**The neonatal epidermal barrier: development of superficial chymotrypsin-like protease activity and natural moisturising factors**

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**Background:**The infant stratum corneum (SC) is thinner, and immature in both structure and function compared to adults throughout the first year of life. This vulnerable period coincides with the onset (<1 year of age) of skin manifestations such as atopic dermatitis. From birth, the SC enters a maturation phase of rapid hydration and acid mantle formation. Considering the reported homeostatic action of these functional properties, the observations suggest underdeveloped or transitional mechanisms underlying neonatal epidermal barrier differentiation and desquamation.

**Objective:** To monitor the functional properties of the SC throughout the neonatal period, in conjunction with the determination of superficial chymotrypsin-like protease activity (such as kallikrein-7 [KLK-7]) and the level of filaggrin-derived natural moisturising factors (NMF).

**Methods:** Full-term, healthy neonates (*n*=115) recruited to the oil in baby skincare (OBSeRvE) randomised controlled trial underwent a full SC assessment at birth (<72 hours old) and at 4 weeks of age (*n*=39, no oil control group) using a portfolio of minimally invasive instrumentation, techniques and methodology. To place the results in neonates into context, a cohort of unrelated adults (*n*=20) was recruited.

**Results:** In conjunction with the increase in SC hydration and skin-surface acidification over the neonatal period, transepidermal water loss (TEWL), superficial KLK-7 activity and NMF significantly elevated from birth beyond the levels observed in adult skin. At birth, KLK-7 activity and NMF both significantly correlated with TEWL (r=0.26 [KLK-7]/-0.38 [NMF]), SC hydration (r=-0.30/0.50) and skin-surface pH (r=0.25/-0.54). Neonates with impaired epidermal barrier function at birth (>75th percentile TEWL) demonstrated significantly elevated KLK-7 activity (1.41 nU/µg) and reduced levels of NMF (139.80 nmol/mg) compared to subjects within the lower TEWL percentiles (KLK-7: 0.90 nU/µg; NMF: 277.90 nmol/mg).

**Conclusions:** The biophysical, biological and functional properties of the developing neonatal SC are transitional from birth to 4 weeks of age and differ to adults. The elevation in KLK-7 activity during this period occurs via a mechanism seemingly independent from skin-surface pH. The presence of impaired barrier function with elevated protease activity and reduced NMF at birth suggests why certain infants are predisposed to epidermal barrier breakdown and the development of AD.