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The Importance of a Healthy Skin Barrier From the Cradle to the Grave Using Ceramide-Containing Cleansers and Moisturizers: A Review and Consensus

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ABSTRACT

Introduction: Inflammatory skin disorders compromise skin barrier health. Early and daily skincare use aims to maintain a life-long healthy skin barrier. Racial/ethnic and age variations in skin barrier properties, cultural differences, and clinical presentation of the inflammatory skin disorder influence the choice of treatment and skin care. Ceramide-containing skin care may play a role in restoring and maintaining a healthy skin barrier.

Methods: A panel of 6 dermatologists met to develop consensus statements based on their 8 previous publications on promoting skin barrier health throughout life using ceramide-containing skin care. The publications covered skin barrier integrity in the newborn and infant, and the role of the skin barrier in mitigating atopic dermatitis (AD); racial/ethnic variations in the skin barrier and implications for skin care; the role of the skin barrier in inflammatory skin conditions including acne, AD and psoriasis in skin of color (SOC) populations; skin barrier integrity in patients with rosacea; and xerosis in patients with diabetes mellitus. The panel synthesized the 8 publications, selected information from a literature review, and their expert opinions and experiences to create the statements. The consensus was reached through a modified Delphi method where the panel met face-to-face and followed up virtually.

Results: The panel adopted 6 consensus statements highlighting the importance of skin care in restoring/maintaining a healthy skin barrier in the populations mentioned above. Skin care suited to this role is gentle, has near-physiologic pH, is pleasant to use, and contains ceramides. This type of skin care can promote a healthy skin barrier and attenuate or delay inflammatory skin conditions.

Conclusions: Adjunctive daily skin care throughout life promotes a healthy skin barrier and is beneficial in managing various inflammatory skin disorders in all populations. However, when choosing optimal treatment and skin care, physicians should consider variations in age, skin properties, presentation of the condition, and cultural differences.

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INTRODUCTION

The skin is the largest organ of the human body, accounting for approximately 16% of total body weight, and has numerous critical functions. It retains water in the body, thermoregulates, blocks external pathogens and foreign substances, and transmits sensations.[1]

The skin's protective and regulatory barrier function is primarily achieved within the top layer of the epidermis, the stratum corneum (SC).[2] The SC is the outermost layer of the skin and consists of 10 to 15 layers of corneocytes (enucleated protein-rich cells) and highly organized intercellular lipids. The corneocytes are the building blocks, and the water-resistant lipid lamellae are the matrix, forming a "brick-and-mortar"-like structure that prevents excess water loss and protects against external toxins and microorganisms.[1,3]

Skin lipids play a significant role in SC barrier function. Close to 20% of the volume of the SC is made up of lipids. These lipids consist of 40% to 50% ceramides, 25% cholesterol, and 10% to 15% free fatty acids.[3,4] Maintaining physiologic SC composition is important to preserving SC hydration and healthy skin from the cradle to the grave.

Harsh chemicals, surfactants, exfoliants, aggressive cleansers, trauma, and inflammatory skin diseases can damage the SC.[3,5] Ceramide abnormalities change the SC's physiologic properties

and can lead to barrier dysfunction. Ceramide levels are reduced or structurally altered in inflammatory skin diseases such as acne, atopic dermatitis (AD), psoriasis, and rosacea.[3]

This paper offers insights into promoting a healthy skin barrier throughout life using ceramide-containing skin care. In particular, this paper focuses on skin barrier integrity in the newborn and infant and on mitigating atopic dermatitis (AD); racial/ethnic variations in the skin barrier and implications for skin care; Skin of color (SOC) and acne, AD, and psoriasis; skin barrier integrity in patients with rosacea; and xerosis in patients with diabetes mellitus.

Project on Promoting Skin Barrier Health

The project aims to offer insights to promote a healthy skin barrier throughout the different phases of life.

Status of the Project

Previously, the panel participating in the project published 8 papers addressing skin barrier integrity in a range of patient populations and exploring the role of ceramide-containing cleansers and moisturizers.[3,6-12] The publications included newborn and infant skin barrier integrity and management of atopic dermatitis (AD). The series on skin of color (SOC) patients included racial/ethnic variations in the skin barrier and implications for skin care, acne in SOC patients, AD in SOC patients, and psoriasis in SOC patients. Further publications were on rosacea and skin barrier integrity and patients with diabetes mellitus-related xerosis.

Consensus Statements

A panel of 7 dermatologists (6 from the US and one from Europe) met on February 13th, 2022, to give an overview of the published papers and to develop consensus statements for promoting a healthy skin barrier using ceramide-containing cleansers and moisturizers.

The project used a modified Delphi method and combined a face-to-face meeting with a virtual follow up. The selected information from literature searches and the 8 previous publications was coupled with the panel's opinions and experience to adopt 6 consensus statements.

Overview of the Previously Published Articles by the Panel

The panel members' publications reviewed the importance of a healthy skin barrier and how to maintain and restore the skin barrier in the following populations: neonates, young children, people of different races/ethnicities, people with SOC and acne, people with SOC and AD, people with SOC and psoriasis, people with rosacea, and people with diabetes mellitus (Table 1).

Consensus regarding the importance of ceramide-containing skin care for normal and sensitive skin conditions in neonates and infants[6]

The newborn and infant's skin is immature and vulnerable to skin barrier disruption. To better understand the role of ceramide-containing skin care in this population, a group of pediatric dermatologists and dermatologists met to develop a consensus paper. The panel discussed information gleaned from systematic literature searchers and their own experiences and opinions and used a modified Delphi technique to reach a consensus. They agreed that given the newborn and infant's vulnerable skin, cleansers should be mildly acidic or neutral, and skin care should have barrier-supporting ingredients such as ceramides that improve the skin's lipid content and be safe, effective, and free of perfume and sensitizers.

The importance of skin care for neonates and infants: an algorithm[7]

Given that the skin of the newborn and infant is prone to barrier disruption, a panel of pediatricians, pediatric dermatologists, and dermatologists met to develop an algorithm for the use of over-the-counter (OTC) skin care to promote a healthy skin barrier in this population. To prepare the algorithm, the panel used a modified Delphi process where they first met virtually to discuss the selected literature on the use of OTC skin care in neonates and children with healthy skin, then coupled this information with their expert opinion and experience. Later, the panel finalized the algorithm through an online process. The final algorithm focuses on the use of skin care in newborns and infants to address erosion/bulla, erythema, and xerosis. Skincare recommendations include using gentle cleansers and moisturizing after bathing with ceramide-containing moisturizers (Figure 1A and 1B).[7]

Racial/Ethnic variations in skin barrier: implications for skin care recommendations in skin of color[8]

Given that skin barrier properties can vary across populations of different self-identified race/ethnicity, a panel of skin experts met to evaluate the available literature on racial/ethnic differences in the skin barrier, specifically, the stratum corneum, and whether these differences translate into a need for population-specific skincare considerations. The panel of 7 dermatologists met virtually and created statements on skin care for health care providers taking care of diverse populations. By synthesizing the reviewed literature with their expert opinion, the panel determined that better studies are needed to provide specific recommendations on skin care in people with SOC.

Racial/Ethnic variations in acne: implications for treatment and skincare recommendations for acne in patients with skin of color.[9] While acne vulgaris is very common, its clinical presentation may vary depending on the population (eg, in patients with SOC). To gain insight on acne in patients with SOC, 6 dermatologists met to answer 3 questions: 1) Are there racial/ethnic differences in the clinical presentation and sequela of acne? 2) Are there racial/ethnic differences in the therapeutic endpoint of acne treatment and patient expectations? 3) Is there a need for specialized

TABLE 1.

Reviewed Articles/Presentations		
Reference	**Subject**	**Outcomes**
Schachner 2020[6]	Consensus on ceramide-containing skincare for neonates and young children with normal or sensitive skin	• The immaturity and the high surface-to-weight ratio of the newborn's skin increase the risk of harm, including infection, chemical and heat damage, and toxicity from topicals.[6] • Using ceramide-containing skincare promotes a healthy skin barrier.[6]
Schachner 2021[7]	Skincare algorithm for neonates and young children	• The newborn and infant skin is vulnerable to SC barrier disruption.[7] • Daily use of non-alkaline cleansers and moisturizing with ceramides can support the skin's barrier and help mitigate AD.[7]
Alexis 2021[8]	Racial/ethnic variations in skin barrier in skin of color	• Studies inconsistently and poorly define race and ethnicity.[8] • Studies on skin barrier properties in different ethnic groups have been inconclusive.[8]
Alexis 2021[9]	Racial/ethnic variations in acne	• Studies report racial/ethnic differences in acne with distinct features in SOC.[9] • Selecting tolerable treatments, treating early, maintaining treatment, using pH-balanced, non-comedogenic cleansers and moisturizers, making clearing acne and avoiding hyperpigmentation treatment goals, and considering cultural differences can improve outcomes in patients with SOC.[9]
Alexis 2022[10]	Skincare in skin of color patients with AD	• Associated genetic factors may vary between self-identified racial/ethnic populations.[10] • Dry skin associated with AD may be more stigmatizing in people with SOC.[10] • In patients with SOC and AD, skincare and prescription treatments should be proactive, align with cultural values, reinforce the skin barrier, and decrease inflammation.[10] • Skincare-containing ceramides can increase the amount of lipids in the skin and improve AD.[10]
Alexis 2022[11]	Psoriasis in skin of color patients; Skin barrier dysfunction and adjunctive skincare	• Skincare as a tool to manage psoriasis may be underutilized, including in those with SOC.[11] • Emollients, including those with ceramides, may help repair the skin barrier and reduce desquamation, pruritus, and TEWL, as well as normalize apoptosis, differentiation, and proliferation.[11]
Baldwin 2021[3]	Barrier deficiency in rosacea and OTC skincare as an adjunct to treatment	• Moisturizers and cleansers that improve barrier function can improve the signs and symptoms of rosacea.[3] • OTC products are recommended adjuncts before, during, and after prescription treatment.[3] • Ingredients such as ceramides, hyaluronic acid, and niacinamide can restore the skin barrier. Irritating ingredients should be avoided.[3]
Kirsner 2019[12]	Diabetic skin changes and benefits of moisturizer and cleanser use	• Skin problems in diabetes are common and underappreciated.[12] • It is important to treat skin problems in patients with diabetes to improve patients' health, including quality of life.[12] • Use of ceramide-containing skin care may improve pruritus and dry Skin.[12]

Atopic dermatitis (AD), skin of color (SOC), Stratum corneum (SC), Trans epidermal water loss (TEWL), Over-the-counter (OTC)

approaches to therapeutic options and skin care in acne patients with SOC?

Using a modified Delphi process where the panel incorporated their expert opinion and experience with a review of the literature, the panel determined that clinical and therapeutic nuances exist in the management of acne in SOC, and special considerations in treatment approaches and skin care are warranted. Selecting tolerable treatments, treating early, maintaining treatment, using pH-balanced, non-comedogenic cleansers and ceramide-containing moisturizers, clearing acne, and avoiding hyperpigmentation are treatment goals, and considering cultural differences can improve outcomes in patients with SOC (Table 2).[9]

Insights on atopic dermatitis in patients with skin of color and the role of skin care in improving outcomes[10]

To synthesize the available information on AD in people with SOC and provide recommendations on the use of skin care in this population, a panel of 6 dermatologists met virtually. Following a literature review, the panel used a modified Delphi process to determine the best way to treat AD in patients with SOC, including the role of gentle cleansers and moisturizers. The panel determined that the skin barrier, clinical features, and impact of AD may vary between racial/ethnic subpopulations. In people with SOC, AD can lead to pigment changes, which can greatly impact quality of life. Since dry skin can be more visible on richly

FIGURE 1A. Algorithm for skin care in newborn and infant skin.

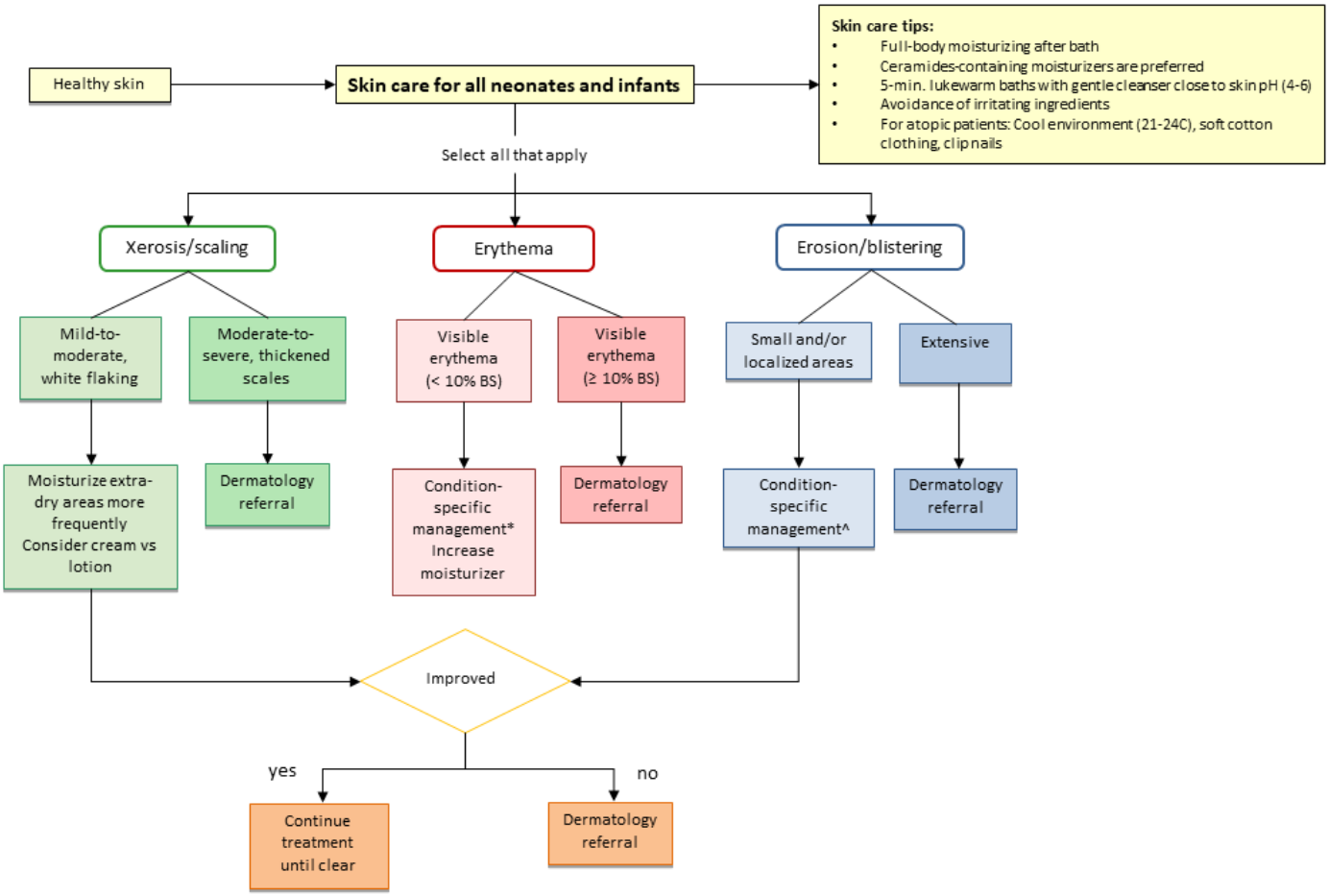


FIGURE 1B. Newborn and infant skin presentation, clinical features, and skin care.

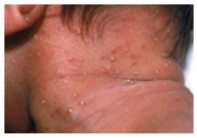
	Erythema	Clinical features	Duration Treatment
	Erythema Toxicum Neonatorum	Various combinations of erythematous macules (flat red patches), papules (small bumps) and pustules. Location: generalized.	Typically lasts for several days, requires no treatment.
	Miliaria	1- 3mm papules or vesicles. Location: typically, truncal and/or in areas of occlusion.	Remove from heated humid environment. Cool bathing or apply cool compresses. Topical steroids may be used to facilitate relief.
	Neonatal cephalic pustulosis Pityrosoprum Folliculitis	Erythematous dome shaped papules and superficial non-pruritic pustules arise in crops. Location: Cheeks, nose and forehead, neck, upper chest.	Will resolve within weeks without treatment. If extensive, can treat with topical antifungals.
	Transient neonatal pustular melanosis	More common in infants with skin of color. Small pustules that resolve into hyperpigmented macules.	Gradually fade without treatment over several weeks to months.

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TABLE 2.

Features of Safe and Effective OTC Cleansers and Moisturizers for Acne in SOC Patients	
Type of OTC acne treatment	**Action/features of the products**
Monotherapy: Mainly used for mild acne	Well tolerated, anti-inflammatory, easy and comfortable to use, cosmetically pleasant texture
Adjunctive therapy: Mainly used for moderate acne in combination with prescription treatment	Non-irritating, well tolerated, anti-inflammatory, repairs skin barrier, addresses hyperchromia post-acne, follicular occlusion, seboregulatory, and pleasant texture.
Maintenance therapy	Anti-inflammatory action, prevention of acne flares, oil control, and minimization of scars. Features include pleasing texture, non-oily, and nonirritating.
BPO containing products	Available as creams, gels, lotions, and washes, it can treat mild acne or can be used as adjunctive treatment or as a component of fixed combinations. Is effective but may cause irritation.
SA containing products	Salicylic acid, available in creams, lotions, and pads, helps resolve the irregular shedding of cells. For mild acne, it can unclog pores, and it is fat soluble but has no antimicrobial activity.
GA containing products	Available as creams, gels, and lotions. There is a risk for increased UV-induced pigmentation when using these products.
Retinoid containing products	Topical retinods decrease the formation of acne. They are used to treat moderate-to-severe acne, often in combination with other products, such as BPO and oral antibiotics. AEs include dryness, pruritus, and erythema.
Azelaic acid-containing products	Azelaic acid helps normalize follicular hyperkeratinization and may decrease pigment and proliferation of *C. acnes*. Effective for mild to moderate papular-pustular acne, particularly in patients with sensitive and richly pigmented skin, as well as in adult acne in women.
Ceramides containing cleansers and moisturizers	Acne-affected skin may have reduced ceramide levels resulting in skin barrier dysfunction, which correlates with hyperkeratinization and comedone formation. A ceramides-containing skincare regimen supports the removal of excess sebum and debris on the skin surface (cleansing) and improves skin barrier (moisturizing) function.
Cleansers and moisturizers containing TSW	May help restore the skin microbiome reducing inflammation.
AHA and BHA-containing products	Available as creams, gels, serums, and lotions, they are both exfoliants and moisturizers and may have antiaging properties. In OTC products, low concentrations (4%-10%) are used.
Sunscreen with an SPF of at least 30	Sunscreens help prevent UV-induced inflammation and PIH.
HA containing products	HA encompasses a large volume of water, giving solutions high viscosity, even at low concentrations. Used as a moisturizer to help improve skin hydration.

Benzoyl peroxide (BPO); Alpha hydroxy acid (AHA); Beta hydroxy acid (BHA); Glycolic acid (GA); Salicylic acid (SA); Sun protection factor (SPF); Hyaluronic acid (HA); Adverse events (AEs); Thermal spring water (TSW), Post-inflammatory hyperpigmentation (PIH)
Reproduced from Alexis et al[9] with permission.

TABLE 3.

Skincare for SOC Patients With AD	
Cleansers and bathing	• Use nonsoap cleansers (e.g., syndets, aqueous solutions) with a neutral or low pH that are less allergenic, nonirritating, and fragrance-free. • Soap-based cleansers, which have a high pH and contain surfactants, should be avoided because they can cause dry skin and irritation. • Antiseptic-containing cleansers are not recommended due to the limited duration of action of antiseptics and limited clinical data regarding their effectiveness. • Consider a bleach bath for specific cases such as infections. • After bathing, gently pad the skin with a soft towel, avoiding rubbing. Next, apply moisturizer while the skin is still moist (within 3 min).
Moisturizers	• A moisturizer should be used at least twice daily and more frequently during acute flare-ups. • Consider patient tolerance and preferences for a moisturizer to enhance treatment adherence. • Cream-type moisturizers containing lipids are suitable, and during winter, higher lipid contents are preferred. • Adult patients with AD should use approximately 250 g or more of moisturizer per week and apply it to their whole body, regardless of the presence of lesions, since barrier defects and subclinical inflammation may also be present on lesion-free skin. • During acute flare-ups, moisturizers should be used more frequently in conjunction with anti-inflammatory treatment and continued as maintenance therapy.

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TABLE 4.

Skincare for SOC Patients with AD	
Education	**Details**
Educate SOC rosacea patients on the avoidance of:	• Triggers • Skincare products with elevated pH • Excessive cleansing and exfoliating
Educate SOC rosacea patients on the importance of:	• Daily using gentle cleansers • Frequently using quality moisturizers • Choosing skincare that promotes a healthy skin barrier • Using sun protection with SPF ≥ 30

pigmented skin, it may also be more stigmatizing in people with SOC. In patients with SOC, AD treatment should reinforce the skin barrier, control inflammation, be proactive, and align with cultural practices. Moreover, higher-quality studies of AD in patients with SOC are needed (Table 3).[10]

Evolving concepts in psoriasis: special considerations for patients with skin of color, skin barrier dysfunction, and the role of adjunctive skin care[11]

Data on psoriasis in people with SOC, on the skin barrier in psoriasis, and on the impact of skin care in managing psoriasis are lacking, and skin care as an adjunctive treatment may be underutilized. To better understand these issues, a panel of 6 dermatologists met to review the available literature and use a modified Delphi technique to develop 10 statements on the role of skin care in managing psoriasis generally and in patients with SOC. The panel identified studies finding racial/ethnic differences in psoriasis and noted that disparities could result from the underrecognition of these differences. The panel also noted that patients with SOC and psoriasis might experience a greater impact on quality of life. Finally, some studies indicate skin care can play a role in managing psoriasis.

Evidence of barrier deficiency in rosacea and the importance of integrating OTC skincare products into treatment regimens.[3]

Rosacea is an inflammatory dermatosis that is less frequently described in patients with richly pigmented skin. Clinical features may be less conspicuous in patients with SOC and rosacea and, therefore, more challenging to detect. To better understand the role of OTC products in controlling rosacea symptoms, a panel of dermatologists completed a survey on which OTC products they use for their patients with rosacea. The panel met to discuss the survey results and the recommendations from the literature on skin care and rosacea in patients with SOC. Drawing from 14 draft statements, the advisors agreed on 5 statements. All patients with rosacea can benefit from education on their condition and daily skin care use (Table 4). The panel concurred that adjunctive moisturizers and cleansers could improve rosacea signs and symptoms by bolstering the skin's barrier and are central to successful rosacea treatment. Skin care with components such as ceramides, hyaluronic acid, and niacinamide can help restore the skin barrier and are beneficial, along with humectants.

Diabetic skin changes can benefit from moisturizer and cleanser use: a review[12]

Diabetes mellitus-related cutaneous disorders such as xerosis frequently occur in both patients with type 1 and type 2 diabetes mellitus (DM). A panel of physician experts across various specialties in the care of patients with DM met to discuss the role of skin care in ameliorating diabetes-associated skin problems. The panel discussed the relevant literature and their expert experiences and opinions and agreed that patients with diabetes often have cutaneous disorders, including diabetic foot syndrome, keratosis pilaris, and xerosis. Recognition and management of DM-related skin conditions are im-portant in maximizing patients' quality of life and in avoiding severe complications. Maintaining an intact skin barrier by preventing and treating xerosis using gentle cleansers and moisturizers may improve skin conditions in patients with diabetes. Skin care containing lipids such as ceramides and humectants such as urea may reduce xerosis and pruritus. Supporting the education of health care professionals and patients about the use of ceramide-containing gentle cleansers and moisturizers in xerosis prevention and treatment and promoting a healthy skin barrier can improve patient comfort and prevent complications.

Consensus Statements

This section explores challenges in promoting a healthy skin barrier, treatment, and skincare approaches throughout life. The statements and recommendations aim to provide insights that may support clinicians in improving patient outcomes.

MATERIALS AND METHODS

The project used a modified Delphi method and combined a face-to-face meeting with a virtual follow up. The selected information from literature searches and the 8 previous publications was coupled with the panel's opinions and experience to adopt 6 consensus statements.

During the meeting, the panel discussed the summary of the previously published papers. The panel's systematic assessment and refinement of the pre-prepared statements followed established standards. Starting from a list of 9 statements, the panel developed and agreed affirmatively on 6 statements.

Statement 1: *Gentle skin cleansers, moisturizers, and application of lipids can promote homeostasis of the permeability barrier. The ideal moisturizer has a near-physiologic pH and is pleasant to use. Ceramides in skincare regimens promote a healthy skin barrier.*

The skin plays an important role in preventing dehydration, and the integrity of the SC's corneocytes and intercellular lipid layers can be evaluated by measuring SC hydration (SCH) and transepidermal water loss (TEWL).[13] An impaired epidermal barrier is associated with a decrease in SCH and an increase in TEWL. Therefore, an ideal cleanser should clean the skin while leaving the skin hydrated and biologically intact; it should preserve the skin's pH, sebum, lipids, and natural moisturizing factor (NMF).[14] An appropriate cleanser and moisturizer can significantly impact skin health, healing, and patient wellbeing.[14]

Most cleansers rely on surfactants to clean. Surfactants form micelles when placed in water, directly dissolve oils, and damage both the "bricks" (corneocytes) and "mortar"(lipids) of the SC's protective barrier. This damage can lead to increased penetration of exogenous compounds and an increased rate of water loss.[15] Gentle cleansers, on the other hand, may reduce skin irritation.[6]

Another important component of skincare products is pH. Skin pH affects the skin's barrier function; lipid processing and formation of lamellar structures require an acidic skin pH.[3] Near-physiologic pH topical skincare products help repair the skin barrier and normalize the skin microbiome.[16]

Moisturizers also play an important role in repairing the skin barrier, increasing water content, and reducing TEWL. An ideal moisturizer should be elegant, hydrating, tolerable for sensitive skin, affordable, rapid-acting, and long-lasting.[17] While moisturizers are designed to improve and maintain skin barrier function and help prevent xerosis, it is a common misunderstanding that they add water to the skin. Instead, moisturizers prevent or reduce water loss.[14]

Ceramide-containing moisturizers are designed to mimic the skin's natural components to enhance and maintain skin barrier integrity.[18] Ceramides play essential roles in SC structure and regulation of skin barrier homeostasis, and studies have found decreased ceramide levels or altered ceramide profiles in dry skin conditions.[5] Data have demonstrated that topical application of lipid mixtures improves skin diseases, and a recent meta-analysis concluded that ceramide-containing formulations reduced TEWL, improved SC structure, and increased SC lipid content.[1,5]

Statement 2: *Compared to the adult skin barrier, the skin barrier of infants and young children is thinner and more subject to TEWL and issues pertaining to hydration. Using moisturizers with humectants and ceramides reduces the rate of flares and the need for topical steroids. When started shortly after birth, skin care can attenuate or delay the development of AD. Gentle cleansers and topical application of physiologic lipids may promote homeostasis of the skin barrier. The ideal moisturizer is hypo- or non-sensitizing, has a near-physiologic pH, and is pleasant to use.*

Skin maturation starts at birth and continues over the first years of life.[6] In utero, the SC is a hydrophobic lipid matrix containing fetal corneocytes giving it distinct biomechanical and water-binding properties.[6] After birth, the SC has a slightly acidic pH which helps protect against pathogens and influences the composition of cutaneous bacterial flora.[2,6,19] In turn, microbial colonization influences the development of the skin's immune function—a healthy skin microbiome is crucial to protecting against pathogens.[2] Microbial colonization may also affect the development of other skin barrier functions and the systemic immune system.[20] Likely for these and other reasons, pH-neutral or mildly acidic cleansers have been shown to be beneficial to neonates and infants.[6]

The skin of newborns and infants has distinct anatomical and functional skin properties that increase the susceptibility to skin barrier disruption.[2] The SC is about 20% to 30% thinner in neonates and infants compared to adults.[6,21] Furthermore, the SC of neonates and young children does not reach the thickness of adults until at least 3 years of age.[6]

Adaptations after birth include changes in SCH, TEWL, and acidification of surface pH.[2,22] Overall, the skin of newborns has less SCH compared to adults, but this reverses during the first few months of life, resulting in increased skin hydration in older infants.[23] SCH stabilizes at about 90% of capacitance levels measured in 3-month-old infants in healthy preschool and school-aged children. In contrast, children and adults with AD have significantly decreased SCH in both affected and unaffected skin.[23,24]

Pooled TEWL data reveals that in healthy neonates and infants, the basal epidermal permeability barrier functions well at most anatomical sites.[2] Notably, there is significant TEWL variability depending on body region and age. In areas of the body, TEWL is comparable to that of adults as early as day 2.[22]

In short, the infant's and young child's skin is more fragile and susceptible to infections and chemical and thermal damage.[2] For the first years after birth, skin is more permeable to topical agents, and what could be harmless in an adult could be toxic to an infant or young child. Therefore, caution is required when choosing topical skin care in this age group.[6] Skin care should be safe, effective, inexpensive, and free from fragrances and sensitizing

TABLE 5.

Investigational Products*	
Investigational Product	**Main Ingredients**
Test cream[a]	Ceramides 1, 3, and 6-II; triglycerides; cholesterol; glycerol
Test lotion[b]	Ceramides 1, 3, and 6-II; triglycerides; cholesterol; glycerol
Reference cream 1[c]	Liquid paraffin, soft white paraffin, cetostearyl alcohol
Reference cream 2[d]	Liquid paraffin, soft white paraffin, cetostearyl alcohol
Reference cream 3[e]	Liquid paraffin, soft white paraffin, cetostearyl alcohol

[a]CeraVe cream, L'Oréal; [b]CeraVe lotion, L'Oréal; [c]Zerobase cream, Thornton & Ross Ltd; [d]Epimax cream, Dermato-Logical; [e]Aquamax cream, Intapharm Laboratories. *Adapted from Danby SG, Andrew PV, Brown K, et al. *Dermatol Ther (Heidelb).* 2020;10(5):1031-1041.[29]

TABLE 6.

Cutaneous Manifestations in DM[36]	
Category	**Finding**
Associated skin findings	Acanthosis nigricans, diabetic bullae, diabetic dermopathy, eruptive xanthomas, lichen planus, necrobiosis lipoidica, oral leukoplakia, perforating disorders, yellow skin
Associated infections	Bacterial, fungal
Cutaneous complications	Microangiopathy, macroangiopathy, neuropathy
DM treatments with potential for dermatological reactions	Sulphonylureas, insulin

Adapted from de Macedo et al[36] with permission.

agents. Additionally, skincare products should be pleasant to use and contain ingredients that benefit the lipid and water content of the SC, such as those products containing ceramides.[6]

Newborns and infants with xerosis or AD greatly benefit from frequent moisturizing. Moisturizer use decreases pruritus and the symptoms and severity of AD.[25] Moreover, regular use of ceramide-containing skin care reduces the number of AD flares and time to flare.[26] Topical ceramide-containing formulations mimic physiological lipids that support homeostasis and improve skin conditions. Clinical guidelines and consensus papers on AD worldwide recognize the benefits of daily use of moisturizers to reduce inflammation and restore skin barrier function.[6]

Statement 3: *A defective skin barrier contributes to AD pathogenesis and chronicity. Moisturizers with ceramides can restore and preserve skin barrier integrity, improve clinical signs and symptoms of AD, are corticosteroid-sparing, and can be used alone or as an adjunct to treat and prevent disease exacerbation.*

Currently, AD affects more than 26 million people in the United States.[27] Treatment of AD includes managing pruritus while minimizing skin barrier disruption and maximizing barrier repair with topical steroids and frequent moisturizer use.[28] A review of independently published guidelines for AD from across the world recommends moisturizing lesional and nonlesional skin at least twice a day.[28] The National Institute for Health and Care Excellence (NICE) guidelines on AD management recommend applying moisturizers 4 times a day, which can be a significant burden.[29]

Ceramides, cholesterol, and free fatty acids are important components of the SC. These components form a highly ordered matrix that is crucial to the barrier function of the skin.[29,30] Decreased levels of ceramide in the SC are associated with reduced skin barrier function, leading to dry skin conditions such as AD.[31] Therefore moisturizing with skin lipids, such as ceramides, is essential for supporting skin barrier function.[32]

To evaluate if products containing skin lipids delivered via a multivesicular emulsion (MVE) controlled-release system can hydrate the skin long enough to decrease the number of applications needed per day, researchers conducted a double-blind, intra-subject, vehicle-controlled, phase 1 RESTORE trial.[29] RESTORE compared the skin barrier-restoring effects of a ceramide-containing cream and lotion in patients with dry, AD-prone skin to 3 reference creams and a no-treatment control. Both test products contained various skin lipids, including ceramides 1, 3, and 6-II, triglycerides, and cholesterol.[29] Table 5 lists the investigational products evaluated.

Danby et al found that a single application of the test moisturizer (cream or lotion) significantly increased skin hydration by 10% for more than 24 hours compared to other investigational products.[29] After baseline skin hydration measurements were recorded, the products were applied to the lower legs, 3 sites per leg. Skin hydration and visual dryness were then measured 3, 6, 12, and 24 hours after treatment.[29] Compared with the no-treatment control, both the test cream and lotion increased hydration ($P<0.0001$) and decreased dryness ($P<0.05$) for at least 24 hours following 1 application.[29]

Further, in the RESTORE study phase 2, an observer-blind, intrapatient-controlled, randomized study of 34 participants with dry, eczema-prone skin showed a test cream containing ceramides, triglycerides, and cholesterol in a multivesicular emulsion reinforced the skin barrier. Patients were treated on the right or left forearms and lower legs twice a day for 4 weeks with the test cream or a reference cream without physiological skin lipids. Compared with the reference cream, skin barrier integrity and hydration were higher, and TEWL and sodium lauryl sulfate sensitivity were lower with the test cream.[33]

The RESTORE phase 1 and phase 2 studies demonstrate that a ceramide-containing cream and lotion with MVE technology are superior to similar simple emollient creams in delivering long-lasting hydration. This property has the potential to reduce the burden of frequent moisturizer application, in particular for patients with AD-prone skin.

Statement 4: *Hyperglycemia contributes to skin changes, though the mechanisms of action are unclear, and other factors are likely involved. A defective skin barrier exposes the skin to water loss and invasion of pathogens and may lead to dry/hyperkeratotic skin and inflammation. Recognition and management of diabetes mellitus (DM) skin conditions are important in maximizing patient quality of life and in avoiding serious adverse effects. Appropriate care of the skin barrier and early-stage treatment of skin barrier dysfunction may help prevent complications.*

Approximately 30% to 70% of patients with DM have associated skin disease.[12] Spravchikov et al reported that hyperglycemia and impaired insulin signaling might be involved in the chronic skin complications associated with DM by inhibiting glucose utilization of skin keratinocytes, skin proliferation, and differentiation.[34] DM-related skin conditions vary in severity and can lead to major complications, including amputation.[35] Cutaneous manifestations in DM are classified into 4 categories and listed in Table 6.

In DM, the SC may be altered, impacting its barrier function.[35] A defective skin barrier predisposes the skin to water loss and pathogen invasion leading to dryness, hyperkeratosis, and inflammation.[12] Furthermore, dry skin is often associated with pruritus and an increased risk of infection.[12] Maintaining an intact skin barrier and hydration with routine gentle cleaning and moisturizing may help improve skin conditions in patients with DM.[12] Additionally, cleansers and moisturizers that mimic natural lipids may reduce the need for other medications.[12]

Recognizing that appropriate cleansers and moisturizers are crucial to optimal patient outcomes is an important part of DM management and education. For example, cleansers with an alkaline pH can be irritating, lower lipid production, and increase the risk of Candida intertrigo.[12] Appropriate cleansers and moisturizers, on the other hand, help achieve physiological pH in DM-affected skin.[12]

Daily use of gentle cleansers and moisturizers is recommended to restore and preserve skin barrier integrity for patients with dry skin conditions.[37] Future integration of skin care specifically geared toward diabetic skin, including antiaging ingredients, urea, essential ceramides, and MVE technology, may be beneficial to treat common DM skin conditions.[12]

Statement 5: *Evidence of skin barrier dysfunction in rosacea includes increased TEWL, increased SC pH, increased allergic dermatitis, decreased hydration, and increased patient-reported itching, burning, and stinging. Gentle cleansers, moisturizers, and UV protection are important to relieve/prevent dry skin and irritation and restore skin barrier function.*

Rosacea is a chronic skin condition characterized by inflammation and vasculopathy that affects approximately 2% to 12% of Europeans.[38] Chronic skin inflammation disturbs the skin barrier and contributes to pain, burning, itching, and flushing.[3] Skin barrier impairment is associated with disease occurrence and severity in rosacea.[3] Frequent and repeated flushing may lead to progressive inflammatory changes in the dermis and damage to the endothelium.[39] Appropriate, quality skin care, on the other hand, has reduced symptoms in many inflammatory disorders.[3]

The skin barrier is compromised in rosacea with increased TEWL, decreased skin hydration, increased SC pH, an increased incidence of contact dermatitis, and increased pruritus.[39,40] Patients with rosacea should use gentle, oil-free liquid cleansers with near physiologic pH to support skin barrier repair, normalize the cutaneous microbiome, and decrease inflammation.[3,16] Products with a high pH, such as antimicrobial cleansers, may cause cutaneous dysbiosis, hinder skin barrier repair, and promote skin breakdown.[3] Other ingredients to avoid include alcohol, acetone, benzyl alcohol, propylene glycol, butylene glycol, and acids.[3]

The international ROSacea COnsensus (ROSCO) guidelines recommend gentle cleansers, moisturizers containing humectants (eg, hyaluronic acid), and barrier lipids such as ceramides, and UV protection to manage dry skin, decrease irritation, and restore skin barrier function.[3,41] Moisturizers can be used as monotherapy or as adjuncts to prescription therapies.[40]

Moisturizers with humectants and barrier lipids can replace deficient lipids in inflammatory skin, attract water, seal in moisture, and soften the skin.[3] In fact, a study found that a ceramide-containing cream increased total ceramide content, free fatty acids, and cholesterol up to 48 hours after application.[42] In short, the ideal moisturizer for patients with rosacea is safe, effective, affordable, fragrance-free, and pleasant to use.[3]

Lastly, guidelines recommend sun avoidance and the use of sunscreen with a sun protection factor (SPF) of at least 30 for patients with rosacea.[3] Sun exposure is the leading flare trigger in up to 81% of patients.[43] A moisturizer with an SPF 50+ was

shown to be beneficial in patients with rosacea-prone sensitive skin. Patients reported a reduced feeling of dryness, itching, and burning after 3 weeks of product application.[44]

Statement 6: *Racial/ethnic differences affecting the skin barrier include variations in ceramide levels, filaggrin null mutations, TEWL, and sensitivity. Certain alterations in skin barrier lipid content correlate with increased TEWL, ceramide deficiency, and enhanced barrier permeability. These findings have implications in the treatment of infant skin and diseases such as acne, rosacea, AD, and psoriasis, including in patients with SOC. Cultural considerations are also important when addressing skin care in patients with SOC.*

Several studies have found that genetic and environmental factors influence SC barrier function and properties. Although studies comparing White skin to Black skin have found comparable SC thickness, the SC of Black skin has been found to have more cell layers that are more densely arranged.[8] Increased cell layers may indicate a stronger SC barrier and more rapid recovery from barrier damage, as evidenced by requiring more tape strips to disrupt the SC.[45]

Studies have also found that Black skin has increased spontaneous desquamation compared with White and Asian skin.[8] However, Alexis et al note that the studies vary by anatomic location or methodology and may not be generalizable to the range of SOC populations.[8] Additionally, studies evaluating the pH in SOC are limited and insufficient to draw conclusions on the effects of pH in patients with SOC.[8] Further, data on water content and TEWL amongst various ethnic groups is inconclusive and requires further research.[8]

As noted, skin lipid plays a significant role in barrier function. Studies have suggested that Black SC has greater lipid content than White SC, but ceramide levels were lowest in Black skin.[8,46] Abnormalities in ceramide composition directly affect the water content of the SC and contribute to barrier dysfunction and disease.[8]

Skin diseases may also present differently in patients with SOC. For instance, while psoriasis lesions may be pink in lighter skin complexions, the affected skin in patients with SOC may be dark brown or violaceous.[11] In AD, too, rather than being erythematous, lesions may be more hyperchromic, violaceous, reddish-brown, or gray. Furthermore, rather than being on the flexural surface, as is more common in White skin, AD lesions in people with SOC may be more common on extensor surfaces.[10]

Even though pruritus and related conditions such as prurigo nodularis and AD are more common in Black patients, erythema in patients with SOC may still be under-detected due to alteration by background pigment.[8,47] Unrecognized or undertreated excoriations in patients with SOC and AD may result in long-term (or even permanent) post-inflammatory pigment alteration and associated distress.[10] It is essential to recognize that AD presents differently in different populations and to offer patient-specific skin care.[10]

Although Alexis et al reviewed clinical practice guidelines, consensus papers, and algorithms on AD treatment and maintenance from various regions with different racial and ethnic populations, guidelines on AD management in people with SOC are limited. A clinical practice guideline from South Africa recommends avoiding soap and applying an aqueous cream moisturizer.[10] Guidelines and algorithms from North America recommend gentle cleansers and moisturizers that contain humectants, lipids, and ceramides to reduce itching, improve dry skin, and maintain the skin barrier in patients with AD regardless of skin color.[10] Additionally, clinicians should integrate guideline recommendations with cultural practices to improve treatment adherence and patient outcomes.[10]

Acne vulgaris is another skin condition that requires tailored treatment for people with SOC. While acne is the eighth most common skin disease worldwide, a US study found it is the most common dermatologic diagnosis in people with SOC.[9] Acne therapies with retinoids, alpha, and beta hydroxy acids, or benzoyl peroxide can cause xerosis and increase the risk of post-inflammatory hyperpigmentation.[9] Post-inflammatory hyperpigmentation and keloid formation associated with severe acne are more common in SOC than in White populations.[48]

Considering these risks, acne treatment for patients with SOC should reduce inflammation and avoid irritation that may result in post-inflammatory hyperpigmentation.[9] Gentle OTC cleansers and non-comedogenic moisturizers are useful adjuncts to topical acne therapies.[9] Acne-affected skin has fewer ceramides than healthy skin in all ethnicities, so ceramide-containing moisturizers should be considered.[9] Clinicians should be aware that certain skincare and haircare products commonly used in SOC populations may exacerbate acne; furthermore, skin care should be tailored to individual and cultural preferences.[9]

Similar recommendations apply to other dry skin conditions, including psoriasis. Psoriasis, a chronic inflammatory disease associated with alterations in skin barrier function, affects about 3.2% of people worldwide.[49] Psoriasis may be challenging to recognize in patients with SOC. Inflammation and lesions, typically pink or red in lighter skin, may appear violaceous or deeply brown-red in darker skin types.[47]

Although current therapies for psoriasis are considered safe and effective in diverse ethnic groups, data regarding psoriasis management in populations with SOC are limited, and skin care as an adjunct in management is underutilized.[11] However, a panel of experts recently proposed a potential role for pH-balanced, nonirritating cleansers and ceramide-containing moisturizers

to reduce dry skin and itching in psoriasis patients. Topical moisturizers increase hydration, decrease desquamation, reduce scale, improve PASI-50, and delay relapse in psoriasis.[11,50]

Limitations

Limitations in the number, size, and methodologies of studies on skin care for various conditions and populations do not allow for conclusive recommendations. More robust studies are needed to support clinical observations that population-specific regular skin care using gentle cleansers and moisturizers is an effective strategy to improve patient outcomes.

CONCLUSION

International clinical practice guidelines recommend barrier-supporting products (including those that contain ceramides) to promote a healthy skin barrier and reduce the symptoms and severity of various inflammatory skin diseases. Gentle cleansers and ceramide-containing moisturizers are beneficial and safe in neonates, young children, and adults. Additionally, they have demonstrated benefits in patients maintaining a healthy skin barrier, and managing skin disease or the cutaneous manifestations of systemic diseases, such as diabetes.

This review demonstrates a crucial need for robust clinical studies to understand and quantify differences in skin properties, across ages, races, and ethnicities, including the complex relationship between the skin's barrier function and skin health.

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