6 Factors influencing the skin pH

Until today, we do not know exactly all mechanisms regulating skin surface pH, however, we do know that there are a number of endogenous (physiological) and exogenous factors affecting skin pH. The most important ones (Table 4) are discussed in more detail.

Table 4 Factors affecting skin pH [according to Rippke et al., 2003; Yosipovitch and Maibach, 1996; Jacobi et al., 2005]

Endogenous factors	Exogenous factors
Age	Detergents/Soaps
Anatomical site	Cosmetic products
Genetic/ethnic predisposition	Skin irritants
Sebum	Topical antibacterials
Skin moisture	
Sweat	

Age

Age has long been assumed to have an influence on skin pH. Previous studies indicated that the skin undergoes a process of adaptation and maturation postnatally. From childhood through age 70, however, pH appears relatively constant while it rises significantly thereafter [Diktein et al., 1984; Fluhr et el., 2000; Waller and Maibach, 2005; Wilhelm et al., 1991]. Fluhr and coworkers used a skin pHmeter to measure pH on volar forearms of 44 adults, aged 21–44 (mean 34.6), and 44 of the adults` children, aged 1–6 (mean 3.5). They found no significant difference in pH of children`s skin versus adult`s skin, however, the age range in this study was not broad enough to assess changes in elderly skin [Fluhr et al., 2000]. The group of Diktein tested forehead skin of 500 female patients, aged 20–70. They used a planar dura probe electrode for their measurements and found no significant correlation between age and pH within this age spectrum [Diktein et al., 1984]. Wilhelm and coworkers studied 11 anatomic locations in 14 young adults (26.7, SD 2.8 years) and 15 aged adults (70.5, SD 13.8 years). Half of the subjects were male and half female.

Measurements were performed in duplicate with a flat surface glass electrode connected with a skin pH meter. The mean pH value varied from 4.8 (ankle) to 5.5 (thigh) in the young group and from 5.0 (forehead) to 5.5 (abdomen) in aged individuals. pH was significantly higher in the aged group on the ankle and the forehead. However, on all other anatomic regions, no significant differences in skin pH were noted [Wilhelm et al., 1991]. The authors attributed the pH differences in the ankle to stasis and reduced oxygen supply frequently observed on the lower limbs in older individuals. Moreover, their results are in accordance with the findings given above, because Wilhelm and coworkers included adults older than 70 years in their study.

The neutral skin surface pH of human infants was first noticed by Taddei in 1935 [Taddei, 1935]. Two decades later, Behrendt and Green detailed the kinetics of development of an acidic surface pH over the first postnatal month [Behrendt and Green, 1958]. In recent years, experimental studies especially focused on postnatal acidification in neonates. Visscher and coworkers reported relatively neutral surface pH values in neonates with a decrease to about 5.5 over the first 4 postnatal days [Visscher et al., 2000]. These findings were confirmed by Yosipovitch and his group who reported about an elevated initial mean pH value of 7.08 (SD 0.17) in neonates compared with a mean pH value of 5.7 (SD 0.16) in adults including measurements on different body sites. The pH values were significant lower on day 2 in all body sites, but they were still significantly higher than in adults ($p < 0.05$) [Yosipovitch et al., 2000]. Vernix caseosa retention on the skin after birth accellerates skin acidification as compared with vernix free skin, although the vernix itself has a neutral pH [Visscher et al., 2005]. Hoeger and Enzmann assessed skin function parameters including skin surface pH, corneal layer hydration, epidermal desquamation, and surface roughness prospectively in a cohort of 202 healthy term neonates. They found a decrease in surface pH by 0.3–1.1 units, while desquamation increased significantly during the observation period of 12 weeks. In addition, stratum corneum hydration increased significantly, paralleled by a decrease in skin roughness [Hoeger and Enzmann, 2002]. Since the skin surface pH of both full-term and premature infants acidifies rapidly during the first week [Fox et al., 1998; Visscher et al., 2001], the progressive postnatal adaptation of stratum corneum pH to ex-utero conditions occurs independent on foetal age at birth.

The neonatal development of the stratum corneum pH gradient and the underlying mechanisms were thoroughly investigated in rat experiments by Behne and coworkers [Behne et al., 2003]. Since the 1990s, rats have served as a useful model to examine a range of parameters of the peri- and neonatal adaptation process [Aszterbaum et al., 1992; Hanley et al., 1997; Wickett et al., 1993]. These studies had shown that the epidermal permeability barrier develops late in gestation and is linked to an increased expression of pH-dependent, lipid-processing enzymes. As in humans, the pH of the stratum corneum of

neonatal rats is neutral and the development of the stratum corneum acid mantle occurs postnatally in both species.

Behne and coworkers examined the spatio-temporal development and changes in stratum corneum microdomain distribution of acidity during early postnatal development [Behne et al., 2003]. They used their newly developed method of fluorescence lifetime imaging (FLIM) [Behne et al., 2002; Hanson et al., 2002] to localize the events leading to an acidic stratum corneum, and to correlate these changes with acidity-requiring lipid processing in the stratum corneum interstices which is necessary to produce a fully competent epidermal permeability barrier. In brief, FLIM was performed by using a Millenia-pumped Tsunami titanium-sapphire laser system as the two-photon excitation source. Excitation of the sample was achieved by coupling the 820 nm output of the laser through the epifluorescence port of a Zeiss Axiovert microscope. The fluorescence was collected using a photomultiplier placed at the bottom port of the microscope. Areas of 107 μm^2 were imaged. Lifetime data were acquired using the frequency-domain method and fluorescein was used as the reference lifetime standard. Fluorescence-intensity images were adjusted to enhance structural features and to visualize dye distribution and penetration. Afterwards, lifetime-values were converted to pH values. The resulting pH maps were displayed on the same colour-scale to facilitate comparisons. The pH-value distribution within these images was depicted in the corresponding histograms.

Using light microscopy of fixed, H&E stained sagittal sections and electron microscopy, the structural integrity and maturity of rat skin was assessed over the first 5 postnatal days. A continuous sheet of periderm on top of the stratum corneum was found on days 1 and 2. By day 3, this layer became less cohesive and adherent to the underlying stratum corneum. In addition, incompletely processed, extracellular lipids turned up during the first 2 days. By day 3, however, sections revealed a normal pattern of mature, extracellular lamellar bilayers, indicative of complete lipid processing. Next, changes in surface pH over the first postnatal week were assessed using flat electrode measurements. It could be demonstrated that newborn rats develop an increasingly acidic pH over this period of time, which achieves adult levels by day 7 (Fig. 19).

FLIM was used to assess changes in pH distribution in stratum corneum of newborn rats from birth through the fifth postnatal day. During the first postnatal day, only neutral pH values (> 6.5) were present throughout the stratum corneum. Yet acidity was detectable in the periderm layer on the skin surface. By day 3, acidic microdomains were largely, though still incompletely developed at the stratum corneum/stratum granulosum interface. By day 4, surface sections displayed normal stratum corneum structure, and extracellular acidity was present at all levels of the stratum corneum. For a more precise localization of the origin and development of stratum corneum acidity, two-dimensional diagrams of pH distribution were constructed (Fig. 20).

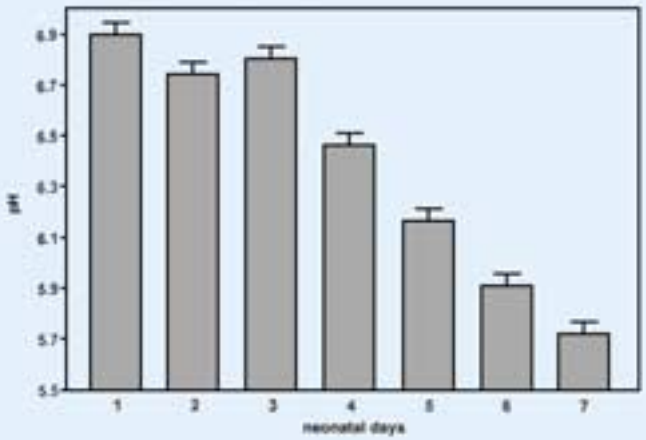

Figure 19 Stratum corneum surface pH develops over the first postnatal week. Flank skin of neonatal rats was measured using a flat electrode at days 1 to 7. A gradial increase in acidity over the first postnatal week was observed [with permission from Behne et al., 2003].

In previous investigations, the same group demonstrated the importance of the sodium/hydrogen antiporter NHE1 for stratum corneum acidification and that this antiporter primarily acidifies the stratum corneum/stratum granulosum interface [Behne et al., 2002]. They, therefore, assessed whether delayed postnatal acidification reflects a parallel delay in the expression of this proton antiporter [Behne et al., 2003]. They found that NHE1 is already fully expressed and apically positioned to influence acidification at birth. However, the stratum corneum/stratum granulosum interface is not acidified at birth even with adequate amounts of NHE1, suggesting that there are additional factors influencing initial stratum corneum/stratum granulosum acidification. To sum up, it could be demonstrated that newborn epidermis of rats is fully equipped with both mechanisms to acidify the stratum corneum, via NHE1 activity, and a mechanism to process lipids in its extracellular compartment, via β-GlcCerase activity. Their experiments demonstrated that postnatal stratum corneum acidification takes place analogous to stratum corneum acidification in the adult, where this inside-out process begins at the stratum corneum/stratum granulosum interface, with acidification proceeding outward to the stratum corneum surface with time. In addition there is speculation that the air exposure after birth furnishes the activating trigger for intrinsic acidification processes, including activation of NHE1, to provide the initial step in establishing stratum corneum acidity at the stratum corneum/stratum granulosum interface [Behne et al., 2003].

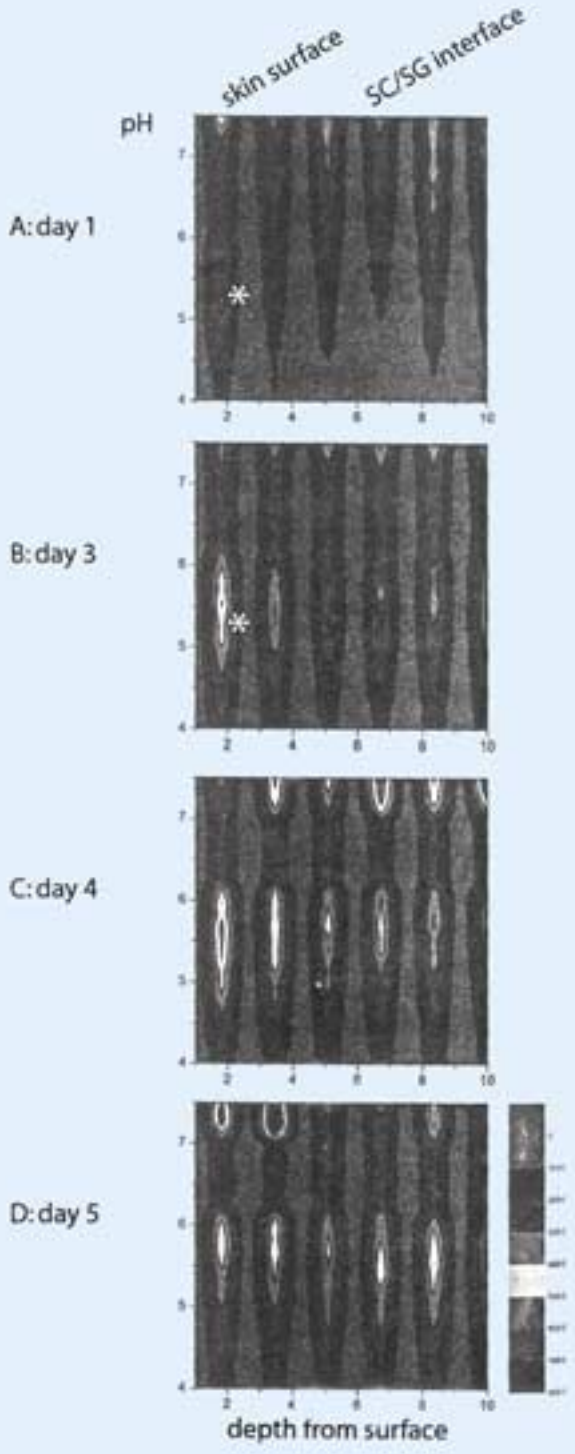

Figure 20 The pH gradient develops between neonatal days 1 and 3. Reconstruction of pH histograms derived from image series of neonatal days 1–5. On display are the peak intensities of the measured pH range, versus the tissue depth, from the skin surface to the stratum corneum/stratum granulosum interface. Day 1 (panel **A**), day 3 (panel **B**), day 4 (panel **C**), and day 5 (panel **D**). The histograms show development of stratum corneum acidity (intensity peak between pH 4.5 and pH 6) from day 1 to day 4 beginning at the stratum corneum/stratum granulosum interface. Surface acidity *(asterixes)* seen on day 1 (panel **A**) and day 3 (panel **B**) is derived from the periderm. All diagrams in comparison show acidity increasing initially at the surface, which peaks at day 4, and in parallel, but separately increasing acidity at the stratum corneum/stratum granulosum interface, which by day 4 forms a continuously spreading extracellular acidic pH domain (panel **C**), while pH distribution inside-out dominated thereafter (panel **D**) [with permission from Behne et al., 2003].