Research letter

Dry skin and skin barrier in early infancy

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Dear Editor, Atopic dermatitis (AD) usually begins in infancy, commonly involving the cheeks and extensor surfaces of the extremities (hereafter, extensors). It is associated with a dysfunctional skin barrier, which can be measured as increased transepidermal water loss (TEWL) in both lesional and nonlesional skin in patients with AD.[1] Dry skin, a cardinal sign of AD, is associated with higher TEWL in adult patients with AD.[2] However, the documentation of the prevalence and manifestation of dry skin in infancy and its association to TEWL is limited. Therefore, we aimed to determine the prevalence of dry skin in early infancy and to assess if dry skin in general, or more specifically on the cheeks and extensors, was associated with a dysfunctional skin barrier.

From the population-based Preventing Atopic Dermatitis and Allergies in children (PreventADALL) study[3] we found that 59% of the 1143 included 3-month old infants had dry skin, defined as roughness and visible scaling without erythema, in at least one of 11 predefined anatomical skin areas. Most infants (47%) had 'dry skin only', while 40% had 'unaffected skin' and 13% had 'possible AD' (of these, 96% had dry skin), defined as doctor-verified dermatitis, excluding differential diagnosis and including only a few infants fulfilling the diagnostic criteria for AD, as the majority were unable to itch at this early age. Among the 540 infants with 'dry skin only' the two most common locations were the cheeks in 62% and extensors in 49%. Dry skin was observed in 96% of the 144 infants with 'possible AD'; most commonly on the cheeks (82%) and the extensors (88%). Standardized TEWL examination, using an open-chamber DermaLab USB (Cortex, Hadslund, Denmark), was measured on the lateral upper arm as previously described,[4] and is presented as mean TEWL (g m^{-2} h) with 95% confidence interval (CI) for the 1019

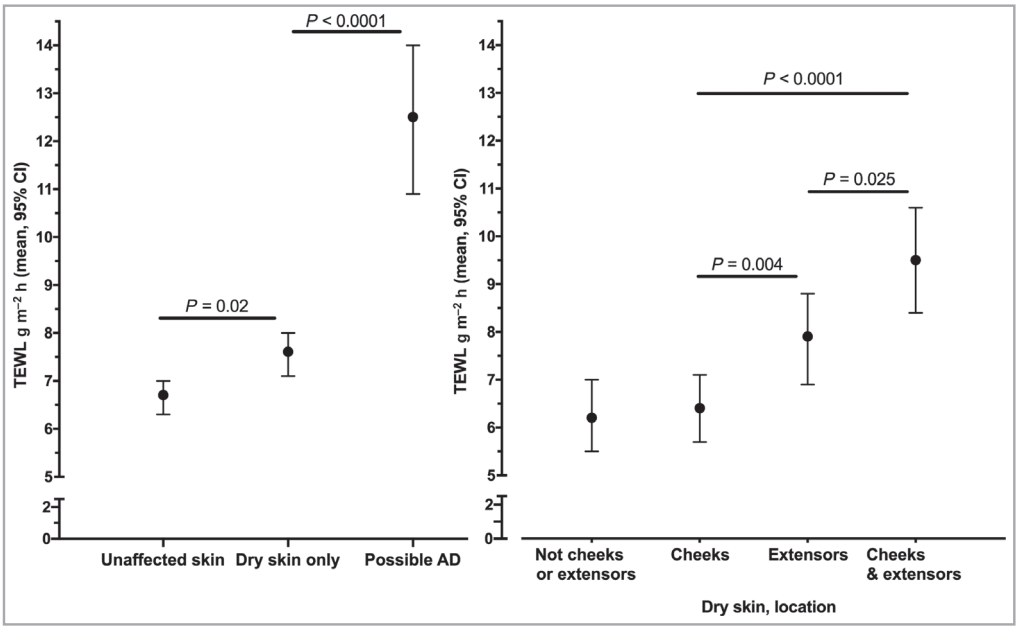

Fig 1. Skin barrier function, given as mean (95% CI) TEWL, measured on left lateral upper arm in 1-month old infants (n = 1019) in the PreventADALL study. (a) Mean TEWL, in 'dry skin only' (n = 483) was significantly higher than in 'unaffected skin' (n = 411, P = 0·02) and significantly lower than in 'possible AD' (n = 125, P < 0·0001). (b) Mean TEWL in infants with dry skin without AD located anywhere but 'not cheeks or extensors' (n = 79) was similar in infants with dry skin anywhere including 'cheeks, but not extensors' (n = 161), and significantly lower in those with dry skin including 'cheeks and extensors' (n = 134, P < 0·0001), as well as in those with dry skin anywhere including 'extensors, but not cheeks' (n = 98, P < 0·004). Mean TEWL in 'cheeks and extensors' was significantly higher than in 'extensors' (P = 0·025). AD, atopic dermatitis; CI, confidence interval; TEWL, transepidermal water loss

(89%) infants with available data. The TEWL was significantly higher among infants with 'dry skin only' (7·6; 7·1–8·0), compared with 'unaffected skin' (6·7; 6·3–7·0) and significantly lower than in infants with 'possible AD' (12·5; 10·9–14·0) (two-way ANOVA) (Fig. 1a). In the subgroup analysis (independent sample Student's *t*-test) shown in Figure 1b, TEWL was similar among infants with 'dry skin – cheeks' (6·4; 5·7–7·1) and 'unaffected skin' (6·7; 6·3–7·0), which was significantly lower than in infants with 'dry skin – extensors' (7·9; 6·9–8·8). The highest TEWL in infants without AD was found in infants with 'dry skin – extensors and cheeks' (9·5; 8·4–10·6), and it was significantly higher also compared with 'dry skin – extensors'. All our results remained significant after adjusting for possible confounders with linear regression analysis: sex, gestational age at birth, age at examination, room humidity and temperature. Statistical analyses were performed in IBM SPSS© v. 25 (Chicago, IL, U.S.A.).

To our knowledge, this is the first study to report on the prevalence of dry skin in early infancy, in a large general population-based study. However, a Swedish case–control study observed dry skin in 40% of 99 healthy 2-year-old children and in all children with AD.[5] The high prevalence of dry skin in children living in Nordic countries may be due to low temperatures in the winter and lower air humidity which is associated with an increase in signs of dry skin, TEWL and flares of AD.[6]

Tight control of room humidity when measuring TEWL in our study was not possible, as the investigations were performed in settings resembling regular clinical practice. Supported by previous findings,[4] all our results remained significant after adjusting for humidity, allowing us to include investigations throughout the different seasons.

The two most common areas of dry skin, the cheeks and extensors, are exposed to wear and tear from environmental factors, possibly impairing the skin barrier, which in turn can manifest as clinically dry skin, and ultimately as AD. This is supported by the outside-inside hypothesis where an initially impaired skin barrier leads to the entry of external stimuli that further drives the T-helper 2 inflammation causing the onset of AD.[7] Studies suggest that increased TEWL in infancy precedes AD development[4] and allergic sensitization[1] and that there is a regional and temporal immaturity in the skin barrier of infant cheeks.[8] Future follow-up investigations in the PreventADALL study[3] may demonstrate if our findings of impaired skin barrier in infants with dry skin, especially when present concurrently on the cheeks and extensor surfaces, may point to a potential role for dry skin examination when selecting children for primary prevention,[1] at risk for long-life allergic diseases.

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[1]*Oslo University Hospital and University of Oslo, Oslo, Norway*
[2]*Karolinska University Hospital and Karolinska Institutet, Stockholm, Sweden*
[3]*Østfold Hospital Trust, Kalnes, Norway*
E-mail: e.m.rehbinder@medisin.uio.no

E.M. Rehbinder[1]
A.J. Winger[1]
L. Landrø[1]
A. Asarnoj[2]
T.L. Berents[1]
K.H. Carlsen[1]
G. Hedlin[2]
C.M. Jonassen[3]
B. Nordlund[2]
L. Sandvik[1]
H.O. Skjerven[1]
C. Söderhäll[2]
R. Vettukattil[1]
K.C.L. Carlsen[1]
on behalf of the PreventADALL study group*

E.M.R. and A.J.W. contributed equally.

*P. Auvinen, K.E.S. Bains, M.H. Carlsen, O.C. Lødrup Carlsen, K.A. Endre, P.A. Granlund, B. Granum, H.K. Gudmundsdóttir, G. Haugen, K. Hilde, I. Kreyberg, C.A.O. Mägi, L.S. Nordhagen, U.C. Nygaard, K. Rudi, C.M. Saunders, I. Skrindo, K. Sjøborg, A.C. Staff, S.G. Tedner, M.R. Værnesbranden and J. Wiik.

Further author, institution and funding details are available directly from the corresponding author.

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Clinical Trial Registration
https://clinicaltrials.gov number: NCT02449850.