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Review Article

Infant skin physiology and development during the first years of life: a review of recent findings based on *in vivo* studies

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Synopsis

Infant skin is often presented as the cosmetic ideal for adults. However, compared to adult skin it seems to be more prone to develop certain pathological conditions, such as atopic dermatitis and irritant contact dermatitis. Therefore, understanding the physiology of healthy infant skin as a point of reference is of interest both from the cosmetic as well as from the clinical point of view. Clinical research on healthy infants is, however, limited because of ethical considerations of using invasive methods and therefore until recently data has been scarce. Technical innovations and the availability of non-invasive *in vivo* techniques, such as evaporimetry, electrical impedance measurement, *in vivo* video and confocal microscopy, and *in vivo* fibre-optic based spectroscopy, opened up the field of *in vivo* infant skin physiology research. Studies incorporating such methods have demonstrated that compared to adult, infant skin continues to develop during the first years of life. Specifically, infant skin appears to have thinner epidermis and stratum corneum (SC) as well as smaller corneocytes at least until the second year of life. The water-handling properties are not fully developed before the end of the first year and infant SC contains more water and less amounts of natural moisturizing factors. Such findings re-evaluate the old notions that skin is fully matured at birth. Armed with this knowledge, we are in a position not only to better understand infant dermatological conditions but also to design better skin care products respecting the distinct qualities of infant skin.

Résumé

La peau de l''enfant est souvent présentée comme l'idéal cosmétique pour des adultes. Cependant, comparé à la peau de l'adulte, elle semble être plus propice au développement de certaines pathologies, comme la dermatite atopique et la dermite de contact. Ainsi, comprendre la physiologie de la peau saine de l'enfant en bas âge est un point de référence intéressant d'un point de vue à la fois cosmétique et clinique. La recherche clinique sur les jeunes enfants avec des méthodes invasives est cependant limitée pour des raisons éthiques rendant jusque récemment les données assez rares. Les innovations techniques et la possibilité de techniques in vivo non-invasives, comme l'évaporimétrie, la mesure d'impédance électrique, la vidéo microscopie confocale, et la spectroscopie à fibre optique, ont ouvert le champ des recherches sur la physiologie de la peau de l'enfant. Les études utilisant de telles méthodes ont montré que comparativement à l'adulte, la peau de l'enfant continue à se développer pendant les premières années de la vie. De façon spécifique, la peau du jeune enfant montre un épiderme et un stratum corneum plus mince ainsi que des cornéocytes plus petits au moins jusqu'à l'âge de 2 ans. Les propriétés cutanées vis-à-vis de l'eau ne sont pas entièrement développées avant l'âge de 1 an et le stratum corneum du jeune enfant contient plus d'eau et des quantités moindres de facteurs naturels d'hydratation. De tels résultats remettent en question les anciennes notions selon lesquelles la peau est entièrement mature à la naissance. Muni de ces données, nous sommes en position non seulement de mieux comprendre les conditions dermatologiques du jeune enfant, mais aussi de concevoir de meilleurs produits de soin en respect des qualités spécifiques de la peau du jeune enfant.

Introduction

Skin fulfils numerous and varied vital functions. Among these are physical and immunological protection from harmful environmental elements (including microorganisms, ultraviolet radiation, humidity, and temperature extremes), sensory perception (pain, temperature, and touch), temperature regulation, water and electrolyte homeostasis, and regulated exchange of gases.

Skin development starts *in utero* during the first pregnancy trimester and continues with the functional maturation of the *stratum corneum* (SC) at around 24 weeks of gestational age; a well-defined SC, however, is not visible before 34 weeks [1]. As part of the barrier maturation during the last trimester, we observe also the formation of the vernix caseosa, a protective coating of the skin, derived from sebaceous secretions and dead corneocytes, and largely composed of water, lipids, and proteins [2]. Skin maturation is a gradual process and the level of maturity is a function of the gestational age. In preterm infants, the epidermal barrier function is weak, as indicated by increased trans-epidermal water loss (TEWL) at ≤28 weeks of gestation [3] and high drug absorption at ≤32 weeks of gestation [4]. Despite that from a histological point of view, epidermal maturation is considered largely complete before

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term [1], full-term infants are not equipped with a fully mature skin at birth. For example, neither sebaceous nor sweat glands are functioning maturely in newborns [5, 6].

A thorough knowledge of healthy infant skin physiology is important as a point of reference for the understanding of dermatological diseases frequently affecting infants such as eczema (atopic dermatitis), diaper dermatitis, etc. Invasive studies in children are not acceptable and the relevance of *ex vivo* studies on human or animal tissue (whole, reconstructed, or excised) or live animal models for human skin physiology is questionable and more data are needed [7–9]. However, the availability of non-invasive *in vivo* techniques has improved the feasibility of studies on infant skin physiology.

In this work, we will focus on structural and functional characteristics of full-term infants (i.e. born between 37 and 42 weeks of gestation). Throughout the text, we will use the term 'infant' to describe individuals between birth and 3 years of age unless otherwise stated. We will review recent findings which show that skin maturation is an ongoing process that lasts well into the first years of life.

Infant skin structure

Skin is a dynamic tissue, engaged in a continuous process of keratinocyte proliferation in the basal layer of the epidermis and desquamation of corneocytes on the skin surface, which involves degradation of tight junctions (corneodesmosomes) that hold them together [10]. In the outermost layer of the epidermis, the SC, the corneocytes are embedded in the intercellular lipid matrix derived from lamellar bodies and consisting of cholesterol, ceramides, and free fatty acids [11]. The organization of the SC has been illustrated as a brick wall, with the corneocytes representing the bricks and the intercellular lipid matrix the mortar [12]. This model was first presented in the 1980s but has evolved since to include structures such as the corneodesmosomes and the lipid and protein components of the cornified cell envelope [13].

Details of infant skin morphology, such as surface structure, skin thickness, and cell size have either been visualized with microscopic methods or calculated with computer-assisted analysis of the microscopy images and of skin imprints in silicone casts and on adhesive tapes [14, 15]. Specifically, video microscopy can be used to take images of the skin surface *in vivo* and of corneocytes removed from the skin surface after adhesive tape stripping [15, 16] to show the density and pattern of microrelief lines. *In vivo* reflectance confocal laser scanning microscopy (CLSM) allows the three-dimensional representation of the skin topography and internal structures by generating sequential optical sections of increasing depth starting at the skin surface and moving in sequential sections parallel to the surface towards the top layers of the dermis. Computerized analysis of the CLSM images has been used to measure infant and adult SC and epidermal thickness, cell projected area, and depth of microrelief lines and to show the shape and density of dermal papillae and the density of dermal collagen fibres [15]. The results from these *in vivo* studies are not always supporting previous studies of *ex vivo* skin preparations, probably because of artefacts arising from handling of the histological samples.

Structure of the skin surface and of the epidermal layer

At birth, infant skin is relatively rough compared to older infants but smoothens during the first 30 days of life as shown by microtopographical analysis of silicone imprints [14]. Skin roughness and hydration appear to be correlated, as surface smoothening is paralleled by an increase in skin hydration [14].

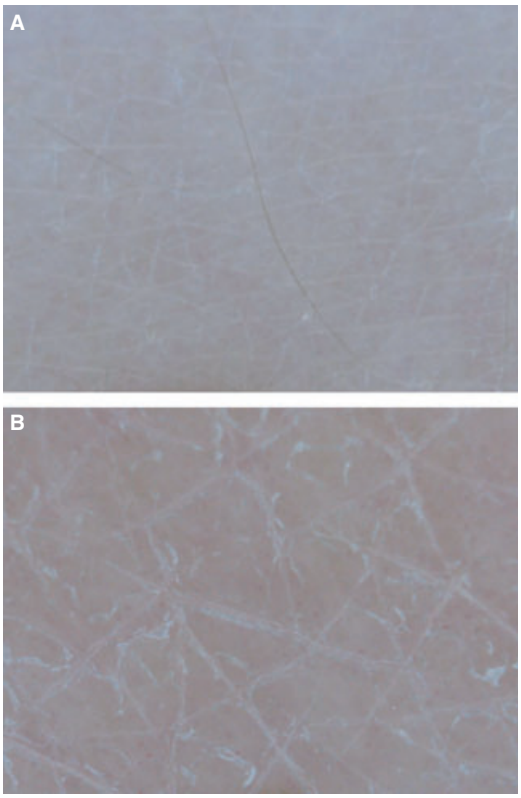

Figure 1 The structures on infant skin surface differ from those of adult skin (volar forearm). These video microscopy images reveal a denser network of micro relief lines in (A) infant skin (30 months of age) compared to (B) adult skin (38 years of age). The size of stratum corneum island structures in between the micro relief lines of the infant skin is markedly smaller than adult. Adult skin surface appears to be drier and more flaky than infant. The image size in both cases is 3.75 × 5.00 mm.

Compared to adult skin, the surface of infant skin looks markedly different as revealed by video microscopy and CLSM [15]. The network of microrelief lines is denser and the 'island' structures (glyphics) of the SC are smaller in size in infants (Fig. 1). It was suggested that the latter might be one factor contributing to the higher hydration state of infant SC compared to adults [17]. The surface glyphics are matched one-to-one with the underlying dermal papillae (collagen structures containing nerve endings and capillary vessels at the dermo-epidermal junction), which are also more homogenous in size, density, and distribution than in adults. There is thus a structural relationship between dermal papillae at the bottom of the epidermis and the skin surface glyphics in infants which is no longer discernable in adults.

SC and epidermal thickness

In infants, both SC and epidermal thickness as calculated from CLSM images are considerably different from adults: the SC is on

average 30% (about 7 μm for infants compared to 10 μm for adults on the volar forearm) and the supra-papillary epidermis 20% thinner in infants 6–24 months of age [15]. Although another study using pulsed ultrasound also showed thinner skin in infants *in vivo* [18], a different conclusion was drawn from a previous *ex vivo* analysis of skin autopsy samples, where no difference between infant and adults SC thickness was observed [19]. As mentioned before, the discrepancy could be attributed to artefacts introduced in the preparation of the histological sample in the *ex vivo* study. Another source of variability between the studies is differences in the body sites investigated.

Corneocyte and keratinocyte size

Corneocytes removed from the SC by applying adhesive tapes to the skin have been analysed by video microscopy and keratinocytes of the granular layer by CLSM. The projected size of both cell types is smaller in infants compared to adults [15]. At the same time, granular cells are more densely packed in infants. The smaller cell size in infants correlated with a higher epidermal cell turnover rate compared to adult skin considering that with a slower turnover-rate, corneocytes will have more time to flatten out.

The implication of smaller corneocytes and thinner SC in infants is that the path that lipophylic molecules have to follow to penetrate this layer and reach the viable epidermis is less tortuous than in adult with obvious implications for the SC barrier function. In the brick and mortar analogy, the bricks are smaller and the wall is thinner for infants.

Dermal collagen

Collagen and elastin fibres, among other structures, scatter any light that enters the skin surface. A difference in collagen and elastin fibre size between the papillary and reticular dermis [20, 21] is thus indicated by a change in the reflected signal in CLSM [15]. Collagen fibres in the upper part of the dermis from skin biopsies of infants are less dense compared to adults [20]. This observation was supported by CLSM, which shows that unlike in adults, no clear transition between papillary and reticular dermis can be observed in infants (the depth limit of CLSM is about 120 μm).

It was suggested that the structural differences outlined earlier might at least partly be the source for the functional differences (including barrier function and water-handling properties) observed between infant and adult skin. For example, the larger surface area because of higher density of the microrelief structures in infants might be the cause for the differences in water absorption and desorption [17] discussed below.

Infant skin composition

The regenerative capacity of skin, as well as its function as protective barrier against harmful substances and against the loss of water is determined by its components. Typical for a biological system, the function of these components is interdependent. The water in the SC enables enzymatic activities for lipid processing, corneodesmolysis, and production of components of the natural moisturizing factor (NMF) [22–25]. In return, corneodesmolysis drives the shedding of the outer skin layers, and the maintenance of an optimal hydration level is provided by the NMF and by the permeability barrier constituted by intercellular lamellar lipids.

From a physical point of view, SC water content determines the flow of electric current through the top layers of the epidermis. This physical phenomenon is exploited by indirectly measuring the skin water content by means of electrical methods: skin impedance, capacitance, and conductance [26]. High-frequency conductance measurements of the skin assess hydration of superficial SC layers, whereas skin capacitance involves deeper layers including parts of the viable epidermis [26, 27]. Although these electrical measurements show some correlation with each other, they are only indirect measures of water concentration. The amount of water in the skin can be directly measured with *in vivo* Raman confocal microspectroscopy down to a depth of about 120 μm within the skin with a resolution of 4 μm [28], which includes the SC and the viable epidermis. This method relies on the inelastic scattering (Raman scattering) of laser light upon interaction with chemical bonds. The shift in energy is characteristic for a given molecule and therefore this technique allows for the identification and quantification of certain molecules, including components of the NMF [29].

Other spectroscopic techniques that measure relative amounts of skin components *in vivo* include attenuated total reflection Fourier-transform infrared (ATR-FTIR) spectroscopy yielding information for the top 1–3 μm and diffuse reflectance spectroscopy (DRS) in the visible part of the spectrum, which measures at depths that include the epidermis and part of the dermis [30]. ATR-FTIR can be used to follow concentrations of SC lipids and sebaceous lipids, whereas DRS allows among others the estimation of epidermal melanin concentration. By comparing the melanin content of ultraviolet (UV)-exposed sites to relatively protected sites, one can distinguish between constitutive pigmentation and facultative pigmentation.

Water content

Infants are born with relatively dry skin as indicated by significantly lower SC hydration at birth compared to older infants [14, 31], children [31], and adults [31, 32]. Skin hydration then significantly increases during the first 2–4 weeks of life [14, 33] with values stabilizing afterwards [14]. It was suggested that the observed increase in skin hydration after birth is related to the increasing functional maturation of eccrine sweat glands [34] although other mechanisms should not be excluded. This increase leads to significantly higher skin hydration in older infants (3–12 months [17] and 8–24 months of age [35], respectively) compared to adults. As skin hydration increases, parameters of skin roughness evaluated with micro-topographical analysis decrease and without any significant differences between the two genders [14]. It was also noticed that both skin hydration and TEWL values are highly variable in infants compared to children or adults, which may be indicative of a fluctuating barrier function [17].

Analysis of water content as a function of skin depth with Raman confocal spectroscopy showed that infants of 3–33 months have a higher water concentration on the skin surface as well as at any assessed depth through the outermost 26 μm, a steeper water gradient at a depth of 4–14 μm and a higher total water concentration within the first 20 μm of the skin surface [17]. Interestingly, even accounting for the difference in SC thickness, the water content remains statistically higher for the top half of the infant SC (unpublished data). These observations are countering the hypothesis that the increased skin hydration is purely because of maturation of the eccrine sweat glands.

Natural moisturizing factor (NMF)

As mentioned earlier, the hydration level of the skin is decisive for enzymatic activity. To retain water and keep skin hydrated,

corneocytes contain hygroscopic molecules (comprising the NMF) that act as humectants [25]. These are produced during the corneocyte maturation process, when the histidine-rich profilaggrin protein is first dephosphorylated to filaggrin, which in turn is proteolyzed to a heterogeneous mix composed of amino acids and their derivatives. NMF also contains organic acids, sugars, and ions. Besides its role in water retention and moisturization, NMF also has an autoregulatory function by controlling protease activity involved in NMF synthesis. Low moisture is increasing the activity of filaggrin breakdown enzymes, which results in more NMF, which in turn increases SC moisture content (as NMF components bind to water molecules), resulting in a negative feedback in the enzymatic activity [36, 37].

Similar to water, NMF concentration can be measured with Raman confocal microscopy as a function of skin depth [29]. Using this method, it was shown that infant skin (3–12 months) has a significantly lower NMF concentration compared to adults in the top 12 μm of the skin that is likely to influence its water-handling properties [17]. However, as infant skin is more hydrated than adult skin despite the low NMF concentration, there must be other mechanisms at work to regulate water homeostasis in infants. Potential candidates are the thinner SC, the relatively high desquamation rate or the skin surface structure particular to infants (water can be trapped in the dense microrelief lines of infants and water filled lacunae in the SC).

Lipid content

Using FTIR, our group has found that the surface of infant skin contains significantly less total lipids (CH stretch in FTIR spectra) and less sebaceous lipids (CO stretch) compared to adults (authors' unpublished results). This correlates with the low sebum levels measured in infants [5]. As mentioned, intracellular lipids in the skin are important regulators of SC hydration and barrier function. The reduced lipid levels on the infant skin surface may thus contribute to the not yet fully matured barrier function of infant skin (discussed later). On the other hand, this finding also underscores the uniqueness of infant skin, which despite this impairment contains higher levels of water than adult skin. Beyond the skin surface, using Raman confocal microspectroscopy we could not see a statistical difference between infants and adults for the lipid-to-protein ratio within the SC (unpublished data).

Melanin content

Melanin is synthesized in specialized organelles, called melanosomes, in dendritic cells that are localized in the epidermis, the melanocytes. The melanosomes are subsequently transferred to the keratinocytes, where the melanin pigment is considered to play a photo-protective role [38].

In a study using DRS, it was found that infants have a significantly lower concentration of melanin compared to adults in body sites exposed to the sun [39]. This is of considerable importance as melanin functions as an UV filter that reduces the penetration of UV light through the epidermis [40]. Lower melanin concentration, together with thinner SC in infants [15], along with increased SC hydration and thus presumably reduced light scattering [17], may contribute to heightened sensitivity to the harmful effects of UV light. In this context, it is not surprising that increased exposure to sunlight and sunburns acquired in childhood correlate with increased risk for malignant skin tumours [41, 42]. Furthermore, effects because of sun exposure are seen in infants beginning at the first year of exposure as demonstrated by an increase in melanin concentration in exposed skin [39]. Such increase in melanin production has been shown to follow UV-induced DNA damage [43]. Thus, early sun exposure may contribute to the cumulative effect and skin damage of UV light.

Infant skin function

Mature skin functions as a protective physical barrier against dryness and other environmental challenges. Moreover, it enables and regulates biochemical processes within the epidermis by controlling hydration, water evaporation, pH, and cell proliferation. At what age this functional maturity is attained is not clear and it may be different for each of these parameters [44].

Another fascinating aspect of skin function is its innate immunity, which has been increasingly the focus of research. However, the development of skin innate immunity during the first years of life is a yet unexplored field where potentially non-invasive *in vivo* methods could be useful.

Skin barrier function

Epidermal barrier function resides primarily (although not exclusively) in the SC and depends, among other factors, on the SC structure, lipid organization, hydration level, and hygroscopic properties [45, 46]. We mentioned for example above that the small corneocytes and relatively thin SC of infants would indicate a weaker SC barrier compared to adults.

The most widely assessed infant skin parameter is TEWL. TEWL measures the loss of water vapour other than sweat from the body via the epidermis and is considered a surrogate marker for the skin barrier function [47]. High TEWL values are indicative of a weak or broken skin barrier, as is the case of eczema and psoriasis [48–50].

The dynamics of water handling by SC, such as absorption and desorption, are also indicative of the quality of barrier function [51]. The water-holding capacity of skin can be assessed by testing the water sorption and desorption rate. In this test, skin hydration levels are assessed by skin conductance or capacitance measurements. The assessment is performed at baseline and at repeated time intervals following application of a drop of water on the skin (for a specific amount of time followed by padding to remove the excess). In another protocol, trans-epidermal water movement can be measured as water build-up under occlusion with the probe head of the capacitance measurement instrument [33]. A further skin parameter, surface pH, is usually measured with conventional surface (flat) pH electrodes.

Skin barrier function and TEWL

Water loss through the skin contributes to the water balance in newborn infants. The values measured are highly influenced by a variety of external parameters as well as factors specific to the individual. This may explain the discrepancies in the literature with high measurements in some and low measurements in other studies. TEWL is higher in preterm infants compared to full term [3, 52]. TEWL has also been found to be high when relative humidity is low [53] and during physical activity [54]. TEWL rates further depend on the anatomical location of the measurement [32], temperature, and nutritional status at birth [55].

Studies comparing infant with adult skin have reported TEWL rates to be lower [31, 32], equal [35], or higher [32]. Our own

studies showed significantly higher TEWL in the arm of full-term infants until 12 months of age compared to adults [17]. This finding was further corroborated by data from the absorption/desorption experiment. Increases in TEWL rates also correlate with skin irritation, as areas afflicted by diaper rash have significantly higher TEWL rates [16].

Interestingly, there is a large inter-person variability, in particular in younger infants, compared to older infants and adults [17]. This indicates that water-handling properties in infant skin are still in a state of flux as the controlling mechanisms are still being developed.

Skin barrier function and water-handling properties

Newborns have been found to have significantly reduced water-holding capacity (water sorption–desorption test) compared to adults [31]. During the first 2 weeks of life, the desorption rate increases and stabilizes thereafter [33]. Skin of older infants absorbs larger amounts of water and loses it initially (during the first 45 s after blotting) more rapidly as adult skin [17]. This increased water absorption is accompanied by significantly higher water concentration in the top layers of the SC, as indicated by Raman spectroscopy [17]. It is possible that the high desorption rate in infants is related to the limited amount of NMF, as these molecules are crucial for binding and retention of water.

Skin barrier function and pH

Babies are born with skin pH close to neutral (ranging from 6.6 to 7.5 depending on the site of measurement) [14, 32, 33, 35]. This is possibly because of the exposure to the slightly alkaline amniotic fluid (pH 7.4) [56] although other mechanisms may also play a role such as lower NMF content (the amino acids in NMF are expected to lower the SC pH), lack of commensal microbial colonization or possible immaturity of the enzymatic system in the SC. In comparison, adults have a much more acidic skin with pH values in the range of 4.5–6.7 [32, 57, 58].

After birth, the skin surface pH turns progressively more acidic, leading to the formation of the 'acid mantle' [59]. Significant changes are noticeable as early as the second day after birth [32]. Subsequently, pH continues to decrease during the first month of life and then remains relatively stable until 3 months [14]. Despite this decrease, skin pH remains significantly higher throughout infancy compared to adults [35]. In particular, the occlusive and humid environment of diapered skin, which is exposed to the activity of faecal enzymes, was found to have high pH [16, 33]. There are no gender-specific differences [14, 35].

Skin acidification is sustained by various processes: generation of free fatty acids either by endogenous phospholipid breakdown by phospholipase A2 [60] or from microbial hydrolysis of sebaceous triglycerides [61], ceramide breakdown by ceramidase activity [62], breakdown of the structural protein filaggrin into amino acids and other derivatives, proton-sodium exchange performed by H^+/Na^+ pumps [60], and lactic acid and lactate production in sweat glands [63, 64].

Acidic skin pH affects several activities such as: a) maturation and maintenance of the epidermal permeability barrier by pH-sensitive enzymes that process constituents of the intercellular lipid matrix, an elementary component of the barrier [65, 66], b) control of the desquamation process by regulation of pH-sensitive serine proteases activity responsible for corneodesmosome degradation [66, 67], and c) regulation of bacterial proliferation on the skin [68, 69]. It is thus not surprising that the near neutral pH of infant skin, in particular in diapered areas, correlates with a propensity to develop skin irritation [70, 71]. Increased skin permeability in consequence of irritation may lead to secondary microbial invasion [72]. Once skin barrier disruption has occurred, infant skin is also possibly less able to promote skin repair [62, 73].

Cell proliferation

The rates of keratinocyte proliferation at the basal layer of the epidermis and corneocyte removal (shedding) on the outermost surface are balanced over the long term to ensure constant thickness of the skin. Corneocytes are 'tied' together by protein aggregates, the corneodesmosomes. The shedding of the corneocytes is driven by the desquamation process, which is the enzyme-dependent degradation of the corneodesmosomes and indicative of epidermal turnover.

Table I Parameters of infant skin physiology and their comparison to adult skin, as evaluated with non-invasive *in vivo* methods

Parameter	Infant compared to adult skin
Skin structure	
Skin surface	Denser microrelief network [15]
	Glyphics more raised, smaller, less defined [15]
Skin cell size	Corneocytes smaller [15]
	Granular keratinocytes smaller, more densely packed [15]
Skin thickness	SC 30% thinner [15]
	Epidermis 20% thinner [15]
Dermal structure	Dermal papillae more homogenous (size, density, distribution), matched one-to-one with surface glyphics [15]
Collagen fibres	No marked distinction between papillary and reticular dermis [15]
Skin composition	
Water content	Skin drier at birth [31, 32], more hydrated in older infants [17, 35]
	Higher inter-personal variability [17]
	Higher water concentration within the upper 26 μm [17]
NMF	Lower concentration [17]
Surface lipids	Lower concentration (authors' unpublished results)
Melanin	Lower concentration [39]
Skin function	
Skin barrier function	Weaker, as indicated by the findings below
TEWL	Lower at birth, similar or higher in older infants depending on the anatomical location
	Higher inter-personal variability [17]
Water handling	Lower water-holding capacity [31]
	Absorption of greater volumes [17]
pH	More alkaline [32, 35]
Cell proliferation	Higher turnover rate [15]

TEWL, trans-epidermal water loss; SC, stratum corneum; NMF, natural moisturizing factor.

Epidermal cell turnover in healthy skin is linked to the desquamation rate as an imbalance would lead to thinning or thickening of the SC. The desquamation rate can be measured by mechanically removing loose corneocytes from the superficial layer of the SC with adhesive tapes and by computing the opacity of the tapes. It was thus found that during the first 3 months of life, the desquamation rate varied depending on the anatomical location. While there was a significant increase during this period in the facial area and on the forearm, desquamation decreased significantly in the buttocks area [14]. This might be explained by the elevated hydration in this area because of the occlusive environment [33].

In vivo fluorescence spectroscopy can be used to evaluate the rate of epidermal keratinocyte proliferation by measuring the fluorescence intensity of tryptophan species [74–76]. Epidermal cell proliferation decreases significantly during the first year of life and reaches adult levels during the second year of life [15]. The higher cell proliferation rate in young infants can explain the smaller cell size and higher cell density observed in this age group.

Conclusions

We have summarized studies providing evidence that infant skin differs significantly from adult skin with regard to structure, function, and composition (Table I). Infant skin apparently employs distinct mechanisms to regulate water homeostasis, as NMF and surface lipid concentrations are below the levels of adults and can thus not explain the infant skin's high water content and the high capacity to absorb water.

Infant skin is functionally still developing as indicated by the high surface hydration, high TEWL, high pH, and high desquamation and proliferation rates. Consequently, the epidermal barrier function is compromised, leaving infant skin vulnerable to chemical and microbial aggression and skin disease. Impaired barrier function is characteristic of infant skin afflicted with diaper dermatitis [17, 33] and children with atopic dermatitis [77]. Interestingly, epidermal barrier function is already impaired in areas of non-involved skin of children afflicted with atopic dermatitis compared to healthy children as indicated by significantly different pH, TEWL, and hydration rates [77]. It would be of interest to investigate whether a predisposition to skin disease can be detected at an early age in the form of aberrant values of skin barrier function.

Considering the different aspects of skin structure, composition, and function as we discussed earlier, it is evident that the skin maturation process continues after birth and that the adaptation from life inside the womb to the terrestrial environment outside appears to extend over at least the first year of life, significantly longer than previously indicated.

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