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Mini-Review

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Skin Barrier Function in Neonates and Infants

Eung Ho Choi *

Department of Dermatology, Yonsei University Wonju College of Medicine, Wonju, Korea

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Correspondence to
Eung Ho Choi, MD, PhD
Department of Dermatology, Yonsei University Wonju College of Medicine, 20 Ilsan-ro, Wonju 26426, Korea.
Tel: +82-33-741-0623
Fax: +82-33-748-2650
Email: choieh@yonsei.ac.kr

ORCID iDs
Eung Ho Choi
https://orcid.org/0000-0002-0148-5594

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ABSTRACT

This review focuses on the skin barrier function in neonates and infants, emphasizing the structural and functional differences compared to adult skin. Neonatal and infant skin is thinner, more permeable, and less developed, which makes it more vulnerable to irritants, infections, and dehydration. Additionally, the critical role of skin pH in maintaining barrier function is discussed, noting significant changes in pH levels during early life. This review also examines the relationship between the onset of atopic dermatitis and skin barrier function, underscoring the importance of maintaining skin barrier integrity from birth to reduce the risk of atopic diseases. Finally, recommendations are offered for skincare practices in neonates and infants, emphasizing the use of mild, fragrance-free products and the importance of tailoring skincare regimens to meet the specific needs of each neonate or infant.

Keywords: Infant; newborns; skin care; dermatitis, atopic; barrier; epidermis

INTRODUCTION

The onset of the atopic march, often characterized by the sequential development of food allergy, asthma, and allergic rhinitis following the occurrence of atopic dermatitis (AD), is hypothesized to be partially explained by congenital impairment of skin barrier function.[1,2] While a compromised skin barrier can facilitate external antigen penetration, leading to sensitization and subsequent triggering of a type 2 inflammatory response, it is not the only factor and does not apply to all patients. The atopic march is influenced by a complex interplay of factors, including the skin barrier, immune system dysregulation, microbiome composition, as well as genetic and acquired mechanisms. This hypothesis remains a leading framework, and ongoing research is crucial to fully understand the mechanisms underlying atopic disorders. Thus, while understanding the structure and function of the skin barrier is critical, preserving it in newborns should be seen as one of several strategies for preventing the onset of atopic diseases.

The skin barrier is composed of the stratum corneum (SC) and tight junctions. The major components of the SC include corneocytes, intercellular lipid lamellae, and corneodesmosomes (CDs).[1] Filaggrin (*FLG*) is the primary protein in corneocytes, while ceramide is the most abundant lipid in the SC. Proteases, including the stratum corneum chymotryptic

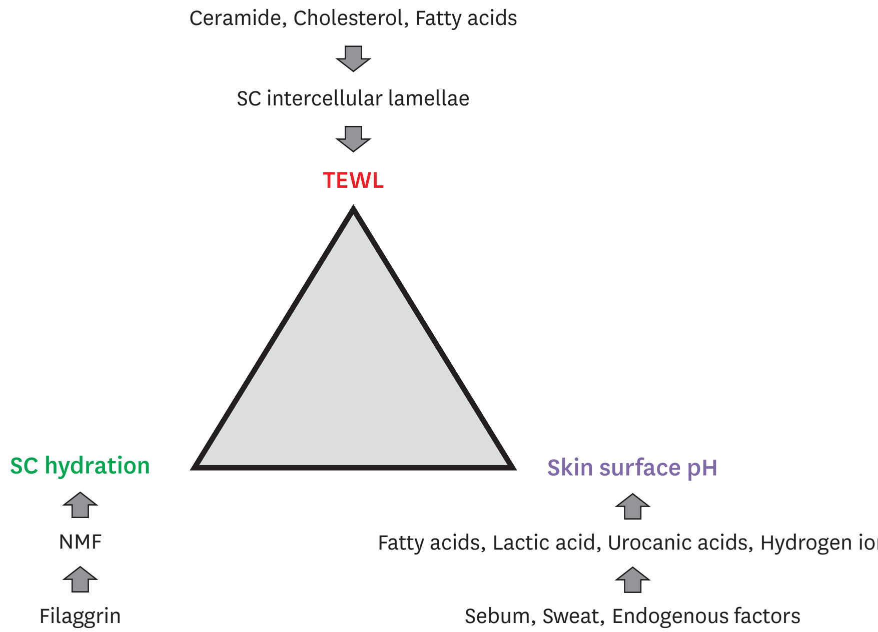

Fig. 1. Three important functions and their components for a healthy skin barrier. The skin barrier consists of the SC and tight junctions. For optimal skin barrier health, 3 key components within the SC must be properly maintained: (1) SC intercellular lamellae, formed by lipids such as ceramides, cholesterol, and fatty acids, which are essential for regulating normal TEWL; (2) NMFs derived from filaggrin, which are crucial for maintaining SC hydration; and (3) a mildly acidic skin surface pH, maintained by fatty acids, lactic acid, urocanic acid, and hydrogen ions derived from sebum, sweat, and endogenous factors.
SC, stratum corneum; TEWL, normal transepidermal water loss; NMF, natural moisturizing factor.

enzyme encoded by the KLK7 gene, degrade CDs. Serine protease inhibitors, such as lymphoepithelial Kazal-type-related inhibitor encoded by the SPINK5 gene, regulate protease activity. For a healthy skin barrier function, 3 components must be properly maintained: SC lipids for normal transepidermal water loss (TEWL), natural moisturizing factors (NMFs) for SC hydration, and an acidic SC for skin surface pH (**Fig. 1**).[3] Research on the role of the skin barrier in the etiology of AD is believed to have begun with a seminal study conducted by Imokawa and colleagues in 1991. This study demonstrated that both lesional and non-lesional skin in AD patients exhibited reduced ceramide levels, highlighting the essential role of lipids in maintaining skin barrier function.[4]

Maintaining an acidic pH in the SC is crucial for a healthy skin barrier. The SC exhibits a pH gradient, with pH levels decreasing closer to the surface. To maintain the acid mantle of the SC, sebum-derived free fatty acids and sweat-derived lactic acid play important roles, alongside 3 key endogenous mechanisms: (1) the non-energy-dependent Na^+/H^+ antiporter, (2) the generation of free fatty acids from phospholipids by secretory phospholipase A2, (3) the production of urocanic acid from histidine by histidase. Disruption of any of these pathways leads to an increase in SC pH, which is associated with impaired permeability barrier homeostasis and compromised SC integrity/cohesion (**Fig. 2**).[2] Under acidic conditions of the SC, ceramide-generating enzymes such as β-glucocerebrosidase and acidic sphingomyelinase are activated. These enzymes play a crucial role in breaking down glucosylceramides and sphingomyelin, lipid precursors located between corneocytes, into ceramides. This process is essential for maintaining the lipid composition of the SC and ensuring proper skin barrier function.[3,5]

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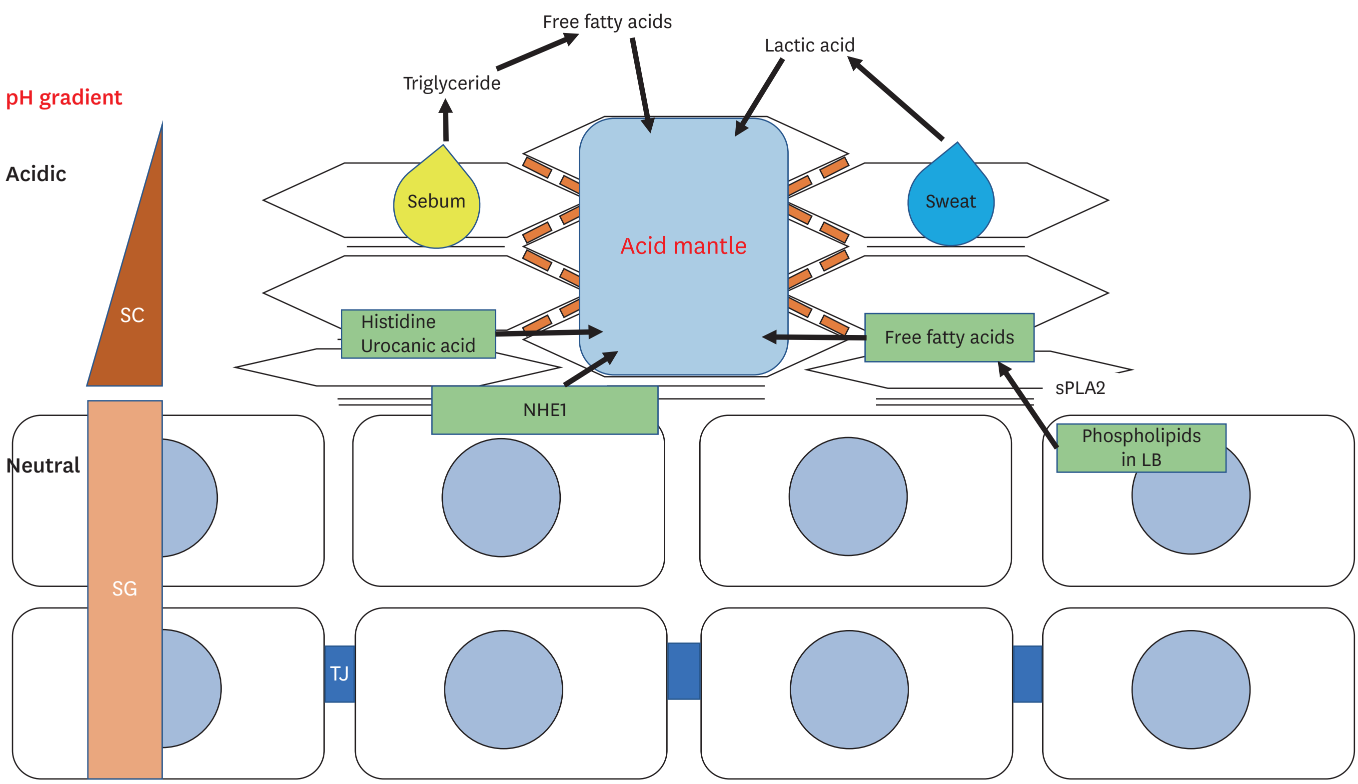

Fig. 2. Mechanisms maintaining an acidic pH in the SC. The SC exhibits a pH gradient, with pH levels decreasing closer to the skin surface. The acid mantle of the SC is maintained by multiple factors, including sebum-derived free fatty acids, sweat-derived lactic acid, and 3 endogenous pathways: (1) the non-energy-dependent NHE1; (2) the generation of free fatty acids from phospholipids by sPLA2; and (3) the production of urocanic acid from histidine via histidase. Deterioration of any of these pathways can elevate SC pH, leading to disruptions in permeability barrier homeostasis and compromised SC integrity and cohesion. SC, stratum corneum; NHE1, Na^+/H^+ antiporter-1; sPLA2, secretory phospholipase A2; LB, lamellar body; SG, stratum granulosum; TJ, tight junction.

NMFs in neonatal skin may serve as biomarkers for predicting the development of AD. *In vivo* Raman spectroscopy effectively distinguishes between *FLG* loss-of-function carriers and wild-type individuals in neonates aged 1 to 4 days, aiding in the assessment of *FLG* mutations.[4] Since NMF levels are inversely related to TEWL, they have potential as predictors of AD development.[6] Research indicates that measuring TEWL during infancy can forecast the future development of AD, regardless of *FLG* mutations. Specifically, a significant decrease in the probability of remaining AD-free was noted in the high TEWL group. Additionally, the use of emollients was associated with an increased likelihood of remaining AD-free, particularly among infants with high TEWL.[7]

The application of emollients from birth, while subject to debate, has been shown to potentially prevent the development of AD. In 2014, Simpson *et al.*[8] conducted a pivotal clinical trial supporting this approach. Their randomized controlled trial included 124 neonates at high risk for AD, who were divided into 2 groups: one received regular emollient applications, while the other group did not. After 6 months, the cumulative incidence of AD was evaluated, revealing a roughly 50% reduction among those who used emollients. This study underscores the potential of early emollient use in significantly lowering the risk of developing AD.[8] However, a comprehensive clinical trial involving 1,394 newborns yielded disappointing results, showing no evidence that daily emollient use during the first year of life prevents eczema in high-risk children. The emollients used in this study included Diprobase® cream (pH 4.92) and Doublebase® gel (pH 7.13), neither of which contained ceramides.[9] In contrast, promising results have been reported from another clinical trial focusing on emollients for preventing AD. In this

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study, 321 high-risk infants were divided into 2 groups: one group applied a specialized emollient containing ceramides and oat ingredients (pH 5.54) daily for 3 weeks. The cumulative incidence of AD was assessed at 6 and 12 months. The results indicated that short-term use of this specialized emollient during the neonatal period reduced the incidence of AD within the first year of life.[10] In 2022, a meta-analysis of data from 10 randomized controlled trials concluded that emollient use in high-risk infants effectively prevents the development of AD.[11] An analysis of large datasets from Korea revealed a significant decrease in the incidence of AD among children aged 5 and under over the past decade.[12] This trend may be attributed to the high level of education among Korean women—approximately 75% are college graduates—combined with a low birth rate of 0.78 births per woman. Consequently, most mothers likely use high-end moisturizers that are mildly acidic and contain ceramides for their one or 2 children.

Therefore, it is crucial to accurately summarize and understand the characteristics of skin barrier function in neonates and infants compared to adults.

SKIN STRUCTURE OF NEONATES AND INFANTS

Skin maturation begins during embryogenesis, with barrier development progressing alongside gestational age and culminating in the full maturation of the epidermis by 34 weeks of gestation.[13] As a result, preterm infants have a thinner epidermis and SC compared to adults. Studies show mixed results regarding full-term neonates: some report that their epidermal and SC thickness is similar to those of adults, while others observe that their epidermis remains thinner.[14] In summary, neonates and infants have distinct differences in skin structure and composition compared to adults, reflecting their developmental stage and functional immaturity. Their SC is notably thinner and less compact, with higher water content, leading to increased permeability and a less effective barrier function compared to adults.[15,16] The infant epidermis has fewer layers of keratinocytes compared to adult skin. At birth, the differentiation of these cells is not fully mature, resulting in a less effective barrier function. The infant epidermis is characterized by underdeveloped desmosomes and reduced keratinization, contributing to a weaker protective layer. Additionally, the dermis in infants shows higher turnover of collagen and elastin and contains immature fibroblasts, indicating ongoing development and structural instability (**Table 1**).[17]

Table 1. Structures, components, and function of skin barrier in neonates and infants compared to adults

Variables	Description
1. Structures	
Epidermal thickness	Thinner up to 20%
SC thickness	Thinner up to 30%
Keratinocyte size	Smaller
Corneocyte size	Smaller
Cell turnover	Faster
2. Components	
NMF	Lower
Water	Lower at birth, gradual increase throughout the first year
SC lipids	Lower levels of ceramides and free fatty acids
3. Function	
Hydration	Lower at birth, peaks between 3–12 mon
Water holding capacity	Lower
TEWL	Higher at birth, gradual decrease throughout the early years
pH	Higher at birth, fast decrease within 2 mon
Sebaceous activity	Higher at birth, fast decrease within the first few days

SC, stratum corneum; NMF, natural moisturizing factor; TEWL, normal transepidermal water loss.

In contrast, adult skin is characterized by a thicker and more compact SC with lower water content, providing a more robust barrier against environmental factors. The adult epidermis features fully developed desmosomes and higher levels of keratinization, which enhance its protective capabilities. Additionally, the adult dermis contains mature fibroblasts and stable collagen and elastin structures, contributing to greater structural integrity and resilience. These differences highlight the need for specialized skincare that addresses the unique needs of infants compared to adults.

MAJOR MESURABLE FUNCTION IN NEONATE AND INFANT SKIN BARRIER

The physiological characteristics of neonates and infants significantly impact their skin barrier and immune functions compared to adults. Barrier functions in neonates and infants differ considerably from that in adults, affecting skin health and vulnerability to external factors (**Table 1**, **Fig. 1**).

SC hydration

SC hydration, as measured by capacitance values, is crucial because it influences both the mechanical properties of the skin barrier and percutaneous absorption. At birth, the skin surface is generally rougher and drier compared to that of older infants. During the first 30 days of life, the skin smooths out in correlation with increased hydration. Over the following 3 months, SC hydration levels continue to rise and may even exceed those found in adults.[18] The functional maturation of sweat glands is likely a key mechanism driving the postnatal increase in skin hydration.[19] Between the ages of 3 and 12 months, infant skin is significantly more hydrated than adult skin, with this difference being particularly pronounced at the skin surface. The functional immaturity of the SC in newborns results in a reduced water-holding capacity compared to that of adults. Additionally, infant skin exhibits higher rates of water absorption and desorption compared to adult skin.[20]

The SC preserves skin hydration primarily through intercellular lamellar lipids, ceramides bound to CDs, and NMFs–hygroscopic molecular complex present both intracellularly and extracellularly.[21]

TEWL

TEWL is a key indicator for quantifying the amount of water evaporating from the skin surface and serves as a marker for barrier function. Several methods are available for assessing TEWL, and there is notable inter-individual variability, particularly in infants aged 3–6 months, who show greater variation compared to older infants and adults.[20] TEWL values are generally higher in preterm infants compared to full-term infants, with an inverse correlation between TEWL and gestational age.[22]

Most studies indicate that TEWL values in full-term newborns are similar to those in adults,[23] although some have reported either lower or higher TEWL in infants.[24] Elevated TEWL observed immediately after birth is likely due to the skin's functional adaptation to the dry, gaseous extrauterine environment.[25] TEWL also varies by anatomical site, with newborns exhibiting higher values in the forearm, palms, and inguinal region. This may be related to sweating and the predominant flexor positioning of extremities in newborns.[26] After the first

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week of life, higher TEWL values are observed in the diaper region, suggesting that the high humidity associated with diapering may impair barrier function.

Although there is no consensus on TEWL levels during this period, most studies agree that TEWL measurements show greater variability, likely due to heterogeneity within the infant population.[27,28] Regardless of TEWL levels, infant skin exhibits increased permeability to irritants[14] and is more susceptible to cutaneous infections and dermatoses, including AD and allergic contact dermatitis compared to adult skin.[29] This increased susceptibility during the period of skin barrier optimization suggests that strategies to accelerate optimization could potentially minimize the risk of developing these conditions.[30]

Skin pH

Normal pH values on the intact adult skin surface are mildly acidic due to the presence of the acid mantle, while interstitial fluid typically has a neutral pH values.[2] Infant skin pH levels are higher than those of adult skin, which typically ranges between 5 and 5.5. Newborn skin pH values are neutral, ranging from 6.34 to 7.5, depending on the anatomical site. The following section will provide detailed information on the mechanisms contributing to the neutral skin pH observed at birth as well as the critical role of acidification in barrier maturation and the activation of enzymes involved in lipid processing, including both endogenous and exogenous factors.

MAJOR COMPONENTS FOR NEONATE AND INFANT SKIN BARRIER

NMFs

NMFs, including amino acids, urea, and lactate, are critical for maintaining skin hydration. During corneocyte maturation, profilaggrin is dephosphorylated into *FLG*, which is then proteolyzed into amino acids and derivatives. These amino acids, along with ions, organic acids, and sugars, combine to form the NMFs. *FLG* breakdown enzymes become more active when moisture levels are low. Although NMF concentrations are generally lower in infants than in adults, contributing to dryness and increased sensitivity,[31] some studies have reported higher NMF levels during the first 2 weeks of life. This elevated NMF may serve as a compensatory mechanism to help rebalance alkaline pH and skin hydration during the early postnatal period.[25] However, these levels subsequently decrease to below those found in adults for approximately 12 months before eventually recovering.[20] Lactate, a component of NMF derived from sweat and the viable epidermis, shows an inverse relationship with overall NMF levels. Due to changes in NMF levels and lipid composition in the SC, infant skin exhibits different water-holding and handling properties compared to adult skin.[31]

Sebum levels

Sebum production is another crucial factor for skin barrier function in neonates and infants. Sebum levels are high during the first week of life due to strong androgenic stimulation of sebum secretion before birth, but decrease over time. Infant skin contains fewer total lipids than adult skin, which correlates with lower sebum levels observed at 6 months of age.[32] Epidermal desquamation, which reflects epidermal turnover, is inversely correlated with sebum levels on the skin surface. During the first 3 months of life, desquamation increases, particularly in facial areas, due to heightened epidermal turnover. However, desquamation is less pronounced in the diaper region due to the occlusive effect of the diaper. The lower

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rate of desquamation on the cheeks compared to the forehead may be related to the higher density of sebaceous glands in the cheeks.[18]

In infants, low sebum production impacts skin hydration and barrier function.[33] During adolescence, sebum production increases, leading to changes in skin texture and health. By adulthood, sebum production stabilizes, contributing to the maintenance of an effective skin barrier.[33] These differences underscore the need for age-specific skincare to maintain optimal skin health and protection.

Lipid composition of the SC

The lipid composition of the SC is essential for maintaining barrier function. Neonatal and Infant skin has a distinct lipid profile compared to adult skin, characterized by lower levels of ceramides and free fatty acids.[34] These lipids are crucial for maintaining the integrity and hydration of the skin barrier. The reduced lipid content in infants contributes to increased TEWL and greater vulnerability to environmental stressors. The composition and structure of SC lipids in infants differ from those in adults due to dynamic changes in sebum production and reduced lipid processing rates immediately after birth.[18,32] Notably, there is a deficiency in the essential omega-6 fatty acid linoleic acid, a component of omega-hydroxy ceramides, during this period.[35] Changes in the lipid composition of the lipid lamellae can affect both the structural integrity of the SC and its permeability barrier function. In contrast, adult skin features a well-balanced epidermal lipid composition, including an optimal ratio of ceramides, cholesterol, and free fatty acids, which supports effective barrier function and moisture retention.

THE ROLE OF ACIDITY IN THE BARRIER FUNCTION OF NEONATAL AND INFANT SKIN

Epidermal barrier maturation begins *in utero*[36] and is completed after birth. During the intrauterine environment, fetal skin is coated with vernix caseosa, and both vernix caseosa and amniotic fluid are mildly alkaline (pH > 7).[37] It is suggested that these factors contribute to the neutral pH (6.6–7.5) observed on the newborn's skin surface. After birth, skin acidification begins immediately, with pH levels decreasing to a range of 5–6 within the first few days and continuing to decline over the first month.[25] The alkaline pH observed on the first day after birth may be attributed to residual vernix caseosa on the skin surface.

Vernix caseosa, a protective coating of the skin, develops during the last trimester of gestation coincides with the terminal differentiation of the epidermis and formation of the SC. It is composed of approximately 80.5% water, along with proteins, sebum lipids, and antimicrobial peptides (AMPs) that provide biomechanical support and water-binding properties.[38] Vernix caseosa has a pH ranges of 6.7 to 7.4, whereas the underlying skin has a pH of 5.5–6.0.[39] Corneocytes are embedded in a hydrophobic lipid matrix that contains wax, sterol esters, squalene, cholesterol, triglycerides, and free sterol. Despite its high water content, the abundance of water-filled fetal corneocytes makes the vernix caseosa a highly viscous material. Neonates born before 28 weeks of gestation or those with low birth weight have an immature epidermal barrier and lack the protective vernix caseosa, resulting in a higher risk of hypothermia.

By one month of age, the average skin pH typically approximates that of adult skin, ranging from pH 4 to 6.[40] The birth process and the subsequent months are crucial for the transition

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from the intrauterine environment to the relatively dry, gaseous extrauterine environment. This adaptation is evident in changes observed in physiological functions and adjustments in biochemical and biophysical parameters, including skin surface pH, SC hydration, and innate immunity. The acid mantel of the epidermis is essential for regulating defensive functions, including resistance to bacterial invasion, chemical irritants, and mechanical damage (**Fig. 2**).[2] During fetal development, the skin is immersed in amniotic fluid and remains unexposed to external environmental factors. Birth marks a sudden and significant transition characterized by the drying and cooling of the skin surface. This biophysical shift triggers a cascade of cellular and molecular events that drive the adaptive maturation of the skin's defensive functions. It is well-established that the skin of healthy newborns undergoes progressive changes in epidermal barrier properties throughout the first months of life.[41]

The maturation of the acid mantle of the epidermis in newborns is a critical aspect of skin adaptation. While the surface pH of adult human skin is typically acidic, ranging between 5 and 5.5, term newborns exhibit higher pH levels, as their skin is not fully acidified at birth. This elevated pH can predispose newborns to various dermatoses during infancy, such as diaper dermatitis. Gradual postnatal acidification of the skin is essential for enhancing its protective functions and reducing the risk of dermatoses.[42] An acidic pH of the SC is crucial for the formation and maintenance of an intact skin barrier. Although basal permeability barrier function is competent at birth, the skin surface pH is nearly neutral in newborns, as observed in both humans and animal models.[42] SC acidity plays a vital role in maintaining epidermal barrier homeostasis, particularly in facilitating recovery after acute disruption.[43] At neutral or elevated pH levels, this recovery process is delayed due to disturbances in the enzymatic processing of extracellular SC lipids, even though the secretion of these lipids remains unaffected.[44] Such disruptions in lipid processing enzymes have also been observed in neonatal skin, highlighting the importance of pH in barrier function during early life.[41] Barrier homeostasis in neonates and infants is impaired because key lipid-processing enzymes in the upper SC, such as β-glucocerebrosidase and acidic sphingomyelinase, function optimally at acidic pH levels. When the pH increases, it leads to disruptions in the activity of these enzymes, resulting in incomplete lipid processing. This, in turn, compromises the structural integrity of the skin barrier and its ability to maintain homeostasis, making the skin more vulnerable to environmental stressors and increasing the risk of skin conditions.[45]

Acidification of the skin surface pH has several critical effects, particularly in regulating corneocyte desquamation, which maintains the integrity and cohesion of the SC. The enzymes primarily responsible for this process, kallikrein 5 (SC trypsin-like enzyme) and kallikrein 7 (SC chymotrypsin-like enzyme), are most active at normal-to-alkaline pH levels. Therefore, maintaining an acidic skin surface pH modulates the activity of these enzymes, preventing excessive desquamation and preserving the SC integrity and cohesion.[42] At higher pH levels, increased activity of kallikrein 5 and 7 degrades desmoglein 1—a key component of desmosomes—and reduces CD density, thereby accelerating the desquamation process. Acidification of the skin surface helps normalize lipid processing and inhibits CD degradation, thereby maintaining the structural integrity of the SC and preventing excessive desquamation. This balance is crucial for preserving an effective skin barrier and overall skin health.[46] The acidic buffer system of the SC plays a vital role in modulating non-specific antimicrobial protection, a key component of innate immunity. When the skin surface pH is elevated, it creates a more conducive environment for the growth of pathogens like *Staphylococcus aureus* and *Candida albicans*, which increase the risk of infections. In contrast, normal skin flora, which acts as a protective barrier against harmful microorganisms, thrives

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in an acidic environment. This highlights the importance of maintaining an acidic pH on the skin surface to support effective antimicrobial defense and overall skin health.[47] The absence of an acidic SC at birth is linked to an increased risk of bacterial and yeast infections in neonates, with this risk being even higher in preterm infants.[48] This is clinically evident in the pathophysiology of diaper dermatitis during infancy. Incomplete acidification of the SC, combined with ammonia-induced alkalization, activates stool enzymes such as trypsin and lipases. This activation leads to skin irritation, further disruption of the barrier, and initiation of an inflammatory cascade.[49]

THE SKIN BARRIER OF PRETERM NEONATES

The skin barrier of preterm neonates is significantly underdeveloped compared to that of full-term infants, presenting unique structural and functional challenges. These differences have critical clinical implications, including increased risks of infection, fluid imbalance, and thermal instability.

Structural immaturities

The epidermal thickness of preterm neonates is significantly reduced compared to full-term infants, reflecting critical structural immaturity. The SC, the outermost layer of the epidermis, is thinner in preterm neonates. In very preterm neonates (< 28 weeks of gestational age), this layer can be underdeveloped or even absent, exposing the underlying skin layers and leaving them vulnerable. The overall epidermal layers in preterm infants lacks the compact organization seen in full-term infants, making them more susceptible to environmental damage and impairing barrier function.[27,50]

The lipid composition and organization in the skin of preterm neonates are underdeveloped compared to full-term infants. Due to incomplete lipid production and impaired lamellar body secretion, the formation of lipid bilayers in the SC is poor. This deficiency leads to insufficient ceramide synthesis, which is crucial for maintaining water retention and barrier function in the skin. As a result, preterm neonates are at higher risk of TEWL and compromised skin barrier function, making their skin more susceptible to dehydration and irritation.[15,27]

Adhesion between the epidermis and dermis in preterm neonates is weaker than full-term infants, making their skin more prone to mechanical injury. This weak adhesion leads to increased fragility and a higher risk of skin breakdown from minor traumas, such as friction caused by clothing or medical devices.[51,52]

Immature sweat and sebaceous glands in preterm neonates impair the skin's ability to regulate moisture and lipid content. This results in increased TEWL and difficulty maintaining adequate skin hydration. As a consequence, these infants are more susceptible to dryness, irritation, and infections due to the compromised skin barrier function. Underdeveloped glands also reduce the production of protective lipids, which are crucial for maintaining skin barrier function.[15,53]

Functional immaturities

Increased TEWL due to incomplete barrier function leads to dehydration and electrolyte imbalances. This heightened permeability increases the risk of toxin absorption and

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infections by opportunistic pathogens, making preterm neonates more susceptible to external aggressors.[15,54]

The thin skin and reduced subcutaneous fat in preterm neonates compromise their ability to maintain body temperature. As a result, they lose heat rapidly through the skin, which requires external thermal support, such as incubators or specialized care environments to prevent hypothermia.[55,56]

Preterm neonates often exhibit reduced levels of AMPs and an immature acid mantle, both of which are essential for combating microbial invasion. This makes them more vulnerable to infections, as their skin lacks effective protection against pathogens.[57,58]

Delayed skin maturation and repair mechanisms prolong the period of skin vulnerability in preterm neonates. Slower recovery from minor injuries and wounds highlights the need for careful management to avoid complications like infections or skin breakdown.[52]

SKINCARE FOR NEONATES AND INFANTS

Skincare for neonates and infants is crucial because their skin is more permeable and fragile compared to adult skin.[15,59] It should prioritize mild, fragrance-free products to protect their delicate skin barrier.[60] Key practices include gentle cleansing, regular moisturization, proper diaper care, appropriate clothing, and environmental control. Bathing infants should be done 2–3 times a week to prevent excessive skin dryness. Daily baths are unnecessary unless the baby is noticeably dirty. Using lukewarm water for 5–10 minutes is ideal.[61] Regular moisturization is essential to maintain skin suppleness, prevent dryness, and minimize flaking. Effective moisturizers usually contain humectants, emollients, and occlusives, which provide lasting hydration throughout the day. Moisturization is an essential step in maintaining healthy skin, particularly for infants. It is recommended to apply fragrance-free, hypoallergenic, and mildly acidic moisturizers immediately after bathing to lock in moisture and protect the skin barrier. Emollients containing ceramides or hyaluronic acid are especially beneficial for infant skin.[62] To ensure optimal skin hydration, moisturizers should be applied at least once daily, with more frequent application if the skin appears dry. Due to the delicate nature of infant skin, it is easily irritated by harsh chemicals such as detergents, surfactants, and preservatives and fragrances.[15] Therefore, using products specifically formulated for infants is crucial. Ideally, these products should be hypoallergenic and free of potential irritants to reduce the risk of allergic reactions or skin irritations.[15] Regular application of barrier creams and emollients, particularly after diaper changes, helps preserve skin integrity and prevent the development of rashes.[54] Maintaining an optimal environment is crucial for infant skin health. Moderate humidity levels should be maintained to prevent excessive skin dryness. Room temperature should be kept comfortable to prevent excessive sweating or chilling, both of which can irritate sensitive skin. Protecting infants from sun exposure is essential for their delicate skin. Infants should be kept out of direct sunlight using protective measures such as clothing, hats, and staying in shaded areas. For infants over 6 months old, applying a broad-spectrum sunscreen with an sun protection factor of 30 or higher to exposed areas is recommended to safeguard their skin from harmful ultraviolet rays (**Table 2**).[63,64]

Premature infants, who often require extended stays in the neonatal intensive care unit (NICU), are especially vulnerable to skin breakdown due to their underdeveloped epidermal

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Table 2. Recommendation for neonate and infant skincare

Variables	Description
1. Cleansing	
Use mild cleansers	Opt for gentle, soap-free, and fragrance-free cleansers specifically formulated for infants. These products help maintain the natural pH balance of their skin.
Avoid harsh soaps	Harsh soaps can strip the skin of its natural oils, leading to dryness and irritation.
2. Bathing	
Frequency	Bathe infants 2–3 times a week to avoid over-drying their skin. Daily baths are generally not necessary unless the infant is visibly dirty.
Water temperature	Use lukewarm water, as hot water can exacerbate dryness and irritation.
Duration	Keep baths short, ideally 5–10 min, to minimize water loss from the skin.
3. Moisturization	
Apply emollients	Apply fragrance-free, hypoallergenic, and mild acidic moisturizers immediately after bathing to lock in moisture. Emollients containing ceramides or hyaluronic acid are especially beneficial.
Frequency	Moisturize the skin at least once daily, and more frequently if the skin appears dry.
4. Diaper area care	
Frequent diaper changes	Change diapers frequently to prevent prolonged exposure to moisture and irritants.
Barrier creams	Apply a thin layer of barrier cream containing zinc oxide to protect the skin from diaper rash.
Fragrance-free wipes	Use fragrance-free and alcohol-free wipes to gently clean the diaper area.
5. Clothing	
Soft fabrics	Dress infants in soft, breathable fabrics such as cotton to minimize the risk of irritation.
Avoid overheating	Overdressing can cause sweating and heat rash. Dress infants appropriately for the surrounding temperature.
6. Environmental control	
Humidity	Keep the humidity level moderate in the infant's environment to prevent skin dryness.
Temperature	Maintain a comfortable room temperature to prevent excessive sweating or chilling.
7. Sun protection	
Shade and clothing	Keep infants out of direct sunlight by using protective clothing, hats, and shade.
Sunscreen	For infants over 6-month-old, apply a broad-spectrum sunscreen with an SPF of 30 or higher to exposed areas.

SPF, sun protection factor.

barrier. Their skin is particularly susceptible to TEWL, making it crucial to use highly effective emollients and employ gentle handling techniques to reduce the risk of skin breakdown. A randomized controlled trial demonstrated that emollient therapy not only improves skin barrier function but also reduces the incidence of nosocomial infections and mortality in preterm infants.[65] Emollients such as petrolatum, Aquaphor, and sunflower seed oil have been extensively studied for their efficacy and safety in neonatal skincare.[48,66-68] These products help reduce TEWL[69] and improve hydration, which is crucial for maintaining skin integrity. Additionally, a systematic review highlighted that structured skincare protocols, including the regular application of barrier creams and the minimization of adhesive use, are effective in preventing skin damage in NICU settings.[70] Individualized skincare regimens tailored to the specific needs of each infant are crucial,[71] particularly in adapting practices according to the neonate's gestational age and health status. Clinical protocols frequently emphasize minimizing the use of adhesives and avoiding rough fabrics to prevent skin damage and ensure optimal skin protection.[72] Therefore, skincare products for neonates and infants should be carefully selected to ensure they are pH-appropriate. Ideally, these products should be pH-balanced (close to 5.5) to support the natural development of the acid mantle. Products with an unsuitable pH (*e.g.*, too alkaline) can disrupt barrier function and delay the formation of acid mantle, thereby increasing the risk of irritation and infection.

Clinical guidelines and recommendations for infant skincare, particularly for high-risk infants are as follows. Emollients enhance skin barrier function by providing hydration and replenishing lipids, potentially reducing TEWL and exposure to environmental allergens. Recent clinical trials have shown mixed results regarding the efficacy of emollients in preventing AD. While some findings suggest a modest benefit, others do not demonstrate a significant protective effect. For infants without specific risk factors, routine use of emollients is not generally required for AD prevention but may be recommended to maintain skin hydration and barrier integrity. For high-risk infants with a family history of atopy, guidelines suggest considering early application of emollients, particularly within the first few weeks of life, with closely monitoring for any adverse reactions. Emollients should be free of fragrances, preservatives, and allergens, with a preference for formulations containing ceramides or other lipid-replenishing components.

CONCLUSION

Neonatal and infant skin is thinner, more permeable, and less developed than adult skin, rendering it more susceptible to irritants, infections, and dehydration. Understanding these differences, along with the critical role of skin pH in maintaining barrier function and the developmental changes occurring in neonates and infants, is essential for effectively protecting and caring for their delicate skin. While significant progress has been made in understanding the neonatal and infant skin barrier, several gaps in knowledge remain. Addressing these gaps could improve clinical care and enhance health outcomes for this vulnerable population. First, it is essential to identify the most effective moisturizer formulations and application regimens to improve skin barrier function and prevent conditions such as AD. Secondly, it is necessary to explore how interventions, such as probiotics or microbiome-friendly skincare products, can strengthen skin barrier integrity and reduce disease risk. Thirdly, it is imperative to design personalized skincare regimens tailored to genetic predispositions, gestational age, and environmental factors. Such knowledge is critical for developing evidence-based skincare practices and therapeutic strategies that optimize skin health and overall well-being in neonates and infants.

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