

## Clinical Communications

### Bathing frequency is associated with skin barrier dysfunction and atopic dermatitis at three months of age

Tom Marrs, PhD<sup>a,b</sup>, Michael R. Perkin, PhD<sup>c</sup>, Kirsty Logan, PhD<sup>a</sup>, Joanna Craven, MPH<sup>a</sup>, Suzana Radulovic, MD<sup>a,b</sup>, W.H. Irwin McLean, DSc<sup>d</sup>, Serge A. Versteeg, BSc<sup>e</sup>, Ronald van Ree, PhD<sup>f</sup>, Gideon Lack, MD<sup>a,b</sup>, and Carsten Flohr, PhD<sup>g</sup>; on behalf of the EAT Study Team

#### Clinical Implications

- Higher bathing frequency was associated with a stepwise increase in skin barrier dysfunction and a greater prevalence of atopic dermatitis at 3 months of age. Interventional work is required to assess the impact of bathing on atopic dermatitis development alongside other skin care routines.

It is widely believed that bathing practices have an impact on the development and progression of atopic dermatitis (AD). Skin barrier impairment, filaggrin (*FLG*) mutation carriage, and AD are strongly interrelated.<sup>1</sup> The former, as determined by transepidermal water loss (TEWL), has been shown to be linked to the development of AD<sup>2</sup> and food allergy.<sup>3</sup> AD management guidelines recommend that bathing should be minimized<sup>4</sup>; however, the evidence base for the impact of bathing on skin barrier function, AD, and its development is limited.

We hypothesized that increased bathing frequency at 3 months of age was associated with raised TEWL and AD. We recruited a cohort of 1303 three-month-old healthy babies from England and Wales to test a dietary intervention for the prevention of food allergy (EAT Study; ISRCTN no. 14254740).<sup>5</sup> Parents completed an online questionnaire at enrolment and 12 months, assessing frequency of bathing (“hardly ever,” “once a week,” “2-4 times a week,” “5-6 times a week,” “daily,” or “more than daily”), frequency of moisturizing, the use of shampoo, soap, bubble baths, bath oils, and baby wipes, and whether they felt their baby had dry skin. We collected information on ethnicity, family history, siblings, and domestic water hardness (CaCO<sub>3</sub> mg/L) for each household. Participants were genotyped for *FLG* mutations (R501X, 2282del4, R2447X, S3247X, 3673delC, and 3702delG) by the TaqMan allelic discrimination assay (ABI 7900 HT; Applied Biosystems, Foster City, Calif) and were examined for AD at 3 and 12 months in accordance with the UK diagnostic criteria—based photographic ISAAC protocol.<sup>6</sup> Skin barrier function was measured through TEWL on uninvolved skin of participants’ left volar forearm at 3 and 12 months. TEWL was reported as medians with interquartile ranges and dichotomized to generate an elevated TEWL variable using a threshold of  $\geq 15$  g/m<sup>2</sup> h (75th percentile of TEWL distribution with no AD at 3-month visit), as previously

reported.<sup>7</sup> Categorical data were compared using  $\chi^2$  analyses. Continuous TEWL was log-transformed before adjusted linear regression and presented as geometric mean ratios with 95% confidence intervals. Variables showing borderline ( $P < .10$ ) associations were included in adjusted models. Food sensitization to cow’s milk, egg, peanut, sesame, cod fish, or wheat was measured by specific IgE ( $\geq 0.35$  kIU) at 3 months.

At 3 months of age, few families bathed their infant “hardly ever” ( $n = 23$ ) or “more than daily” ( $n = 3$ ), and these categories were therefore combined with the adjoining category (once weekly and daily, respectively). A binary bathing frequency variable comparing bathing once a week or less with more frequent bathing was also generated. Continuous numbers of baths were inferred from the categories of bathing frequency to assess the impact of each additional bath per week.

Bathing frequency was correlated between 3 and 12 months (nptrend  $P < .001$ ). Half of participants were bathed at the same frequency (51.9%; 567 of 1093) at both time points, whereas one-third were bathed more frequently at 12 months (36.0%; 393 of 1093).

One quarter (24.4%; 317) of participants had AD on skin examination at 3 months. TEWL was skewed and the median value was 12.8 g/m<sup>2</sup> h (interquartile range [IQR], 10.8-16.1 g/m<sup>2</sup> h). TEWL was significantly higher among participants with AD (median, 15.7 g/m<sup>2</sup> h; IQR, 12.3-22.0 g/m<sup>2</sup> h) compared with those without (median, 12.4 g/m<sup>2</sup> h; IQR, 10.4-15.0 g/m<sup>2</sup> h,  $P < .001$ ).

Bathing frequency was associated with having an elevated TEWL with daily bathing being associated with a crude odds ratio for raised TEWL ( $\geq 15$  g/m<sup>2</sup> h) of 4.62 (2.61-8.21,  $P < .001$ ) when compared with bathing up-to-weekly. There was a dose-response progression across bathing categories, whether participants had AD or not (trend  $P < .001$ ; Figure 1).

Bath oils were used more often among children with elevated TEWL (24.1% vs 14.8%,  $P = .001$ ), as were emollients (84.0% vs 75.0%,  $P = .002$ ), whereas shampoo use was less common (26.1% vs 35.4%,  $P = .004$ ). After adjustment for these skin care variables in addition to participant AD, sex, non-European ethnicity, siblings, parental report of dry skin, water hardness, *FLG* mutation, parental history of AD, frequency of emollient application, and use of wet wipes, elevated TEWL remained significantly associated with daily bathing (adjusted odds ratio [aOR], 4.32 [2.27-8.22],  $P < .001$ ) when compared with up-to-weekly bathing.

In an unadjusted regression model, log-transformed TEWL was significantly associated with increasing bathing frequency. The geometric mean ratio of TEWL per unit increase in bathing frequency was 1.03 (95% confidence interval, 1.02-1.04,  $P < .001$ ), with a baseline (bathing less than weekly) TEWL of 11.93 g/m<sup>2</sup> h. After adjustment, the relationship remained statistically significant with a geometric mean ratio of TEWL per unit increase in bathing frequency of 1.03 (1.02-1.03,  $P < .001$ ) with a baseline (bathing less than weekly) TEWL of 10.63 g/m<sup>2</sup> h. A sensitivity analysis excluding infants with AD at enrolment or parental report of ever having had dry skin yielded the same results (geometric mean ratio of 1.02 [1.01-1.03],  $P < .001$ , with a baseline [bathing less than weekly] TEWL of 10.89 g/m<sup>2</sup> h).

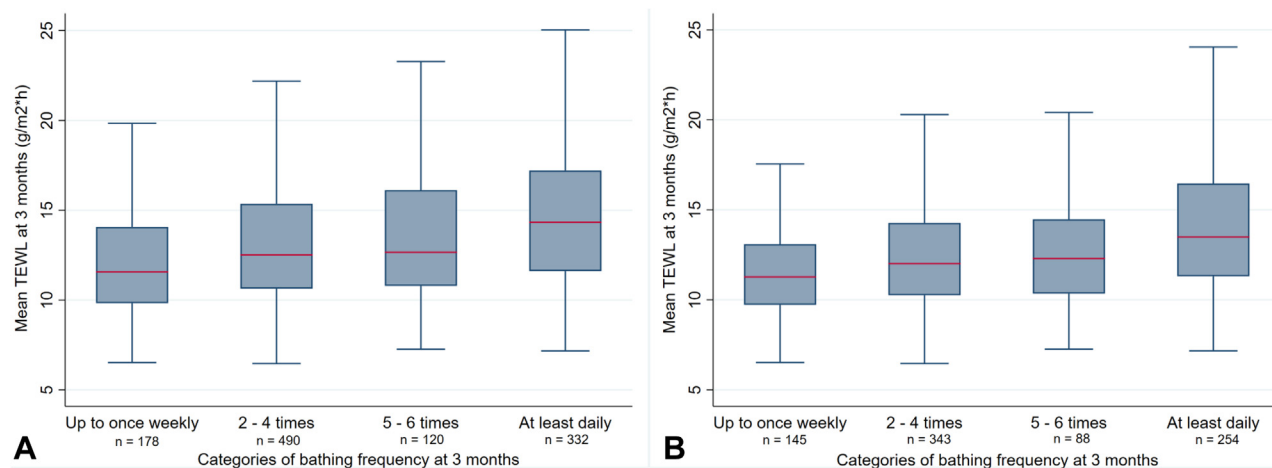


**FIGURE 1.** Box plot showing median transepidermal water loss (TEWL) at 3 months in relation to bathing frequency at 3 months (A) in all participants and (B) among those without signs of atopic dermatitis on skin examination.

**TABLE I.** Adjusted associations between bathing frequency, transepidermal water loss (TEWL), atopic dermatitis (AD), and serum food sensitization at 3 months of age

| Clinical outcome             | Outcome definition                 | Clinical outcome prevalence % (n/N) | Weekly bathing frequency |              |                 |                   |                |                   |                 |                   | Binary bathing   |                   |
|------------------------------|------------------------------------|-------------------------------------|--------------------------|--------------|-----------------|-------------------|----------------|-------------------|-----------------|-------------------|------------------|-------------------|
|                              |                                    |                                     | Up to once weekly        |              | 2-4 times       |                   | 5-6 times      |                   | At least daily  |                   | More than weekly |                   |
|                              |                                    |                                     | % (n/N)                  | aOR (95% CI) | % (n/N)         | aOR (95% CI)      | % (n/N)        | aOR (95% CI)      | % (n/N)         | aOR (95% CI)      | % (n/N)          | aOR (95% CI)      |
| Skin barrier dysfunction     | TEWL; $\geq 15$ g/m <sup>2</sup> h | 31.6% (299/946)                     | 14.6% (16/110)           | 1.00         | 26.4% (104/394) | 1.85 (0.99-3.47)* | 30.4% (35/115) | 2.34 (1.23-4.84)* | 44.0% (144/327) | 4.32 (2.27-8.22)* | 33.9% (283/836)  | 2.53 (1.38-4.62)* |
| AD                           | Examination                        | 24.0% (227/946)                     | 14.6% (16/110)           | 1.00         | 26.9% (106/394) | 2.21 (1.16-4.22)  | 25.2% (29/115) | 1.87 (0.86-4.06)  | 23.2% (76/327)  | 1.63 (0.82-3.24)  | 25.2% (211/836)  | 1.98 (1.06-3.71)  |
| Any serum food sensitization | sIgE $\geq 0.35$ kIU               | 6.1% (53/867)                       | 6.0% (6/100)             | 1.00         | 6.9% (25/360)   | 0.58 (0.19-1.74)* | 4.8% (5/104)   | 0.35 (0.09-1.41)* | 5.6% (17/303)   | 0.53 (0.17-1.70)* | 6.1% (47/767)    | 0.52 (0.18-1.51)* |

AD, Atopic dermatitis; aOR, adjusted odds ratio; CI, confidence interval; sIgE, specific IgE.

All odds ratios adjusted for sex, non-European ethnicity, having siblings, parental report of participant having dry skin, *FLG*, water hardness, *FLG* mutation inheritance, parental history of AD, frequency of emollient application, and use of bath oil, shampoo, soap, and wet wipes.

\*Denotes adjustment for participant examined AD at 3 months in addition to the above.

Bathing frequency showed a nonlinear relationship with AD at 3 months. Babies bathed up-to-weekly demonstrated a 14.6% AD prevalence, whereas the prevalence associated with more frequent bathing categories varied between 23.2% and 26.9% (Table I). In an adjusted logistic regression analysis, bathing more often than weekly, compared with bathing weekly or less, was significantly associated with AD at 3 months (aOR, 1.98 [1.06-3.71],  $P = .03$ ), but not associated with food sensitization ( $\geq 0.35$  kIU) at the same time point (aOR, 0.52 [0.18-1.51],  $P = .23$ ).

A subgroup analysis was undertaken among participants who were bathed at the same frequency at both 3 and 12 months of age to avoid reverse causality. Investigating the relationship in this subgroup between bathing frequency and TEWL at the 12-month visit, there was a statistically significant relationship with the geometric mean ratio of TEWL per unit increase in bathing frequency of 1.03 (1.01-1.04,  $P < .001$ ) with a baseline (bathing weekly or less) geometric mean TEWL of 12.51 g/m<sup>2</sup> h. AD on

examination and bathing frequency were not associated at 12 months (aOR, 0.70 [0.24-2.03],  $P = .51$ ).

In summary, bathing frequency was significantly associated with a dose-response increase in skin barrier dysfunction at both 3 and 12 months of age, but with AD only at 3 months. There was insufficient statistical power to explore associations with food sensitization or allergy at any time point. The trial was not designed specifically to examine whether bathing frequency may impact skin barrier function, AD, or food sensitization; thus families were not asked whether they applied moisturizer directly after bathing.

These data suggest that increased frequency of bathing may negatively influence the integrity of the immature skin barrier and is associated with AD by 3 months of age. In this context, future studies should investigate the impact of the length of time babies are bathed for and whether moisturizer application directly after bathing can ameliorate the negative

effect on skin barrier function, ideally tested in an intervention study.

<sup>a</sup>Department of Paediatric Allergy, Department of Women and Children's Health, School of Life Course Sciences, Faculty of Life Sciences and Medicine, King's College London, London, United Kingdom

<sup>b</sup>Children's Allergies Department, Guy's and St Thomas' NHS Foundation Trust, St Thomas' Hospital, London, United Kingdom

<sup>c</sup>Population Health Research Institute, St George's, University of London, Cranmer Terrace, London, United Kingdom

<sup>d</sup>Division of Biological Chemistry and Drug Discovery, School of Life Sciences, University of Dundee, Dundee, United Kingdom

<sup>e</sup>Department of Experimental Immunology, Amsterdam University Medical Centers/location AMC, Amsterdam, the Netherlands

<sup>f</sup>Departments of Experimental Immunology and Otorhinolaryngology, Amsterdam University Medical Centers/location AMC, Amsterdam, the Netherlands

<sup>g</sup>Unit for Population-based Dermatology Research, St John's Institute of Dermatology, Guy's and St Thomas' NHS Foundation Trust and King's College London, London, United Kingdom

The main components of the EAT Study were jointly funded by the UK Food Standards Agency (FSA, grant code T07051) and the Medical Research Council (MRC). The skin-related aspects of the study were supported by a Clinician Scientist Award from the UK National Institute for Health Research (NIHR) held by CF (NIHRCS/01/2008/009). The McLean lab is funded by Wellcome Trust Programme (092530/Z/10/Z; to WHIM) and Bioresources grants (090066/B/09/Z; to WHIM). The Centre for Dermatology and Genetic Medicine, University of Dundee, is supported by a Wellcome Trust Strategic Award (098439/Z/12/Z; to WHIM). TM, GL, and CF are additionally supported by the NIHR Biomedical Research Centre based at Guy's and St Thomas' NHS Foundation Trust. The views expressed in this publication are those of the authors and not necessarily those of the Food Standards Agency, the Medical Research Council, the NHS, the UK National Institute for Health Research, the UK Department of Health or the Wellcome Trust.

Conflicts of interest: R. van Ree provided consultancy for HAL Allergy BV, Citeq BV, and Angany Inc, and has received speaker fees from HAL Allergy and ThermoFisher Scientific. G. Lack has received research funding from ALK Abello, the Immune Tolerance Network, US National Peanut Board, Food Standards Agency, Medical Research Council, Food Allergy Initiative, Action Medical Research, and Guy's and St Thomas' Charity; has received sponsorship from Novartis, Sodilac, Spanish Society of Allergy and Clinical Immunology, Danone

Nutricia, and Nestle; and has been a scientific advisor for DBV Technologies and gives voluntary advice to the Anaphylaxis Campaign and US National Peanut Board. The rest of the authors declare that they have no relevant conflicts of interest.

Received for publication September 29, 2019; revised April 14, 2020; accepted for publication April 15, 2020.

Available online ■■

Corresponding author: Carsten Flohr, PhD, Unit for Population-based Dermatology Research, St John's Institute of Dermatology, Guy's & St Thomas' NHS Foundation Trust and King's College London, London SE1 7EH, United Kingdom. E-mail: [carsten.flohr@kcl.ac.uk](mailto:carsten.flohr@kcl.ac.uk).

2213-2198

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<https://doi.org/10.1016/j.jaip.2020.04.043>

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