

Newborn Transepidermal Water Loss Values: A Reference Dataset

Maeve M. Kelleher, M.D.,* Michelle O'Carroll, M.D.,* Aine Gallagher, R.G.N.,*
Deirdre M. Murray, Ph.D.,*,† Audrey Dunn Galvin, Ph.D.,* Alan D. Irvine, M.D.,†,‡
and Jonathan O'B Hourihane, M.D.,*†

*Department of Paediatrics and Child Health, University College Cork, Cork, Ireland, †National Children's Research Centre, Our Lady's Children's Hospital, Dublin, Ireland, ‡Clinical Medicine, Trinity College Dublin, Dublin, Ireland

Abstract: Transepidermal water loss (TEWL) is a simple noninvasive measurement of inside-out skin barrier function. The goal of this research was to establish normal values for TEWL in early life using data gathered from the Cork BASELINE Birth Cohort Study. TEWL was recorded in a standardized fashion using a well-validated open-chamber system. A mean of three readings was recorded from 1,036 neonates (37–42 weeks gestational age) and 18 late preterm infants (34–37 weeks gestational age) within 96 hours of birth in an environmentally controlled room. Full-term neonatal TEWL measurements have a normal distribution (mean 7.06 ± 3.41 g of water/m² per hour) and mean preterm neonatal TEWL measurements were 7.76 ± 2.85 g of water/m² per hour. This is the largest evaluation to date of TEWL in a normal-term neonatal population. It therefore constitutes a reference dataset for this measurement using an open-chamber system.

The stratum corneum is made up of a dead cell layer of corneocytes that develops to form an insoluble protein structure that acts as a scaffold for lipid binding, preventing epidermal water loss and impedes entry of infectious organisms, toxins, and allergens (1,2). Dysfunction of this barrier leads to increased water loss (inside–outside barrier defect) and entry of microbes, toxins, and allergens (outside–inside barrier defect). Determination of skin barrier function is therefore of great interest in assessing the risk of developing diseases such as atopic dermatitis and other atopic conditions (3).

One widely used method of assessment of skin barrier function (inside-outside function) is measurement of trans-epidermal water loss. A low TEWL indicates intact inside-out skin barrier function, whereas high TEWL levels indicate a nonintact barrier function. High TEWL levels can be found in disease states such as atopic dermatitis (AD), and these changes have been shown to predate the onset of AD (3).

Identification of skin barrier dysfunction as an early step in the disease process of AD could open up novel approaches to identifying individuals at birth who are at risk of developing AD and other atopic

Address correspondence to Jonathan O'B Hourihane, M.D., Professor of Paediatrics and Child Health, Clinical Investigations Unit, Cork University Hospital, Wilton, Cork, Ireland, or e-mail: j.hourihane@ucc.ie.

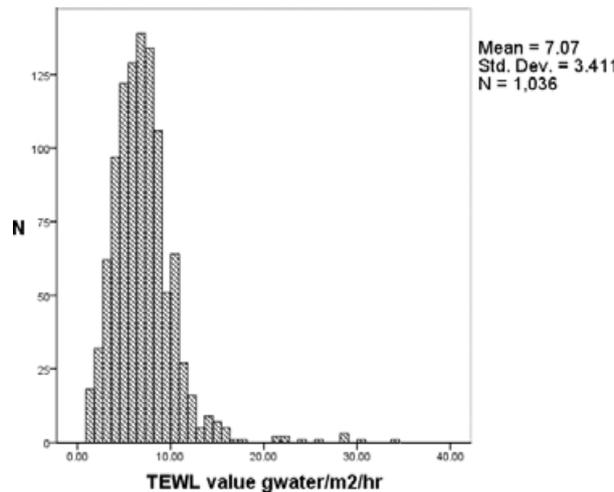


Figure 1. Normal term neonatal transepidermal water loss distribution.

disorders. This could provide an opportunity for early preventative measures and educational management in these infants. The potential would then be there to reduce the incidence of AD and perhaps halt or decelerate the “Atopic March.” With the increasing prevalence of atopic disease, including food allergy in children over the last 2 decades (4), such an intervention would have widespread clinical implications.

For these reasons, knowing what the normal TEWL value is for newborns is imperative, and this paper attempts to fill this gap in knowledge.

MATERIALS AND METHODS

The Cork BASELINE Birth Cohort Study (Babies After SCOPE: Evaluating the Longitudinal Impact using Neurological and Nutritional Endpoints) study is Ireland’s first birth cohort study (5,6). It was established in 2008 as a follow-up to the Screening for Pregnancy Endpoints (SCOPE) pregnancy study (7). The SCOPE study is a worldwide multicenter study involving primiparous low-risk women aimed at establishing biomarkers to assist with prediction and prevention of the major diseases of late pregnancy (8). Women in the SCOPE study were recruited antenatally to the BASELINE Birth Cohort study. Infants recruited into the study from June 2009 on had TEWL measurements taken in the early postnatal period. Recruitment to the study was completed in October 2011.

TEWL measurements were made using a widely validated open-chamber system (Tewameter TM 300, Courage+Khazaka Electronic, Cologne, Germany) (9,10). The subject’s arm was acclimated before

measurement by exposing the arm in a non-environmentally controlled room for 10 minutes. This occurred in the bassinet at the mother’s bedside in the ward room. The mother and child were then accompanied to an environmentally controlled room to wait a further 5 minutes before TEWL was measured in that room. TEWL measurements were taken on the lower volar site of the forearm, and the average of three values was recorded.

All TEWL readings were taken in a windowless room in which an air conditioning system kept temperature set between 20–25°C. Humidity was monitored by a manometer in the room and was maintained between 30–45%.

TEWL measurements were taken only on healthy full-term infants rooming with their mothers on the postnatal wards. According to the local hospital protocol, all infants requiring phototherapy or incubator care are admitted to the neonatal unit, so these infants were excluded from this data set. Occasional recalibration failure of the Tewameter on a given day also resulted in some infants not having TEWL taken within the specified timeframe.

STATISTICAL ANALYSIS

We used a Pearson correlation procedure to determine what independent factors (time at TEWL measurement, birthweight, and gestational age) were significantly related to overall score on TEWL scale and independent sample *t*-tests to examine any differences between the groups (term vs preterm, washed vs not washed).

All statistical analyses were performed using SPSS (version 18.0, SPSS Corp, Chicago, IL). Results were taken to be significant at $p < 0.05$.

RESULTS

Of a possible 1318 infants enrolled during the study period from when TEWL measurements were available, 1054 (80%) had TEWL values measured within first 96 hours of life.

The gestational age of the infants ranged from 34.9 to 42.6 wks (mean 40.1 ± 1.2 wks). Using Pearson correlation, there was no correlation between gestational age and TEWL value ($r = 0.005$, $p = 0.88$). We subsequently divided the cohort into two groups (term > 37 wks gestation, late preterm 34–37 wks gestation). TEWL measurements for term infants showed a normal distribution (Fig. 1). Values for TEWL in the 1036 term infants ranged from 1.00 to 34.00 $\text{g}_{\text{water}}/\text{m}^2$ per hour (mean 7.06 ± 3.41 $\text{g}_{\text{water}}/\text{m}^2$ per hour).

For the 18 late preterm infants, TEWL measurement ranged from 2.00 to 13.00 $\text{g}_{\text{water}}/\text{m}^2$ per hour (mean $7.8 \pm 2.9 \text{ g}_{\text{water}}/\text{m}^2$ per hour).

This difference in mean TEWL measurements between term and late preterm infants did not reach statistical significance ($p = 0.48$, mean difference

$0.64 \text{ g}_{\text{water}}/\text{m}^2$ per hour, 95% confidence interval = -1.15 – 2.42), but because there were only 18 late preterm infants, we cannot infer similar results in a larger late preterm cohort.

Mean postnatal age at time of reading was 41.6 ± 20.8 hours. Again, we used a Pearson

TABLE 1. Summary of previous studies on transepidermal water loss

Study	Population	Area measured	Device used	Findings
Fluhr et al (9) Br J Dermatol 2012	108 subjects 18 in each group 1–15 days, 5–6 weeks, 6 ± 1 months, 1–2 years, 4–5 years, 20–35 years	Right and left volar forearm	Open chamber device, Tewameter (TM 300; Courage & Khazaka, Cologne, Germany)	Mean readings at each age group $<10 \text{ g}_{\text{water}}/\text{m}^2/\text{hour}$ Trend towards increase TEWL at 5–6 weeks
Flohr et al (3) Br J Dermatol 2010	88 infants Age 3 months	Volar Forearm	Closed condenser chamber Biox Aquaflux_ AF200 (Biox Systems Ltd., London, U.K.)	Mean TEWL normal skin 11.24 Mean TEWL Atopic Dermatitis 14.24
Nikolovski et al (16) J Invest Dermatol 2008	19 infants 3–6 months 31 infants 7–9 months 71 adults	Lower dorsal and upper ventral sites of randomly chosen arms of each subject	Closed chamber Delfin VapoMeter (Delfin, Kuopio, Finland).	TEWL lower dorsum 15–30 g water/m/hour Adult recordings significantly less
Boralevi et al (22) Allergy 2008	89 infants (3–12 months) 59 Atopic Dermatitis 30 controls	Volar Forearm	Open Chamber Tewameter	TEWL 27.4 $\text{g}/\text{m}^2/\text{h}$ infants with AD 11.1 $\text{g}/\text{m}^2/\text{hour}$ in control infants
Guisti et al (19) Pediatr Dermatol 2001	70 infants 8–24 months 30 women	Left volar forearm buttocks	Open Evaporimeter (Servomed EP-1)	No differences between adults and infants; infant TEWL: 8–9 $\text{g}/\text{m}^2/\text{hour}$; no regional differences
Yosipovitch et al (23) Paediatrics 2000	44 term neonates; measurements taken: 5–10 h PP and 24 h PP; 20 adults	Forehead, upper back, flexor forearm, palms, abdomen, inguinal region, soles	Tewameter (Courage and Khjazaka, Koln, Germany)	Variability depending on site TEWL taken
Kalia et al (20) J Invest Dermatol 1998	10 infants, 23–32 weeks GA, aged 1–7 days	Calf or thigh	Evaporimeter (Servomed)	23–25 weeks GA: mature barrier not developed 30–32 weeks GA: have adult barrier function as measured by TEWL
Agren et al (26) Acta Paediatrica 1998	13 infants 24–25 weeks DOB, Day 1,3,7,28	Chest, Interscapular area, buttock	Evaporimeter (Servomed)	TEWL decreased after day 1 Still $>$ than more mature infants at 28 days
Saijo and Tagami (27) Pediatr Dermatol 1991	46 term newborns 10 adults 16 children	Dorsa of hand and foot	Evaporimeter (Servomed)	No regional differences; adult TEWL $>$ infants; infant TEWL 8–9 $\text{g}/\text{m}^2/\text{h}$;
Sedin et al (25) Acta Paediatric Scand 1983	18 infants	18 sites Not fully specified	Evaporimeter (Servomed)	Preterm: TEWL gradually decreased in first weeks Term: TEWL almost unchanged in 1 st weeks
Harpin and Rutter (15) J Pediatr 1983	70 infants (25–41 weeks gestation)	Abdomen	Evaporimeter (Servomed)	>37 weeks: TEWL $<10 \text{ g}_{\text{water}}/\text{m}^2/\text{hour}$ 33–36 weeks: normal TEWL levels by 1 st week 30–32 weeks: normal TEWL levels by 10 days <30 weeks: normal levels after 2 weeks
Rutter and Hull (24) Arch Dis Child 1979	78 infants 26–41 weeks	Multiple sites	Evaporimeter (Servomed)	34–41 weeks: high TEWL in 1 st hours of life, falls to 6 $\text{g}_{\text{water}}/\text{m}^2/\text{hour}$ 30–33 weeks: High TEWL first week <30 weeks: high TEWL

correlation to determine whether there was a relationship between postnatal age and TEWL value. No correlation was found ($r = -0.057$, $p = 0.07$).

Four hundred seventy-eight neonates (45.6%) had been washed before measurements were taken. Using the Independent sample T test, there was no significant difference in TEWL values in those who were and were not washed before measurement. Mean TEWL in infants who were washed prior to reading was 7.04 ± 3.22 $\text{g}_{\text{water}}/\text{m}^2$ per hour compared with those not washed prior to reading was 7.10 ± 3.54 $\text{g}_{\text{water}}/\text{m}^2$ per hour ($p = 0.76$).

DISCUSSION

This is the largest study of skin barrier function TEWL in full-term neonates to date. It establishes the normative dataset in full-term infants not selected for atopy or other skin conditions. Our large dataset shows that full-term infants have an intact inside-out skin barrier in the early newborn period. TEWL in full-term newborn infants displays a normal distribution, with a mean of 7.06 ± 3.41 $\text{g}_{\text{water}}/\text{m}^2$ per hour.

We used an open-chamber system, which is based on Fick's Law of Diffusion and estimates water diffusion gradient across an open chamber (11). Because this device is open to the environment, it may be susceptible to changes in environmental airflow, but it offers continuous measurement over a period of time, allowing it to recognize changes to flow (12). In head-to-head comparison against a closed-chamber device, it was more sensitive in detecting changes in TEWL values at lower levels (<45 $\text{g}_{\text{water}}/\text{m}^2$ per hour), but the closed-chamber system was more sensitive in detecting measurements in the high-value range (>80 $\text{g}_{\text{water}}/\text{m}^2$ per hour). Therefore, the data presented here are reliable only as a reference set for open systems (13).

There is previous evidence that full-term infants have an effective epidermal barrier, with TEWL values between 4 and 8 $\text{g}_{\text{water}}/\text{m}^2$ per hour cited in dermatology textbooks (14), but the gestational age at which this barrier becomes effective has been debated. Preterm infants (<32 weeks) have been shown to have higher TEWL values than full-term infants and show more marked drug absorption (15). Other studies have suggested that skin water-barrier development is complete at 34 weeks of gestation (16). This would seem to be reflected in our study by the nonsignificant difference in mean TEWL scores between late preterm (34–37 weeks of gestation) and full-term infants (>37 weeks of gestation), although our late

preterm infant numbers were small, because this was not the primary focus of our study.

The difference in TEWL values between adults and infants is debated. Initial studies suggested that infants had lower TEWL values than adults (17). Since then, studies have shown that full-term infants have similar TEWL values as adults (18–20), whereas others suggest that infants have higher TEWL values than adults (16,27). The stage at which infant TEWL normalize to adult values is not known. These prior studies are summarized in Table 1.

Our study, which was performed under standardized conditions in a single unit and is in scale several orders of magnitude greater than prior studies, brings some clarity to the data regarding normal perinatal skin barrier function. In time, as our population matures, we hope to reveal the time course of normal skin barrier function maturation.

TEWL is used as an indicator of skin barrier dysfunction in AD, and it has been shown that TEWL changes occur in individuals with AD (21,22). These changes can precede and predict a diagnosis of AD. Flohr and colleagues have demonstrated an association between TEWL at 3 months and *FLG* status and coexisting AD, although this was a smaller sample of high-risk infants (3).

Our study has some minor limitations. The small number of infants who were not of white European descent means that our findings cannot be generalized to other ethnic groups. Because TEWL was performed within 96 hours of birth, infants who were admitted to the neonatal unit, and hence unavailable for TEWL, were excluded from our study. Thus, these reference data are for healthy full-term infants only. Finally according to the SCOPE study protocol, all infants were born to primiparous mothers. The effect of parity on skin barrier function is unknown.

This study has established the normative data set for assessment of TEWL as a measure of inside-out skin barrier function in the earliest days of postnatal life, as the skin function transitions from the aquatic intrauterine environment to the dry extrauterine environment. This will inform future intervention trials to maintain or support early-life skin-barrier function.

ACKNOWLEDGMENTS

This study was funded by the Food Standards Agency UK. The BASELINE study is funded by the National Children's Research Centre, Ireland. M O'C received

a studentship grant from the Health Research Board, Ireland.

REFERENCES

- O'Regan GM, Sandilands A, McLean WH et al. Filaggrin in atopic dermatitis. *J Allergy Clin Immunol* 2008;122:689–693.
- O'Regan GM, Kemperman PM, Sandilands A et al. Raman profiles of the stratum corneum define 3 filaggrin genotype-determined atopic dermatitis endophenotypes. *J Allergy Clin Immunol* 2010;126:574–580.
- Flohr C, England K, Radulovic S. Filaggrin loss-of-function mutations are associated with early-onset eczema, eczema severity and transepidermal water loss at 3 months of age. *Br J Dermatol* 2010;163:1333–1336.
- Venter C, Hasan Arshad S, Grundy J et al. Time trends in the prevalence of peanut allergy: three cohorts of children from the same geographical location in the UK. *Allergy* 2010;65:103–108.
- Baselinestudy.net (n.d.) [online] Available at: <http://www.baselinestudy.net> [Accessed: 10 Jan 2013].
- Hawkes CP, Hourihane JO'B, Kenny L et al. Gender and gestational age specific body fat percentage at birth. *Paediatrics* 2011;128:645.
- Scopestudy.net (n.d.) [online] Available at: <http://www.scopestudy.net> [Accessed: 10 Jan 2013].
- North RA, McCowan, Dekker GA et al. Clinical risk prediction for pre-eclampsia in nulliparous women: development of model in international prospective cohort. *BMJ* 2011;342:d1875.
- Fluhr JW, Darlenski R, Lachmann N et al. Additive impairment of the barrier function by mechanical irritation, occlusion and sodium lauryl sulphate in vivo. *Br J Dermatol* 2005;153:125–131.
- Barel AO, Clarys P. Study of the stratum corneum barrier function by transepidermal water loss measurements: comparison between two commercial instruments: Evaporimeter and Tewameter. *Skin Pharmacol* 1995;8:186–195.
- De Paepe K, Houben E, Adam R et al. Validation of the Vapometer, a closed unventilated chamber system to assess transepidermal water loss vs. the open chamber Tewameter. *Skin Res Technol* 2005;11:61–69.
- Darlenski R, Sassning S, Tsankov N et al. Non-invasive in vivo methods for investigation of the skin barrier physical properties. *Eur J Pharm Biopharm* 2009;72:295–303.
- Steiner M, Aikman-Green S, Prescott GJ et al. Side-by-side comparison of an open-chamber (TM 300) and a closed-chamber (Vapometer™) transepidermal water loss meter. *Skin Res Technol* 2011;17:366–372.
- Hoeger PH. Physiology of neonatal skin. In Irvine AD, Hoeger PH, Yan AC, eds. *Harpers textbook of paediatric dermatology*. Oxford, UK: Wiley-Blackwell, 2011:3.1–3.7.
- Harpin VA, Rutter N. Barrier properties of the newborn infant's skin. *J Pediatr* 1983;102:41925.
- Nikolovski J, Stamatas GN, Kollias N et al. Barrier function and water-holding and transport properties of infant stratum corneum are different from adult and continue to develop through the first year of life. *J Invest Dermatol* 2008;128:1728–1736.
- Cunico RL, Maibach HI, Khan H et al. Skin barrier properties in the newborn. *Biol Neonate* 1977;32:177–182.
- Chiou YB, Blume-Peytavi U. Stratum corneum maturation. A review of neonatal skin function. *Skin Pharmacol Physiol* 2004;17:57–66.
- Giusti F, Martella A, Bertoni L et al. Skin barrier, hydration, and pH of the skin of infants under 2 years of age. *Pediatr Dermatol* 2001;18:93–96.
- Kalia YN, Nonato LB, Lund CH et al. Development of skin barrier function in premature infants. *J Invest Dermatol* 1998;111:320–326.
- Holm EA, Wulf HC, Thomassen L et al. Instrumental assessment of atopic eczema: validation of transepidermal water loss, stratum corneum hydration, erythema, scaling, and edema. *J Am Acad Dermatol* 2006;55:772–780.
- Boralevi F, Hubichel T, Leaute-Labreze C. Epicutaneous aeroallergen sensitization in atopic dermatitis infants—determining the role of epidermal barrier impairment. *Allergy* 2008;63:205–210.
- Yosipovitch G, Maayan-Metzger A, Merlob P et al. Skin barrier properties in different body areas in neonates. *Pediatrics* 2000;106:105–108.
- Rutter N, Hull D. Water loss from the skin of term and preterm babies. *Arch Dis Child* 1979;54:858–868.
- Sedin G, Hammarlund K, Strömberg B. Transepidermal water loss in full-term and pre-term infants. *Acta Paediatr Scand Suppl* 1983;305:27–31.
- Ägren J, Sjörs G, Sedin G. Transepidermal water loss in infants born at 24 and 25 weeks of gestation. *Acta Paediatr* 1998;87:1185–1190.
- Saijo S, Tagami H. Dry skin of newborn infants: functional analysis of the stratum corneum. *Pediatr Dermatol* 1991;8:155–159.