skin hydration, and TEWL. Over the subsequent decades, the role of the stratum corneum in maintaining optimal skin hydration and preventing excess TEWL has been further studied, understood, and appreciated. The most recent research has revealed the wide range of physiologic functions of the stratum corneum beyond TEWL, and the term “stratum corneum barrier” is becoming increasingly familiar to clinicians outside of the specialty of dermatology.

Both in vitro and in vivo studies also have demonstrated much about the medical and environmental factors that perturb the stratum corneum, disrupting the many and interdependent functions of the skin barrier, including permeability and defense functions.

Dermatologists and other clinicians have made enormous strides in parent and patient education when it comes to routine cleansing and other skin care measures that help the skin heal and, therefore, restore the barrier function to normal (or as normal as possible in the case of chronic conditions). This is seen particularly in the specific and detailed instructions given to parents of children with atopic dermatitis (AD).

However, in the absence of skin pathology, we have considerable work left to do when it comes to educating ourselves and our patients (or their caregivers). Because of its ordinariness, the routine activities involved in well skin care—cleansing, moisturizing, and sun protection—are almost always underappreciated by both clinicians and patients, unless and until a dermatologic condition emerges. For example, in the care of normal skin, “use mild cleansers” is advice used often and broadly by clinicians, and without advice regarding a specific mild cleanser that is appropriate in a particular patient.

In this supplement, the authors review the physiology of the stratum corneum across the age spectrum and a range of demographic and other variables, consider AD as an exemplar of stratum corneum barrier perturbation, provide an overview of the chemistry of skin cleansers, and offer recommendations for incorporating well skin care into every clinical encounter. Included is an educational handout for parents that may be freely copied and distributed by clinicians; this is designed to allow clinicians to write in their own recommendations for specific products that are appropriate for each patient.

The authors, who are guest editors of this supplement, provide further insight and discussion on these topics in a companion educational webcast titled, “An Evidence-Based Approach to Skin Cleansing: Restoring and Maintaining the Skin Barrier in Diverse Patient Populations.” The webcast is available to healthcare professionals and may be found at www.globalacademycme.com/sdef.

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Understanding Skin Barrier Differences: A Demographic, Cultural, and Medical Diversity Viewpoint

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ABSTRACT Important differences exist in the physiology of the stratum corneum barrier according to demographic, cultural, and medical factors. Understanding these differences is crucial to choosing strategies for optimum clinical management.

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KEYWORDS atopic dermatitis; filaggrin; rosacea; stratum corneum barrier; transepidermal water loss

A review of skin development, beginning in utero, is helpful to understanding current knowledge about the stratum corneum barrier. In this article, we will review important information about the skin barrier according to age, and we also consider other important contributors, such as culture and demographic factors, to the structure and function—or dysfunction—of the stratum corneum barrier.

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Skin Development in Utero

Skin development begins at 36 days of gestational age, with the formation of an epidermis consisting only of a basal layer of cells and a superficial periderm. Less than 8 months later—assuming normal development—the newborn emerges with soft, moist, resilient skin that provides an excellent barrier that adapts rapidly to the change from immersion in liquid to air and light exposure.

In the time period between those two events, the skin develops in three areas¹: (1) *organogenesis*, with ectodermal tissue forming lateral to the neural plate epidermis, and mesenchymal and neural crest cells forming the dermis; (2) *histogenesis*, with the formation of vascular structures and stratification of the epidermis into layers; and (3) maturation, with the development of structural integrity of the integument. At full gestational maturation, the epidermis has structural integrity and functions as the stratum corneum skin barrier.

The stratum corneum begins to form around hair follicles at about 14 weeks of gestational age, subsequently expanding—between gestational weeks 22 and 24—to include the epidermis between the hair follicles. The stratum corneum is fully developed in utero by 32 to 34 weeks' estimated gestational age.²

Stratum Corneum Barrier in Premature Neonates

The skin of the full-term neonate is somewhat thinner than that of adults, but premature infant skin is even thinner. Barrier maturation to a fully functional state is associated more with maturation of the epidermis than with the weight of the baby. For example, children who are small for their gestational age—including those with intrauterine growth retardation—usually have epidermal maturation and barrier competence that are expected for their gestational age.

It has been known for some time that when the stratum corneum is immature, a number of problems may occur, including fluid and electrolyte loss, temperature dysregulation, increased vulnerability to injury and infection, and increased uptake of potentially toxic agents that come in direct contact with the skin.³ These issues are seen especially in very low birth weight (VLBW) infants (<30 weeks' gestational age). In addition to a poorly developed stratum corneum, epidermal-dermal adhesion is diminished (a result of fewer fibrils, spaced farther apart), and dermal collagen levels are lower in these infants. As a result, VLBW infants have increased transepidermal water loss (TEWL) and normal barrier function is delayed.

As Kalia and coworkers⁴ demonstrated on measures of TEWL and low-frequency impedance spectroscopy, infants born at 30 to 32 weeks' gestational age develop barrier function within 2 to 4 weeks that is comparable to that seen in adults, whereas in those born at 23 to 25 weeks' gestational age, functional maturation may require significantly more time than that—up to 9 weeks.

In an infant born at about 24 weeks of gestational age, clinical signs of immaturity of the skin are obvious. The skin is translucent and friable, and no lanugo is evident. The absence of a fully functional stratum corneum—and, thus, a fully functional skin barrier—has clinical consequences that must be appreciated and addressed. These include superficial breakdown of the skin (sometimes from adhesives applied to hold tubing in place) and an increased risk for opportunistic infections.⁵

Stratum Corneum Barrier in Full-Term Infants and Babies

In the transition from intrauterine to extrauterine life, the stratum corneum undergoes extensive adaptation. Research with animal models has demonstrated that several stimuli cause the epidermis to change at birth, adapting from a liquid to a dry environment. The most important of these is exposure to air.

At birth, the pH of the skin is neutral or slightly alkaline. In the process of normal skin maturation after birth, the skin acidifies, forming what is called the “acid mantle.”⁶ The acid mantle improves epidermal permeability function and maintains bacterial and chemical resistance.

The process of infant skin adaptation has been well studied recently, using a variety of measures, including those to assess hydration (TEWL) and pH, and capacitance measurements and Raman confocal microscopy to assess skin thickness. Fluhr and colleagues⁷ used these noninvasive techniques to evaluate the stratum corneum of 108 subjects in six age groups: 1 to 15 days, 5 to 6 weeks, 6 months, 4 to 5 years, and 20 to 35 years of age. These investigators found that, in normal neonates, basal epidermal function is competent very early, within the first 2 weeks after birth. They also found that, over the first few weeks of life, the stratum corneum becomes less hydrated and that the acid mantle fully develops.

Stratum Corneum Barrier in Children and Adolescents

Few studies have focused on stratum corneum barrier function in children and adolescents, and this is an area of evolving interest. It is known that many factors can influence skin barrier function in the pediatric population, including genetic factors, ambient environment, hormonal changes of adolescence, and an individual's skin biome.

In addition, sebaceous gland activity changes over time. Sebum production probably is low in infants and young children, and it is known that as children mature from preadolescence to adolescence, sebum production increases, providing an environment in which *Propionibacterium acnes* flourishes. Following adolescence, sebum production decreases significantly with age; in a recent article, Leubberding and colleagues⁸ found that the lowest skin surface lipid levels occurred in study subjects older than 70 years of age.

TEWL and Skin Thickness Over Time

Many factors can affect the skin's biomechanical stress responses, influencing skin dryness and hydration. TEWL has been well studied for many years. Briefly, the term describes the measure of flux density of water from deeper layers of hydrated dermis and epidermis and is generally measured as a rate of water loss in grams per meter squared per hour (g/m²/h). TEWL values are affected by the state and the function of the stratum corneum, including how hydrated the stratum corneum may be at the start of the measurement.

Investigators have shown that TEWL tends to differ at various anatomic sites; for example, the highest rate of TEWL is found in the axillae, and the lowest rate is found in the breasts. However, TEWL is a dynamic rather than a static condition. In a study of TEWL in healthy young and elderly individuals, Kottner et al⁹ demonstrated that TEWL decreases after age 65 to a rate that is lower than that observed in individuals 18 to 64 years of age. The reason for this is not clear, but one theory is that the increase in corneocyte surface area seen in elderly skin may cause increased stratum corneum water transit times.

Opinions have differed on stratum corneum thickness at various ages. A number of years ago, Waller and Maibach¹⁰ concluded that there is little or no difference in stratum corneum thickness between young and elderly adults. However, others have demonstrated that stratum corneum thickness decreases with intrinsic aging, but increases with significant photoaging. Although no general conclusion can be drawn at this time about the effects of aging itself on skin thickness, further investigation likely will show that the thickness of the mature stratum corneum is affected by a variety of factors, including ultraviolet radiation and other environmental exposures, as well as genetic influences.

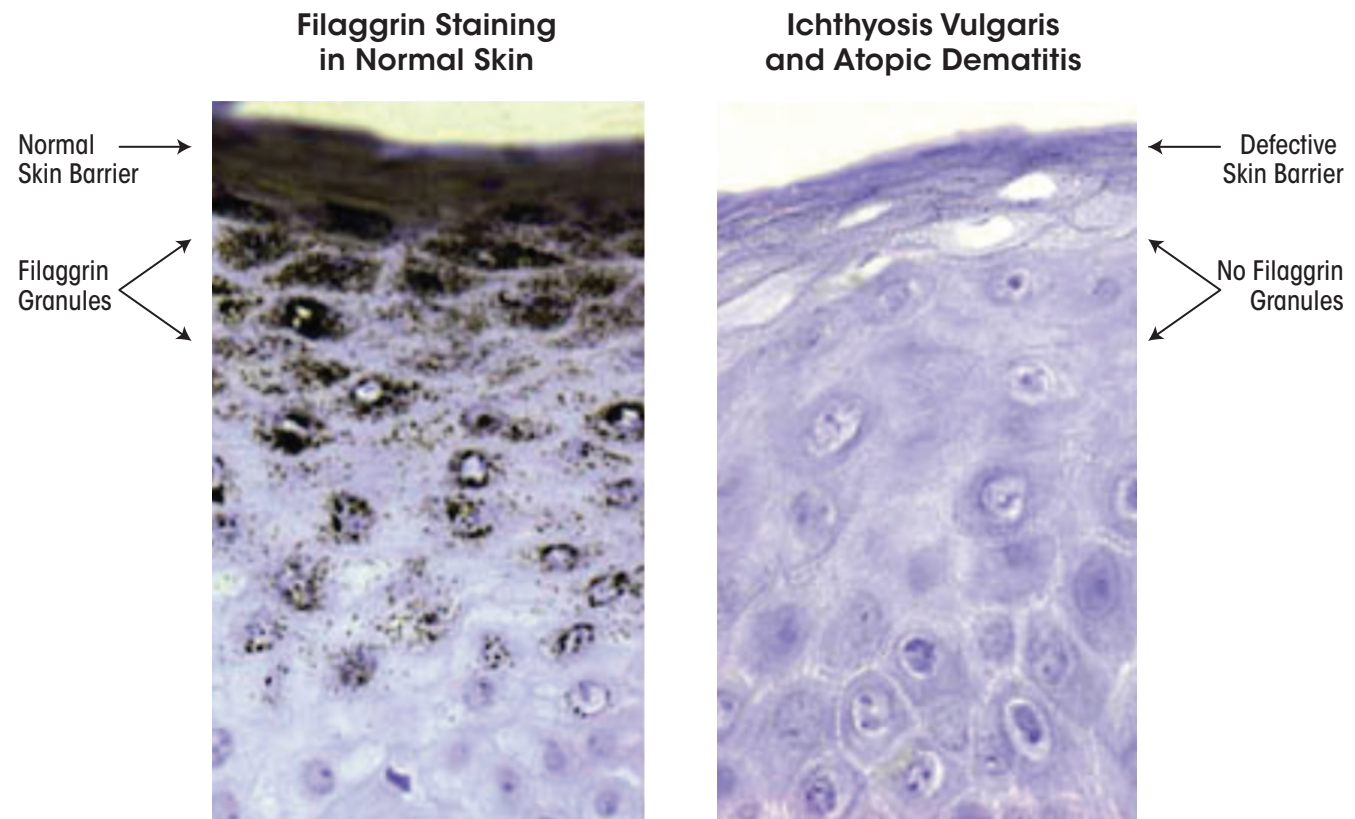


Figure 1. Absence of staining of filaggrin. Note the normal filaggrin staining (left) in a patient without ichthyosis vulgaris versus the reduction in filaggrin staining (right) in a patient with this disease. Used with permission from Sybert et al.¹³

Demographic Differences and the Skin Barrier

In addition to age, other demographic variables may affect stratum corneum function.

Ethnicity and Genetics

The impact of ethnicity on the stratum corneum is a difficult issue to analyze. One study that attempted to provide insight in this area studied three groups of students at several universities in Copenhagen: 25 Asians, 18 Africans, and 28 Caucasian Danes.¹¹ These investigators reported different ceramide-to-cholesterol ratios, with the Asians having the highest and the Africans the lowest. They found no significant differences in ceramide subgroups. However, this study does not take into account the enormous degree of genetic variation that exists within ethnic groups.

Nevertheless, ethnic differences that clearly do matter in terms of stratum corneum function are cultural differences in the way groups of people take care of their skin. For example, different cultural groups may vary in the frequency and method that they use to cleanse and moisturize their skin and the skin of their babies.

Soaking and bathing can influence skin hydration and natural moisturizing factor content. Robinson and colleagues¹² conducted a study in which subjects' arms were soaked and adhesive tape was applied 30 minutes and 4 hours after soaking. Natural moisturizing factor levels

decreased 30 minutes after soaking, accompanied by an increase in skin pH—that is, a compromise of the acid mantle. After 4 hours, the stratum corneum's homeostatic mechanisms had raised natural moisturizing factor and reduced pH to normal levels.

Skin of Color

The Fitzpatrick phototype score, which is based on the propensity of an individual to burn and tan, initially had only four classifications; types V and VI were subsequently added for Asian Indian and African aboriginal peoples, respectively. Data have demonstrated that the Fitzpatrick skin typing does not necessarily correlate with intrinsic skin color or with minimal erythema dose and that many polymorphisms probably influence pigmentary variation as well as the stratum corneum in these individuals.

Genetic Influences on Skin Barrier Function and Dysfunction

Genetic tendencies toward barrier dysfunction or certain diseases that affect the skin barrier have been the focus of a great deal of investigation over the past decade. Filaggrin mutations are the best example we have to date of genetic variation within groups, and differences in filaggrin expression illustrate how genetics may underlie both very significant as well as very subtle changes in base skin function.



Figure 2. Filaggrin mutations. Hyperlinearity of the hands (A) and xerosis on the extensor surfaces of the legs (B) are clinical clues to the presence of filaggrin mutations. Photos courtesy of Lawrence F. Eichenfield, MD.

The earliest insight that filaggrin was clinically important was in 1985, when Sybert and colleagues¹³ proposed that it might be associated with the dry scaly skin condition ichthyosis vulgaris. It was only relatively recently, however, that genetic techniques had developed to the point at which it could be demonstrated that loss-of-function mutations in the filaggrin gene cause ichthyosis vulgaris (**Figure 1**).¹³ Clinical clues to filaggrin mutations include a hyperlinearity of the hands and dry skin on the extensor surfaces of the legs (**Figure 2**).

In the intervening years since the early studies of ichthyosis vulgaris by Sybert et al, it also has become evident that filaggrin gene mutations are associated with an increased risk for the development of atopic dermatitis (AD) as well as asthma secondary to AD, immunoglobulin E (IgE) sensitization, allergic rhinitis, and persistent AD. The functional impact of filaggrin mutations include decreased natural moisturizing factor and increased permeability and pH, the latter adversely affecting cell cohesion, permeability, and inflammation.

In a recent editorial, McLean and Irvine¹⁴ discussed filaggrin mutations as being observable in an ethnosppecific mutation profile—that is, types and prevalences of mutations may differ in various parts of the world. Even in patients with AD who do not have filaggrin mutations, the number of filaggrin copies that are expressed in the genome may influence both their base stratum corneum function and the risk of their development of AD.

Recent work has shown that there is much variation in the prevalence of filaggrin mutations among different populations. For example, Margolis et al¹⁵ published the results of a long-term study of more than 6,000 children with mild to moderate AD who were followed for an average of 4 years. These investigators showed that, in DNA from 850 of these children, filaggrin mutations were present in 6% of African Americans with AD but were seen in 28% of white children. Moreover, they reported that, at any given time, 50% of children with mutations were less likely to have remission of AD than were children without filaggrin mutations.

Genetic influences on skin barrier function also are now appreciated in other diseases, including acne vulgaris, rosacea, psoriasis, and allergic contact dermatitis.

Lipids are known to be bioactive mediators of skin inflammation and immunity. Numerous studies have demonstrated that the cutaneous immune system is influenced and regulated by cytokines and bioactive lipids, and inflammation both affects and is affected by perturbation of the skin barrier. In rosacea, as an example, Meyer-Hoffert and Schröder¹⁶ demonstrated that serine proteases affect epidermal barrier homeostasis. In addition, they showed that, in rosacea, cathelicidin LL-37 levels are increased and that proteolytic fragments—associated with kallikrein-related peptidase—influence the skin barrier, vasoactivity, and inflammation. These findings raise the question of whether some intrinsic tendency toward barrier dysfunction exists in individuals with rosacea. Also, it suggests that rosacea itself may have an impact on skin barrier function.

An interesting clinical correlate is papulopustular rosacea and the skin dryness that often accompanies this condition. Recent research has shown that the fatty acid composition of the sebum may be different in patients with papulopustular rosacea.¹⁷ These individuals may have an abnormal sebaceous fatty acid composition, and this sebum can influence skin barrier integrity. Such studies provide insight into rosacea as a disease but also give an example of the complex interplay that exists among the various components of the skin and the function of the stratum corneum barrier.

Skin Injuries and Barrier Function

Intrinsic barrier function can be perturbed by a variety of extrinsic events, including exposure to ultraviolet radiation, chemical injuries, and traumatic wounds. In a normally functioning stratum corneum, barrier function recovers after insults of many types. Homeostatic and healing mechanisms are triggered as the system responds to injuries and a restoration of normal barrier function.

Conclusion

The stratum corneum skin barrier is a highly complex homeostatic mechanism, subject to perturbation by many variables, including age, cultural differences in skin care, and environmental influences. In addition, genetic factors are a major source of variation in skin dynamics as well as being associated with vulnerability to certain disease states. Clinicians must remain up-to-date with the results of ongoing research that continues to provide essential information about the dynamic process of barrier function.

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Update on the Structure and Function of the Skin Barrier: Atopic Dermatitis as an Exemplar of Clinical Implications

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ABSTRACT The healthy stratum corneum allows optimum permeability of water and provides the first line of defense against pathogenic and environmental assaults. The barrier functions of the stratum corneum are interrelated, coregulated, and interdependent. Research has demonstrated that three lipid species, which usually comprise 10% of the stratum corneum, are crucial to both its structure and its function; these must be present in sufficient quantities and in the correct proportions to provide optimum barrier function. The clinical implications of how the skin barrier works—and is supported and restored—can be seen in the current and emerging understanding of atopic dermatitis management. *Semin Cutan Med Surg* 32(suppl2):S21-S24 © 2013 Frontline Medical Communications

KEYWORDS atopic dermatitis; lipid abnormalities; skin barrier; stratum corneum barrier

The effectiveness of the skin as a protective organ is made possible by a set of critical defensive and protective functions known collectively as “barrier function” (Table). Of these, the *permeability barrier* is the most critical because

it allows humans to live in our dry terrestrial environment. The other functions all are defensive in nature. The most recent research has demonstrated that these defensive functions are not completely discrete; they are interrelated, coregulated, and interdependent to such a degree that if one function is perturbed, the others also are affected. These functions are possible because of the structure and properties of the stratum corneum.

Stratum Corneum Structure

It was first proposed 3 decades ago and now is widely appreciated that the structure of the stratum corneum is analogous to that of a brick wall, with corneocyte “bricks” held in place by the extracellular matrix “mortar.”¹⁻³ The stratum corneum barrier relies predominantly on the extracellular matrix, where lamellar bilayers block the outflow of water into the environment and prevent the ingress of toxic substances, allergens, and microbial pathogens into the body.^{2,3}

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Table. Protective Functions of the Stratum Corneum Barrier

- Permeability barrier (life in a dry milieu)
- Exclusion of noxious chemicals and allergens
- Protection from mechanical insults
- Antimicrobial defense
- Integrity and cohesion (desquamation)
- Antioxidant defense
- Cytokine activation (outpost of immune system)
- Ultraviolet light barrier
- Hydration (pliability)

The lamellar bilayers that fill the intercellular spaces are formed of extracellular lipids, of which three species are key: cholesterol; a family of long-chained, free fatty acids; and ceramides. Normally, they comprise about 10% of the mass of the stratum corneum. Each of these three lipid species is equally important and must be present in sufficient quantities. In addition, they must be present in the correct proportions for the lamellar bilayers to form.^{2,3}

The key lipids are derived from a unique secretory vesicle, the epidermal lamellar body, which is produced by the epidermis. The lamellar bodies produce the precursor elements—including phospholipids, glucosylceramides, cholesterol, and proteins that are essential to the cohesion, desquamation, and conversion of the lipid precursors into the more waterproof lipid products. Epidermal lamellar bodies also deliver at least two critical proteins that are important for antimicrobial defense: human β -defensin 2 and the cathelicidin protein LL-37.^{2,3}

Structurally, ceramides can be considered as two fatty-acid chain links joined together by an amide group. The ceramides in the stratum corneum barrier are highly saturated, with few unsaturated groups; thus, these ceramides are highly hydrophobic and are essential for the waterproofing of the skin—that is, forming a permeability barrier.²⁻⁴

A normal permeability barrier is also an effective antimicrobial barrier. It resists not only the egress of water but also the penetration into the body of pathogenic microbes, allergens, and other noxious substances.^{2,4}

Clinical Implications of Skin Barrier Function: The Atopic Dermatitis (AD) Exemplar

The decades of basic science research have led to the present and growing recognition that barrier function is clinically relevant. It is becoming increasingly clear that many of the important inflammatory dermatoses seen in clinical practice are associated with primary inherited abnormalities in barrier function. Moreover, this understanding has led to the realization that the treatment of these disorders cannot be limited solely to anti-inflammatory therapy. AD provides a clear illustration of how our knowledge and strategies have progressed.

Molecular Background of AD

Filaggrin is the key protein that causes aggregation of keratin filaments in the corneocyte cytosol. As the corneocytes move up through the stratum corneum, filaggrin begins to be degraded into its constituent amino acid components. Next, these amino acids are further de-emanated into a family of organic acids that comprise natural moisturizing factor, a compound that is crucial for corneocyte hydration.

Many patients with AD have an inherited defect in filaggrin, but it is intriguing that AD associated with filaggrin deficiency is found predominantly in individuals of northern European ancestry. Thyssen and Elias⁵ recently proposed a

new theory to explain why filaggrin mutations have persisted and are becoming more common in this population; namely, that it might be related to a need for additional vitamin D production in the skin. It has been commonly believed that less skin pigment found in northern populations allows greater ultraviolet B (UVB) penetration and, thus, generation of additional vitamin D; new evidence suggests instead that it is filaggrin deficiency that allows greater UVB penetration and increased production of vitamin D in the epidermis.⁵

The fact that AD is attributable to inherited abnormalities in barrier function has important and broad implications for the therapy and prevention of AD.

The absence of sufficient quantities of filaggrin results in a defect in corneocyte hydration and a severe dry skin abnormality. In turn, the dry skin itself creates and contributes to the barrier abnormality by increasing the water gradient across the skin (**Figure 1**).

In addition, lack of sufficient organic acids results in an adverse change in the pH of the stratum corneum. The surface pH of the skin is normally highly acidic, a condition necessary for many critical functions. In the absence of sufficient filaggrin breakdown products, the pH rises, which has several dramatic and important consequences for stratum corneum function, including perturbation of the permeability barrier, hydration, antimicrobial defense, and skin cohesion (**Figure 2**). In addition, trans-urocanic acid, a critical filter for UVB radiation, is not formed, a finding that explains the recently reported increased incidence of nonmelanoma skin cancers in patients with a history of AD.⁶

Finally, these abnormalities in the availability of filaggrin breakdown products are accompanied by an activation and initiation of a cytokine cascade.

The epidermal cytokines have two functions. Of benefit to barrier function is that their synthesis and release upregulate necessary processes, such as lipid and DNA synthesis, which help restore the barrier function after it has been perturbed. However, if the barrier abnormality persists, the result is what is called an “outside-inside” cytokine cascade—recruitment of an inflammatory infiltrate into the skin and the initiation of inflammation.⁷

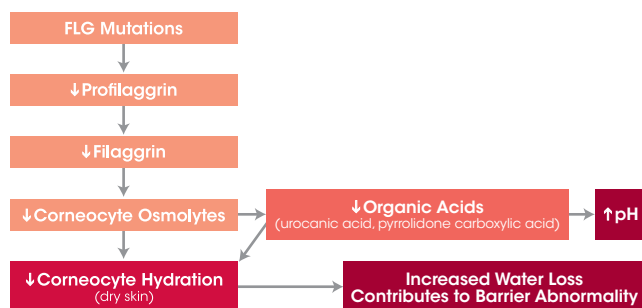


Figure 1. Filaggrin deficiency leading to barrier dysfunction in atopic dermatitis. Filaggrin gene (FLG) mutations in patients with atopic dermatitis result in inadequate production of profilaggrin and filaggrin and in reduced corneocyte osmolytes. The consequent defect in corneocyte hydration causes severe dry skin, which, in turn, creates and contributes to abnormal barrier function by increasing the water gradient across the skin. Figure courtesy of Peter M. Elias, MD.

pH and the Pathogenesis of AD

Study of Netherton syndrome has provided important insights into the pathogenesis of AD. Netherton syndrome is a rare condition associated with a severe type of AD. In Netherton syndrome, mutations occur in SPINK5, a serine protease inhibitor that encodes a critical serine protease inhibitor, lymphoepithelial-Kazal-type 5 inhibitor (LEKTI). In the absence of LEKTI, serine proteases increase markedly and attack structures in the stratum corneum and the underlying epidermis. The result is abnormal barrier function, increased incidence of infection, a thin and poorly cohesive stratum corneum, and a direct initiation of helper T-cell subtype 2 (T_H2) inflammation.⁸

As noted above, an increase in pH also increases serine protease activity. Therefore, in individuals with filaggrin deficiency, the abnormalities associated with Netherton syndrome (including the increases in pH and serine protease activity) are replicated. Conversely, if the pH of the skin can be lowered into an acidic range, many of the features of AD—and, perhaps, the disease itself—can be prevented.⁸

Lipid Abnormalities in AD

Most clinicians who manage patients with AD are aware of the lipid abnormalities inherent in this disease. However, the mechanisms of serine protease and pH increase underlying these abnormalities have been described only recently and may not be as widely understood.

It is now known that the increase in serine proteases blocks lamellar body secretion, so the lipids become trapped in the corneocytes. Because these lipids are not secreted, a global deficiency occurs in all three key lipids (ie, cholesterol, free fatty acids, and ceramides).⁹

A further decrease occurs specifically in ceramide content because the serine proteases attack the enzymes that generate ceramides. In addition, the T_H2 cytokines in AD downregulate ceramide synthesis on a transcriptional level. Finally, the increased pH deactivates the serine proteases, which are mainly active when pH is neutral.⁹

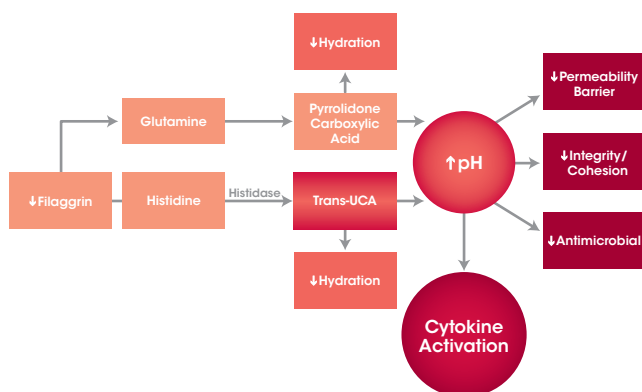


Figure 2. Filaggrin deficiency predisposes to both atopic dermatitis and skin cancer. When filaggrin deficiency is present, trans-urocanic acid (UCA) does not form. Trans-UCA is a critical filter for ultraviolet B (UVB) radiation—more important, in fact, than melanin pigment for protection against UVB radiation. This finding explains the increased incidence of nonmelanoma skin cancers in patients with a history of atopic dermatitis. Figure courtesy of Peter M. Elias, MD.

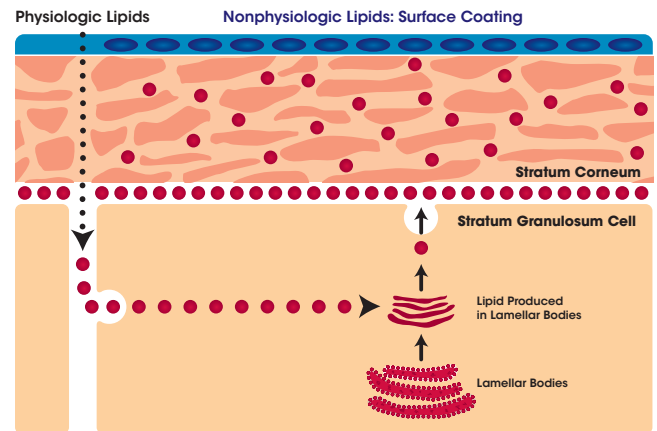


Figure 3. Barrier repair lipids. Nonphysiologic lipids—such as petrolatum—remain on the surface stratum corneum layers. In contrast, physiologic lipids traverse the stratum corneum and enter the nucleated cell layers. Adapted from Man M-Q et al.¹⁰

Barrier-Repair Strategies in AD

The understanding of these underlying mechanisms of lipid abnormalities provides a rationale for therapy with corrective mixtures of physiologic lipids. Corrective barrier-repair therapy can use either nonphysiologic lipids (such as petrolatum and lanolin) or physiologic lipid-based formulations.

Applications of nonphysiologic lipids (“greasing the skin”) has been the mainstay of basic skin care in patients with AD. The mechanism of action is the formation of a coating on the outer layer of the stratum corneum.^{10,11} In contrast, physiologic lipids rapidly traverse the stratum corneum and enter the nucleated layers of the epidermis, where they combine with lipids that are being synthesized in the underlying epidermal cells and are then secreted into the intercellular spaces of the stratum corneum (Figure 3).¹⁰

To be optimal, physiologic lipid formulations must include all three key lipids, which must be delivered in a 3:1:1 molar ratio. The dominant species in any given formulation depends on the disease being treated. In AD, a global deficiency exists in all three key lipids, with a further decline in ceramides; thus, a ceramide-dominant version of the optimal molar ratio should be used to treat this disorder. Such a formulation has been shown to be highly effective—as effective as a midpotency corticosteroid agent—in treating moderate and severe AD.^{12,13}

Physiologic lipid formulations are effective for barrier repair because, in addition to emollient and hydrating effects, these formulations are anti-inflammatory. A number of anti-inflammatory mechanisms have been identified. By normalizing the barrier, the cytokine cascade is decreased and the entry of allergens and haptens into the skin is reduced. In addition, improvement in the permeability barrier results in improved antimicrobial defense function. Also, many of the free fatty acids that are used in these formulations are potent activators of nuclear hormone receptors such as peroxisome proliferator-activated receptor (PPAR)- α and PPAR- β/δ . In animal models of AD, these hormone receptors have been shown to exert anti-inflammatory effects as potent as that seen with clobetasol. Finally, physiologic lipid formulations with a low pH cause a decrease in serine protease activity.¹²

It is important to note that numerous products are being marketed that use the terms *barrier repair* and *ceramides* to support claims of restoration of normal barrier function, but often with few scientific data behind such claims. Many of these products contain incomplete lipid mixtures, often with no ceramides included, and frequently they do not contain sufficient quantities of physiologic lipids; commonly, the lipids in these formulations are not present in the correct molar ratio.¹²

Conclusion

For many years, clinicians routinely have used a number of effective strategies that help repair the stratum corneum barrier. These measures were based largely on empiric and anecdotal evidence that they worked, although the underlying mechanisms for why and how they worked were not always fully understood. For example, in AD, clinicians educated parents and patients about strategies to break the itch-scratch cycle, including avoiding harsh soaps and exposure to potential allergens, the importance of hydration in the form of baths followed by applications of emollient moisturizers, decreasing psychological stress in the family, using antihistamines and topical and systemic corticosteroids when needed, and attention to reducing exposure to microbes, especially staphylococci.

Newer approaches do not replace but enhance these traditional strategies for maintaining and restoring the optimal function of the stratum corneum barrier. These include keeping the skin pH sufficiently acidic, using topical antihistamines (particularly H₂-blockers such as cimetidine), and applying appropriately formulated physiologic lipid amines. In addition, the results of recent research advances in understanding stratum corneum function in diseases

such as AD may, in the near future, lead to the availability of agents that target specific molecular pathways. These include PPAR and liver X receptor activators (which are highly anti-inflammatory and improve barrier function), serine protease inhibitors (which may prevent stratum corneum damage and, ultimately, clinical expression of AD), and protease-activated receptor-2 inhibitors (to inhibit itching and inflammation).

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The Chemistry of Skin Cleansers: An Overview for Clinicians

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ABSTRACT Cleansers and other skin care products can be agents either of stratum corneum damage and skin barrier dysfunction or of maintaining or restoring healthy stratum corneum barrier structure and function. To guide patients toward beneficial choices most suitable for their individual skin conditions and needs, clinicians must be aware of and understand the ingredients in such skin care products and their potential effects on the stratum corneum barrier. In cleansers specifically, clinicians should be aware particularly of the benefits and potential problems associated with chemical components of surfactants, preservatives, and fragrances. *Semin Cutan Med Surg* 32(suppl2):S25-S27 © 2013 Frontline Medical Communications

KEYWORDS cleanser allergies; fragrances; micelles; moisturizers; preservatives; skin cleansers; surfactants

The techniques and agents used to cleanse the skin are important factors in the maintenance and restoration of the skin barrier or, conversely, in causing and continuing damage to the stratum corneum and its important barrier functions. In addition to barrier maintenance issues, recommendations

for skin-cleansing practices should take into consideration individual patient characteristics, including age, gender, and any underlying skin conditions, as well as cultural and personal preferences regarding aesthetics (including the fragrance of products). As examples, individuals with dry skin should use a cleanser that minimizes further drying, and those with eczema or other skin conditions should use nondrying cleansers that may also replenish lipids. In this article, we provide an overview of the goal of skin cleansing, how skin cleansers work, and the ingredients commonly used in cleansers that are important to remember in clinical practice.

Overview of Skin Cleanser Ingredients

Skin cleanser chemistry is not an esoteric topic and does not require in-depth study for clinicians to acquire the necessary foundation for making informed and appropriate recommendations to patients that are tailored to their individual needs. In addition to water (included in almost all skin cleansers), the ingredients also include surfactants, along with any of a number of other possible ingredients such as antimicrobial agents to reduce bacterial colonization, viscosity enhancers that affect the feel of a product (found mainly in shampoos), moisturizers, preservatives, and fragrances (Table 1).

Table 1. Skin Cleanser Components

- Water
- Surfactants—the cleansing agents
- Antimicrobials—reduce colonization
- Viscosity agents—enhance product “feel”
- Moisturizers—reduce drying
- Preservatives—affect shelf life
- Fragrances—enhance aesthetic appeal

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Surfactants

Briefly stated, a surfactant—a term derived from the words “surface” and “active”—is a cleansing agent. The earliest known surfactants were soaps consisting of sodium or potassium salts of fats or fatty acids. Until about the middle of the 20th century, soaps used for bathing were largely crude formulations of a lipid such as tallow (ie, rendered animal fat) plus lye (a strongly alkaline solution usually derived from wood ash). Improvements in these lye-containing formulations were made by substituting various sulfates (such as sodium lauryl sulfate) and carboxylates. The benefit of these earlier generations of soaps was that they were essentially nonallergenic. However, the simple, small long-chain molecules that comprised these soaps tended to cause stinging, burning, and irritation, particularly when used on sensitive skin or when accidentally splashed into the eyes. Also, these types of simple soaps (which are still widely available today) may increase xerosis and worsen the skin condition in patients with eczema.

In today's skin cleansers, a variety of newer surfactants are used (Table 2). These include amphoteric compounds (chiefly, cocamidopropyl betaine, plus others in the betaine family, and related compounds), nonionic compounds (such as cocamide diethanolamine, also called cocamide DEA), and hydrophobically modified (HM) polymers.

Table 2. Newer Surfactants

- Amphoteric surfactants (eg, cocamidopropyl betaine)
- Nonionic surfactants (eg, cocamide diethanolamine)
- Hydrophobically modified polymers

Understanding Micelles

Surfactants are molecules with both a hydrophilic and a hydrophobic region: The hydrophobic component scavenges oils, soil, and other contaminants from the skin; the hydrophilic component allows their removal from the skin by rinsing with water.

In an aqueous solution, surfactants naturally self-organize into groups called micelles. Research has shown that micelle size negatively correlates with irritancy—that is, the larger the micelles, the less irritating the surfactant, because the larger molecules are less able to penetrate the stratum corneum. Product research over the past 5 to 6 decades have yielded methods of chemically altering surfactants to create larger micelles, including ethoxylation and, more recently, pegylation using polyethylene glycol. The largest micelles developed to date are in the HM-polymer surfactant, created by linking groups of micelles together using a polymerizing component.

Antimicrobial Agents

Some cleansers—especially some of the newer hand cleansers and products used in medical and dental offices and hospitals, for example—may contain antimicrobial ingredients. These may include various alcohol formulations and agents such as benzalkonium chloride and iodine solutions.

These agents are not usually found in products that are intended for use in infants and children or for anyone with sensitive skin, although occasionally they are seen in such products. These chemicals tend to be irritating and, in some cases, can be allergenic.

Moisturizers

Many cleansers contain moisturizers to reduce the potentially irritating and drying effects of the other ingredients. Some cleansing products claim that the moisturizers they contain remain on the skin following rinsing; this may be true for some moisturizing ingredients in some cleanser formulations, but it is difficult to determine how much of the moisturizer actually persists. Glycerin, lanolin, various lipids, and petrolatum are commonly used.

Preservatives

Preservatives are almost always included in the formulation of any water-based system to prevent bacterial and fungal growth. Ideally, preservatives should be hypoallergenic and active against a broad range of microorganisms. Few preservatives fulfill both of these requirements, so often combinations of preservatives are used.

Fragrances

Fragrances add to the aesthetic appeal of skin care products and are ingredients in most cleansers, moisturizers, and other products. An entire industry is devoted to the chemistry, psychology, development, and manufacture of fragrances.

The physiology and psychology of smell explains why almost all personal care products contain fragrances. Olfactory receptors communicate with the brain's most ancient center, the limbic system.^{1,2} So strong is the olfactory experience that memories of events or objects are associated with an individual's exposure to pleasant or unpleasant odors; subsequent exposure to the smell—pleasant or unpleasant—often evokes a memory of the event or object or with the feeling associated with the event.²⁻⁴ Smells are associated with autobiographical episodes.⁵ In fact, memories triggered by odors tend to be more emotional than are those evoked by visual or auditory cues.⁶ Human language that describes olfactory stimuli reflects the emotional response to those stimuli: “Odor” usually denotes a less-than-pleasant smell; scent, fragrance, and aroma are synonyms for pleasant smells.

Primarily because of these emotional responses, non-scented products are preferred over those with a smell that is perceived as unpleasant, and pleasantly scented products tend to be preferred over unscented ones.⁷ Studies have shown that fragrances in skin care products can have positive emotional associations, resulting in an improved mood and a heightened overall sense of well-being.^{8,9} Sometimes fragrances even suggest better product efficacy^{1,7}—for example, when certain fragrances are perceived as having a “clean scent” or a “fresh scent,” implying more effective cleansing properties.



Figure. Allergic reaction. This patient had a typical presentation of a shampoo allergy. The eyelids show a severe reaction, although the rest of the face is relatively unaffected. Photo courtesy of Joseph F. Fowler, Jr, MD.

Cleanser Allergies

A relatively frequent skin complaint is dermatitis resulting from allergy to a skin cleanser. Many patients who complain of an “allergy” to skin care products actually are experiencing an irritant reaction, but true allergy does occur. Among the cleanser category of skin care products, preservatives and fragrances represent the most common allergens; surfactants and moisturizing additives can be allergenic, but this is not as common as fragrance and preservative allergy.

An allergic reaction to a facial cleanser or shampoo typically is seen on the face—especially the eyelids (**Figure**)—and sometimes the neck. The scalp, which appears to be more resistant to allergen penetration, is rarely affected, even with shampoo allergies. If an individual is allergic to a cleanser, the intertriginous areas also are affected, if exposed (as in the shower or bath).

Preservative Allergenicity and Irritancy

From the standpoint of allergenicity and efficacy, parabens are close to ideal. In contrast, a variety of preservatives are used that are formaldehyde based, although the term *formaldehyde* is not listed on the cleanser label as an ingredient. These preservatives have some direct antimicrobial effect, but they also work by slowly degrading in solution and releasing small amounts of formaldehyde. The formaldehyde-based preservatives are very effective antibacterial and antifungal agents, but they tend to be allergenic.

Fragrance Allergenicity and Irritancy

Chemically, fragrances can consist of simple single molecules, but they usually consist of mixtures of dozens to hundreds of different molecules. Among the more than 1,000 fragrance chemicals in use are, of course, some allergens.

Professional perfumers are skilled at mixing the various chemicals to achieve a desired scent in everything from floor cleaners to floral room deodorizers. When fragrances are developed for products used on the skin, the goal is to achieve the desired scent using fragrance ingredients that are least likely to be allergenic. However, as with all chemicals to which skin may be exposed, individual sensitivities may result in allergic reactions to even those that might be considered “nonallergenic” or “hypoallergenic” fragrances.

Fragrances also can be irritants, and it may be prudent to recommend that individuals with diseases (such as atopic dermatitis) or very sensitive skin avoid products with fragrances, even if there is no allergy.

Surfactant Allergenicity

The newer surfactants (described in a previous section) are milder to the skin and eyes but tend to be more allergenic than some of the earlier compounds. Although surfactant allergies are not common, those that are seen usually occur with exposure to cocamidopropyl betaine and related compounds.

Diagnosing Allergies to Skin Cleansers

Sometimes when patients experience allergic reactions to a skin care product, they self-treat by changing brands. However, many of the same ingredients—particularly surfactants and preservatives—are used in different types from different manufacturers, and unless the new product does not contain the allergenic compound, the reaction will persist. Patch testing often is necessary to identify a specific allergen so that a patient knows which particular ingredients to avoid when choosing cleansers or other skin care products.

Conclusion

The use of cleansers is a necessary and beneficial part of good skin care throughout life. Because both allergic and irritant contact dermatitis may be caused by components of skin cleansers, it is important for clinicians to be aware of and understand the nature and functions of the ingredients listed on skin care product labels. Fragrances, preservatives, and surfactants are the components usually implicated when contact dermatitis does occur.

Surfactants that are associated with the formation of larger, rather than smaller, micelles are less likely to be irritating to individuals with sensitive skin. The newer surfactants, designed for infant skin and individuals with eczema, are in this category. Products containing preservatives that break down into formaldehyde are more likely to be allergenic in sensitive individuals. Parabens are among the compounds that are not formaldehyde based and are relatively hypoallergenic.

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A Lifetime of Well Skin Care: Practical Recommendations for Clinicians and Patients

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ABSTRACT The skin is an indicator of overall health throughout life, and the skin's lifelong care and environment are reflected with aging. The goal of skin care education by clinicians is to teach and reinforce habits that will support and maintain optimum stratum corneum barrier function throughout life and, when dermatologic conditions or injuries arise, that will aid in recovery of barrier function.

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KEYWORDS sensitive skin; skin cleansing; stratum corneum barrier; well skin care

Healthy skin care habits should begin with the birth of a child. Starting with the first newborn visit, parents should be educated about how to care for the skin. This education should continue during each well child visit throughout adolescence and on into adulthood. This allows information to be customized to the age of the child and the skin care needs of all the family members, and can include information that takes into consideration different skin and hair types and cultural practices. Education that includes

product preferences and appropriateness of products is easily included in a brief visit. In addition, every clinical encounter should be viewed as an opportunity to observe and educate patients and caregivers regarding appropriate skin care.

Parents and patients should know the basics of well skin care that apply at all stages of life. In its simplest form, this message comprises three areas: (1) cleanse, to remove pathogens, irritants, and other contaminants, (2) moisturize, to reduce drying effects from cleansers, low ambient humidity, and other factors, and (3) protect the skin from sun damage, using sunscreens and other sun-protection measures, such as protective clothing.

Parents should be advised about specific products for home use, including shampoos, skin cleansers, and moisturizers for routine care. Initial cleansers for newborns should be recommended that are not drying and that will not disrupt the skin pH and the normal development of the acid mantle, perturb the development of the microbiome, or remove the outermost layers of epidermal cells.

The technique of bathing also should be specifically addressed. A frequent problem in pediatricians' offices is overzealous bathing—skin cleansing by rubbing vigorously with washcloths—seen particularly among new parents of a first-born child. Parents should be told to avoid scrubbing and advised that application of a mild cleanser with the hands alone or with a soft washcloth will provide satisfactory cleansing. Although frequent baths are not needed in the newborn, a regular bath is a practice that parents often engage in to assist with bonding and starting a sleep routine. This practice is acceptable as long as moisturizers containing emollients are used after bathing and the newborn does not have a skin condition that makes frequent bathing inadvisable.

Well Skin Care in the Well Child Visit

Incorporating well skin care education into routine clinical encounters can be done without adding a substantial amount of time to the visit by focusing on a small amount of age-appropriate information each time. This is particularly feasible during the first year of well child visits because

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of the frequency of encounters during this time. For example, during the first visit, (1) give a brief explanation of the role of the skin, (2) list the three basic healthy skin care habits (cleansing, moisturizing, sun protection), and (3) discuss what is meant by “sensitive skin.”

During subsequent visits in the first year, and, assuming that the skin is healthy, the following messages may be considered:

- Liquid cleansers contain cleansing agents (surfactants) and preservatives and may also contain moisturizers, fragrance, and other ingredients. Certain ingredients are more appropriate for cleansing the skin in babies and children. Recommendations can then be made for specific products that are most appropriate for the young child.
- Bathing with water alone and a cloth is not sufficient to properly cleanse the skin of bacteria, oils, and other contaminants and can have a drying effect on the skin. Mild liquid cleansers that contain emollients have protective effects.
- During and after bathing, the use of appropriate emollients helps lubricate the skin and supports the skin barrier.
- The application of a petrolatum-based product to the diaper area after bathing will help prevent diaper rash.

Beyond Product Recommendations

A common issue that requires education is that the same skin care products may not be appropriate for all members of the family. For example, many shampoos that are appropriate for adolescents and adults with healthy skin are too harsh for young children or for individuals with sensitive skin or an inflammatory condition, such as atopic dermatitis (AD) or rosacea.

Environmental issues—specifically, the condition of the water in the household and the ambient humidity in the home, in outside play areas, and at school—are factors that influence skin condition that may not be addressed unless a patient develops a problem, such as AD in younger patients or rosacea, acne, or psoriasis in older individuals. For example, hard water may not remove all nonsoluble substances from the skin or from laundered clothing, possibly resulting in skin irritation. Furthermore, hard water itself also can have a drying effect and may irritate sensitive skin or skin damaged from dermatologic conditions or injuries (such as sunburn).

Ambient humidity affects skin dryness but also has an impact on whether and how recommended skin care products or medications are used. Patients should understand, for example, that if the skin feels sticky, the medication or skin care product (especially moisturizers) is not being absorbed. This is common in humid climates, particularly during the summer months, and the selection of a medication or product may need to change with the weather.

Cleansing “Sensitive Skin”

The concept of “sensitive skin” is confusing to both the lay public and many medical professionals. Many individuals believe that they have sensitive skin^{1,2} and would describe the skin of all babies and children as being sensitive. By definition, however, sensitive skin is an abnormal response to drugs, cosmetics, and toiletries in the absence of visible signs of irritation. The abnormal response usually takes the form of the perceptions of itching, burning, stinging, and/or tightness of the skin when certain products are applied. The cause is poorly understood.³

Clinicians should advise parents of the difference between this medical condition and the need for using products that

support the stratum corneum barrier. Claims for some products that are marketed as “gentle” and “for sensitive skin” are not necessarily supported by data. For this reason, the clinician should be aware of the ingredients in cleansing, moisturizing, and other skin care products that are appropriate for use in babies and children. The article by Fowler et al⁴ provides a concise discussion of skin care product ingredients. Note that preservatives are necessary in any cleansing product that is water-based to prevent bacterial overgrowth in the product. Also note that the inclusion of fragrance in a product does not mean that it should not be used in babies or in those with sensitive skin; the type of fragrance matters with respect to irritancy. Furthermore, the inclusion of fragrance in cleansers and moisturizers has many benefits.⁴

In babies, children, and individuals of any age who have sensitive skin or a dermatologic disease, injury, or other issue, the skin should be cleansed with a soap-free product—that is, a synthetic surfactant, or “syndet”—that has been tested on the appropriate skin.⁵ Patients should be advised not to overrinse these products with water, as this will wash away the protective emollient ingredients and subject the skin to the drying effects of water.

Common Barrier-Compromising Conditions in Older Children and Adults

Many patients experience burning, stinging, and irritation with the use of topical medications prescribed for a number of common skin conditions that compromise the stratum corneum barrier. In addition, these medications—particularly retinoids—contribute to dryness, exacerbating barrier dysfunction. In adult patients, these conditions include adult acne, AD, rosacea, and psoriasis.

An appropriate cleanser and moisturizing regimen tailored to individual patient needs can mitigate the discomfort associated with medication (and, thus, enhance compliance), reduce irritation and inflammation, and promote repair of the stratum corneum.

Patients who experience environmental skin damage—sunburn, minor chemical burns, and contact with botanical and other allergens—also require supportive skin care regimens until the skin heals. Use of a mild nonsoap cleanser and appropriate moisturizers during this time will prevent exacerbation of symptoms from additional irritation and dryness, ideally reducing the risk for secondary complications such as infection.

Conclusion

Educating patients and parents about healthy skin care practices should be part of wellness care throughout the life span. Skin care education that supports the barrier function of the stratum corneum should include proper cleansing, application of moisturizers and emollients, and protection from sun damage.

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Stratum Corneum Skin Barrier Maintenance and Restoration: Evidence-Based Approach to Cleansing and Other Skin Care Practices

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ABSTRACT Good skin care has two overall goals: to support and maintain healthy stratum corneum function and to help restore barrier function perturbed by disease processes or injuries. In this article, we discuss the special attention that is required in the initial skin care of newborns, and we address what measures, beyond the basic skin care principles, are required for patients with conditions such as atopic dermatitis, acne, contact and allergic dermatitis, and diaper rash.

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KEYWORDS acne; allergic contact dermatitis; atopic dermatitis; diaper rash; irritant contact dermatitis; neonatal skin care; sunburn

Caregivers should appreciate the role of the skin as a dynamic organ and, in particular, should understand the basic structure and function of the stratum corneum barrier. Within this context, it will be easier for clinicians

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to explain the principles of good skin care—including skin cleansing—for special pediatric populations. In this article, we provide insights from the pediatricians' viewpoint that are intended to be helpful in counseling parents and other caregivers—and pediatric patients who are old enough—to provide good skin care to (1) aid in the process of restoring barrier function damaged by disease processes or injuries and (2) to support and maintain healthy stratum corneum function once the disease process or damage has been optimally managed. A parent education handout is provided at the end of this article to assist clinicians in this endeavor.

Neonates and Infants

Neonates represent a special pediatric population. The stratum corneum in full-term newborns is 10 to 20 cells thick, the same thickness as in adults. However, the pH of neonatal skin is neutral—typically, 6.5—and does not develop the important acid mantle (a pH of 5.5 to 6.0) until about 2 weeks after birth. (By about 1 month of age, the pH increases to that of adult skin, in the range of 5 to 5.5.) In addition, the microbiome of neonates differs from that of older babies and adults.¹

The initial skin care of a newborn—the first cleansing—should be delayed for 2 to 4 hours after birth and once vital signs have stabilized. Assuming no complications prevent it, the infant should be placed on the mother immediately after birth and should remain in skin-to-skin contact for at least an hour, and breast-feeding should begin within this time. This period, known as the golden hour, has become a familiar concept in neonatal intensive care units (NICUs), underlying the timing of life-saving protocols for premature infants.² More recently, outside

NICUs, the golden hour has become recognized as crucial to maternal-infant bonding, even in uncomplicated births.³ As early as 1990, Lindenberg and colleagues⁴ reported that imprinting that occurs during the golden hour enhances the long-term success of breast-feeding.

Some have suggested that, for the initial bath after birth, cleansing with water alone is sufficient, although this conflicts with the consensus of experts worldwide. Water alone does not remove the bacteria, oils, and vernix; a made-for-baby cleanser with surfactants that has been adequately preserved for safety is required.

Discharge instructions after childbirth should include guidance for healthy skin care, beginning with instructions on parental hand-washing in addition to recommendations for the child's skin care regimen. Patients and parents of young children should understand that the purpose of cleansing the skin is to maintain good hygiene by regularly removing bacteria, viruses, irritants, and other contaminants (such as urine and feces).

The clinician should provide specific information on how to cleanse the skin, including recommendations for products that are appropriate for individual patients' cleansing and moisturizing needs. For example, parents should be advised that firmly rubbing cleanser onto the skin with a washcloth not only is unnecessary but can be irritating in children with sensitive skin and can further perturb the skin barrier in those with dermatologic conditions such as atopic dermatitis (AD). Using the hands alone to apply cleanser is usually adequate to achieve the desired hygienic results.

The article by McLeod et al⁵ offers recommendations for well skin care that will support maintenance of a healthy and optimally functional stratum corneum barrier. Implementing these strategies at the beginning of life can help establish a foundation for lifelong habits of self-care that will serve when the skin is healthy and will help restore barrier function if injuries occur or dermatologic disease develops.

Patients With Special Skin Care Needs

Skin care for patients who develop skin conditions that are acute rather than chronic—that is, for example, a child with a sunburn or diaper rash rather than AD—requires temporary short-term changes to the general principles of well skin care discussed by McLeod et al.⁵ In contrast, children with AD or other chronic skin conditions should adhere to skin care regimens as prescribed for their disease; well skin care principles should guide caregivers during periods of remission.

The following sections discuss some specific observations regarding skin care during times of special needs—when the stratum corneum barrier is perturbed and requires special attention to heal and restore normal barrier function.

Atopic Dermatitis

The underlying changes in the stratum corneum barrier that contribute to the development of AD are reviewed in detail in the article by Elias et al.⁶ This established and emerging understanding of the pathogenesis of AD and

the perturbation of normal stratum corneum function have helped shape both the pharmacologic and the nonpharmacologic management principles in use today.

A frequent problem with AD management is compliance with a skin care regimen. In many cases, an appropriate home care protocol is prescribed and is followed initially, but when the flare clears, aspects of the regimen may be abandoned until the patient flares again. Parents should be advised to adhere strictly to the recommendations for treating AD to bring flares under control, including instructions for bathing and moisturizing the skin. However, they must also understand that attention to appropriate skin care during periods of remission can help restore the skin barrier and reduce the frequency of further AD flares. It is important to emphasize to parents (and patients who are old enough to understand) that AD is a chronic disease and that resolution of a flare does not indicate a cure but signals the need to switch—and adhere—to the recommended maintenance regimen.

Patients with AD should be bathed with soap-free cleansers that do not compromise the skin barrier by contributing to dryness and the itch-scratch cycle and that, at the same time, enhance skin barrier integrity by moisturizing the stratum corneum. In many cases, it is helpful to use additional moisturizers several times a day, particularly during a flare. Adequate moisturization helps decrease the skin's susceptibility to irritation from clothing and from exposure to various products and substances.

Moreover, parents need to know that the characteristics of AD typically change over time. For example, AD may look like one disease in their infant, but may manifest differently when the child becomes a toddler and change again when the child reaches adolescence. (It is worth noting here that eczematous changes during the first month of life generally result from contact irritant dermatitis rather than from an immunoglobulin-E-mediated disease.) These changes in the appearance of the disease also may require changes in the products used in routine skin care.

In addition to following the instructions for skin care, parents must understand that a young child's environment also needs attention. Crawling babies and playing toddlers with AD have an increased risk for skin infections because of a compromised skin barrier function, so keeping rugs vacuumed and other types of floor surfaces reasonably clean of bacteria and other contaminants will reduce exposure to irritants and potential pathogens.

Acne

During office visits with teenagers, clinicians can reinforce, enhance, or correct skin care habits. Patients with mild to moderate acne that responds to first-line treatment often are managed in the pediatrician's or other primary care practitioner's office; those with severe, difficult-to-manage, or refractory acne are appropriately referred to a dermatology specialist. Regardless of which practitioner manages a patient's acne, the nondermatologist who sees that patient for any reason can provide valuable education and reinforcement to support the chosen acne management regimen.

Patients commonly believe that surface oiliness requires the frequent use of harsh, strong cleansers and scrubbing to achieve clean skin. Many use abrasive cleaners that

contain fine granules and are labeled as “pore cleansers,” believing that these products will clear current lesions and prevent the emergence of additional acne lesions. Cosmetic products that many patients use to cover acne lesions can make the condition worse and add to dryness.

Furthermore, many patients believe that oils on the skin should be “dried up” to enhance appearance, and thus they avoid using a much-needed, lipid-rich moisturizer. Clinicians frequently hear comments such as, “I don’t use any lotions or creams—my skin is already so greasy,” and “I want to stop the shine, not make it worse.”

The use of harsh, abrasive, or excessively drying products on the skin alters the barrier function, changes the microbiome, and more generally changes the normal physiology of the skin in patients with acne. Excessive washing can lead to further irritation and distorted physiology, which can potentially worsen the condition.

Patients should be told that harsh products and scrubbing irritate the skin and contribute to the inflammatory process of the underlying disease. They also need to know that consistent regimens involving the use of mild cleansers (limiting cleansing to twice daily), using medications as prescribed, and moisturizers and sunscreens comprise the best strategy for managing their disease.

In addition, clinicians should guide patients in choosing specific products for routine cleansing, as well as other agents such as makeup removers. The function and importance of moisturizers should be explained and appropriate products recommended. Moisturizers are especially important for patients who are using topical retinoid medications. Products containing sunscreen should be considered.

Allergic and Irritant Contact Dermatitis

Identification and elimination of the offending allergen or irritant is, of course, crucial to managing allergic and irritant contact dermatitis. In young children who spend time crawling or playing on the floor, environmental cleaners may be a source of allergic contact dermatitis in the home. Other common sources of dermatitis include adhesive bandages and the use of skin care products that contain ingredients to which a child may be sensitive (usually, products intended for adult use). Laundry detergents and fabric softeners also may be responsible.

Floor mats used in daycare or school play areas and gymnasiums and skin care products that contain ingredients to which a child may be sensitive may be a source of dermatitis. Toddlers in daycare or school-age children also may experience dermatitis from exposure to products used to disinfect desktops and other work surfaces in the classroom. Outdoors, certain plant, animal, and landscaping chemicals are other potential culprits at home, in the school yard, and other outdoor recreational areas.

The use of anti-inflammatory medications may be needed to bring the inflammatory process under control. However, caregivers should understand that irritants and allergens are harmful only if they penetrate the stratum corneum barrier and reach the skin cells farther down in the epidermis.⁷ Therefore, the restoration of an intact and optimally functional stratum corneum barrier is necessary to prevent skin infection during the current episode and to reduce the risk



Figure. Diaper rash. In most cases, diaper rash can be effectively managed—and normal stratum corneum function can be restored—with frequent diaper changes, gentle cleansing followed by air-drying, and application of a barrier agent such as 40% zinc oxide or petrolatum.

for contact dermatitis in the future. Again, the same principles for well skin care apply to support healing and enhance restoration and maintenance of the stratum corneum barrier.

Sunburn and Diaper Rash

In cleansing sunburned skin, it is important to avoid scrubbing to prevent pain and additional damage to the stratum corneum, as well as to reduce the chances of secondary infection. The presentation of sunburn in a child also offers an important opportunity to emphasize the importance of sun protection and to teach parents that ultraviolet radiation causes DNA damage to the skin that lasts a lifetime.

The same is true for the care of skin damaged by diaper rash. Although yeast may sometimes be the cause, in most cases diaper rash essentially is a chemical burn (**Figure**). Some of the enzymes secreted into the gut to digest food are excreted in the stool and can damage skin on contact. In addition, the pH of the stool and the bacterial content also lead to skin damage. In most cases, home care is sufficient to resolve the problem, including frequent diaper changes, gentle cleansing, allowing the buttocks to air dry, and the application of a barrier agent (such as 40% zinc oxide or petrolatum). These measures are appropriate curative steps that also will restore normal skin barrier function and prevent further outbreaks of diaper rash.

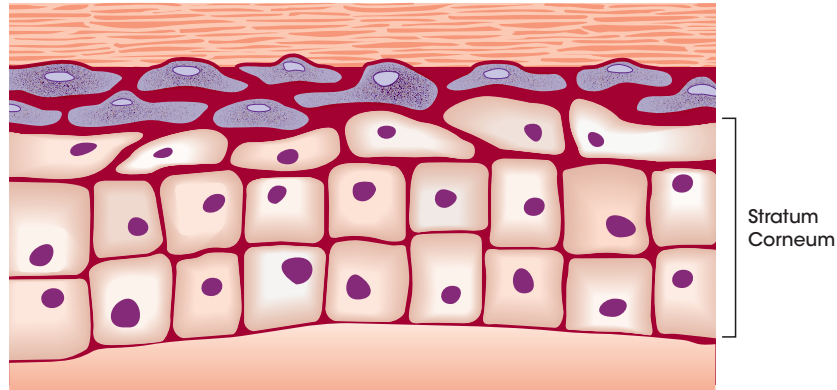
Conclusion

Good skin care practices, beginning in early childhood, include the use of cleansers and moisturizers that are appropriate to the individual. All babies and children should be bathed with gentle cleansers; scrubbing and abrading the skin should be avoided. The use of moisturizers following gentle cleansing will support the structure and function of a healthy stratum corneum barrier and will help restore healthy function in patients whose skin is compromised by illness or injury.

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The Basics of Skin Care: Cleanse, Moisturize, Protect



Understanding the Skin

The skin is not just a covering for the body. Instead, it is an organ that is responsible for many tasks that help keep the entire body working properly. The skin regulates the amount of moisture that enters and leaves the body, and it ensures that the body temperature remains stable. The skin also blocks the entrance of harmful bacteria and other organisms. It also is the first line of defense against other potentially harmful invaders, such as dirt, chemicals, fumes, and radiation from the sun.

The outermost portion of the skin is called the epidermis (EP-eh-DER-miss). The surface of the epidermis is known as the stratum corneum (STRAT-um CORN-ee-um). The cells of the stratum corneum are produced in deeper layers of the epidermis and, over a period of weeks, move gradually to the surface. Dead skin cells are shed, and cells from below take their place. In this way, the surface of the skin is constantly renewed.

Basics of Lifelong Healthy Skin

Parents and patients should know the basics of well skin care that apply at all stages of life. In its simplest form, this message comprises three areas: (1) **cleanse**, to remove pathogens, irritants, and other contaminants, (2) **moisturize**, to reduce drying effects from cleansers, low ambient humidity, and other factors, and (3) **protect** the skin from sun damage, using sunscreens and other sun-protection measures, such as protective clothing.

Never use products on your child that are intended for adult skin. If your budget does not allow you to buy different cleansers, moisturizers, and sunscreens for your young children and older family members, “go young.” Buy what is recommended for the youngest in your family. Let those products become the “family” skin care products, used by everyone.

This two-sided handout developed by Renee P. McLeod, PhD, APRN-BC, CPNP, FAANP, Paul Horowitz, MD, FAAP, Joseph F. Fowler, Jr, MD, Lawrence F. Eichenfield, MD, and Peter M. Elias, MD, may be freely duplicated and distributed, without charge, to patients and parents. Other uses, such as inclusion in published materials or presentations, require proper attribution for the authors and permission from the publisher.

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Tips for Cleansing

- Never scrub the skin.
- Use warm rather than hot water to rinse.
- Use a cleanser that is best for your child. Your clinician recommends the following cleanser(s):

Tips for Moisturizing

- Apply moisturizer after every cleansing.
- Apply moisturizer more often during “dry conditions”
 - Before and after children play outside in cold weather.
 - When you use heat in your home.
 - If you live in or visit a dry region of the country (such as desert areas).
- Use a moisturizer that is best for your child. Your clinician recommends the following moisturizer(s):

Tips for Sun Protection

- Use sun protection every day, even if you don’t expect your child to be exposed to the sun. Get into the habit of protecting your child’s skin and eyes from sun damage.
- Clothing is sun protection, too. Children who play outside should wear hats and sunglasses. When playing in sunny areas—especially near pools, lakes, or the ocean—make sure your child covers up with a hat, shirt, and long pants.
- Some moisturizers contain sunscreen. Your clinician will let you know if this type of product is right for your child.
- Use a sunscreen that is right for your child. Your clinician recommends the following sunscreen(s):

Stratum Corneum Skin Barrier Maintenance and Restoration: Evidence-Based Approach to Cleansing and Other Skin Care Practices CME Post-Test Answer Sheet

Original Release Date: June 2013 • Most Recent Review Date: June 2013
Expiration Date: June 30, 2015 • Estimated Time to Complete Activity: 3.0 hours

Physicians: To get instant CME credits online, go to <http://uoft.me/skinsupp13>. Upon successful completion of the online test and evaluation form, you will be directed to a Web page that will allow you to receive your certificate of credit via e-mail. Please add cmepd@louisville.edu to your e-mail "safe" list. If you have any questions or difficulties, please contact the **University of Louisville School of Medicine Continuing Medical Education (CME & PD)** office at cmepd@louisville.edu.

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CME Questions: For each question or incomplete statement, choose the answer or completion that is correct. Circle the most appropriate response.

1. **All of the following are considered defensive functions of the stratum corneum barrier except:**
 - A. Cytokine activation
 - B. Hydration
 - C. Integrity and cohesion
 - D. Permeability barrier
2. **To be optimal in supporting the stratum corneum in patients with atopic dermatitis, physiologic lipid formulations must include ceramides, cholesterol, and free fatty acids, respectively, in which molar ratio?**
 - A. Ceramides, cholesterol, free fatty acids, 1:1:3
 - B. Ceramides, cholesterol, free fatty acids, 1:3:3
 - C. Ceramides, cholesterol, free fatty acids, 3:1:1
 - D. Ceramides, cholesterol, free fatty acids, 3:3:1
3. **Large surfactant molecule groups are known as _____.**
 - A. Hydrophobic cleansers
 - B. Irritant molecules
 - C. Micelles
 - D. Moisturizing factors
4. **The key lipids in the stratum corneum are derived from _____.**
 - A. Epidermal lamellar body
 - B. Filaggrin
 - C. Glycosylceramides
 - D. Phospholipids
5. **At what anatomic site is transepidermal water loss usually lowest?**
 - A. Back
 - B. Breasts
 - C. Lower extremities
 - D. Upper extremities
6. **The earliest insight that filaggrin was clinically important was in 1985, when Sybert and colleagues proposed that it might be associated with _____.**
 - A. Atopic dermatitis
 - B. Ichthyosis vulgaris
 - C. Psoriasis
 - D. Xeroderma pigmentosum
7. **Viscosity enhancers are ingredients primarily found in which of the following categories of skin care products?**
 - A. Cleansers
 - B. Emollients
 - C. Moisturizers
 - D. Shampoos
8. **Cocamidopropyl betaine and hydrophobically modified polymers are which types of compounds?**
 - A. Emollients
 - B. Preservatives
 - C. Surfactants
 - D. Viscosity enhancers
9. **Among the cleanser ingredients listed below, those least likely to be allergenic are _____.**
 - A. Fragrances
 - B. Preservatives
 - C. Stabilizers
 - D. Surfactants
10. **By about 1 month of age, the pH of an infant's skin is in the range of:**
 - A. 4 to 4.5
 - B. 4.5 to 5
 - C. 5 to 5.5
 - D. 5.5 to 6

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EVALUATION FORM

We would appreciate your answering the following questions in order to help us plan for other activities of this type. All information is confidential.

Please print.

Name: _____

Specialty: _____

Degree: ☐ MD ☐ DO ☐ PharmD ☐ RPh ☐ NP ☐ RN ☐ BS ☐ PA

☐ Other _____

Affiliation: _____

Address: _____

City: _____ State: _____ ZIP: _____

Telephone: _____ Fax: _____

E-mail: _____

Signature: _____

CME CREDIT VERIFICATION

I verify that I have spent _____ hour(s)/_____ minutes of actual time working on this CME/CNE activity. No more than 3.0 CME credits will be issued for this activity.

COURSE EVALUATION: GAPS

This activity was created to address the professional practice gaps listed below. Please respond regarding how much you agree or disagree that the following gaps were met:

- It is challenging for clinicians to remain up-to-date with the numerous recent laboratory and clinical studies that have significantly advanced understanding of the physiology and function of the skin barrier.
- Skin cleansing currently is viewed predominantly as an activity that promotes good skin appearance and reduces the number of microbes on the skin surface. The role of cleansing in maintaining a healthy skin barrier must be more widely recognized and understood by clinicians.
- With the extensive array of skin cleansers available to consumers, it is difficult for clinicians to maintain an awareness of which agents are appropriate for particular clinical applications.
- Many clinicians tend to accept "umbrella" descriptions of cleansing agents that indicate a product is "mild," "made for sensitive skin," or "gentle" and make similar broad generalizations when recommending cleansing regimens to patients (such as the admonition to "use a mild cleanser").
- For clinicians to make evidence-based recommendations to patients regarding skin cleansing and cleansing agents, they must have available a means of easily accessing and synthesizing the clinically relevant information that is now available and will continue to emerge on this topic.

Did participating in this educational activity improve your **KNOWLEDGE** in the professional practice gaps that are listed on the left?

Strongly Agree	Agree	Somewhat Agree	Disagree	Strongly Disagree
1	2	3	4	5

Please elaborate on your answer. _____

Did participating in this educational activity improve your **COMPETENCE** in the professional practice gaps that are listed on the left?

Strongly Agree	Agree	Somewhat Agree	Disagree	Strongly Disagree
1	2	3	4	5

Please elaborate on your answer. _____

Did participating in this educational activity improve your **PERFORMANCE** in the professional practice gaps that are listed on the left?

Strongly Agree	Agree	Somewhat Agree	Disagree	Strongly Disagree
1	2	3	4	5

Please elaborate on your answer. _____

Please identify a change that you will implement into practice as a result of participating in this educational activity (new protocols, different medications, etc).

How certain are you that you will implement this change?

Strongly Agree	Agree	Somewhat Agree	Disagree	Strongly Disagree
1	2	3	4	5

What topics do you want to hear more about, and what issue(s) in your practice will they address? _____

Were the patient recommendations based on acceptable practices in medicine? ☐ Yes ☐ No

If no, please explain which recommendation(s) were not based on acceptable practices in medicine. _____

Do you think the articles were without commercial bias?

☐ Yes ☐ No

If no, please list the article(s) that was/were biased. _____