TEWL Studies

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Presentation Plan

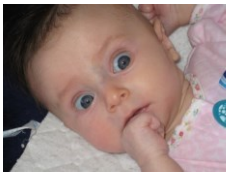
1a. Introduction: The Skin Water-loss Barrier

What is the Skin Water-loss Barrier ?

The skin water-loss barrier resides in the outermost layer of the skin, the Stratum Corneum (SC).

The SC is a layer of dead skin cells that protects the viable cells of the epidermis from water loss and ingress of harmful substances.

The SC is typically 10-20 microns thick, except on the palms & soles, where it is typically 1mm thick.



Presentation Plan

1b. Introduction: TEWL

What is TEWL ?

The skin water-loss barrier is not perfect. Water from the viable epidermis can escape through the SC into the ambient air. This is TransEpidermal Water Loss (TEWL).

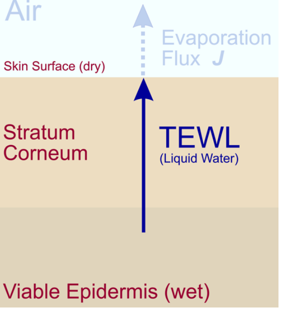
TEWL can be measured to give information about the quality of the skin water-loss barrier.

The lower the TEWL, the better the barrier.

1b. Introduction: TEWL

Definition

TEWL is the flux of (liquid) water diffusing through the SC, from the Viable Epidermis (wet) to the surface (dry).



NB:

1. For the skin surface to remain dry, the TEWL water must evaporate into the adjacent air.
2. Diffusion is a key word for both TEWL and for evaporation flux. More next ...

Presentation Plan

1c. Introduction: Diffusion

Fick's Laws of Diffusion

Diffusion is the net movement of molecules (particles) from a region of high concentration (chemical potential) to a region of low concentration as a result of random thermal motion.

According to Fick's 2nd Law of Diffusion:

$$\frac{\partial c}{\partial t} = D\left(\frac{\partial^2 c}{\partial x^2} + \frac{\partial^2 c}{\partial y^2} + \frac{\partial^2 c}{\partial z^2}\right) \quad \text{or in 1-dimension} \quad \frac{\partial c}{\partial t} = D\left(\frac{\partial^2 c}{\partial x^2}\right)$$

where c = concentration, *D* = diffusion coefficient.

For steady-state diffusion (no time dependence) the above reduces to Fick's 1st Law:

$$J = -D\frac{dc}{dx}$$

where *J* = steady-state flux density.

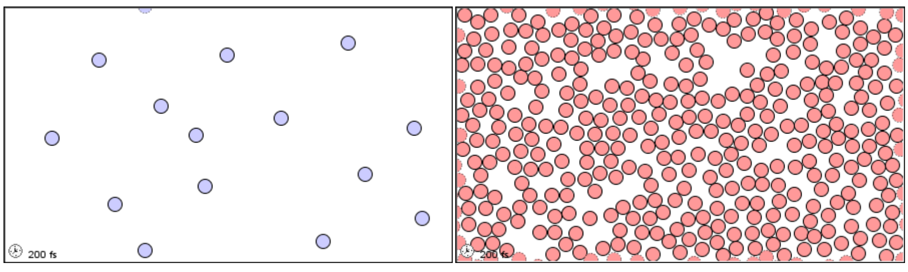
Note that *J* is proportional to the concentration gradient *dc/dx*.

J Crank. ***The Mathematics of Diffusion***. 2nd ed. Oxford: Oxford Science Publications; (1975).

1c. Introduction: Diffusion

Random Thermal Motion

Gas | **Liquid**

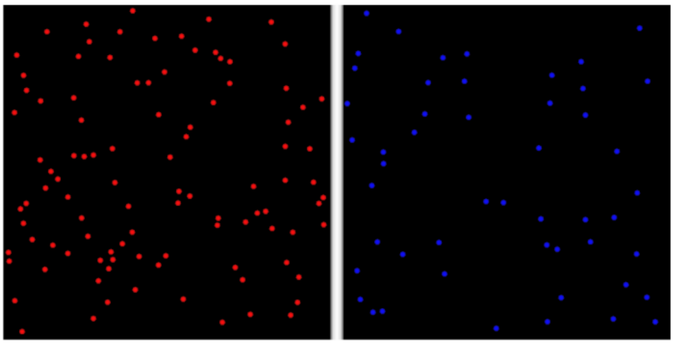


NB: No external forces, no favoured direction.

1c. Introduction: Diffusion

Mixing of Two Gases

high concentration | **low concentration**

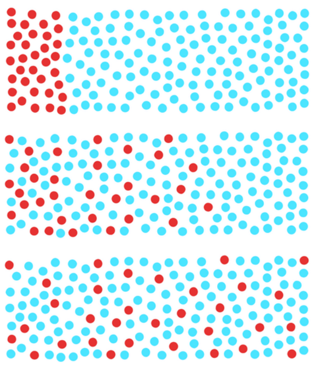


No external forces, no favoured direction, no bulk movement, just random thermal motion.

What? No favoured direction? What about ...from **high** to **low** concentration?

1c. Introduction: Diffusion

No external Forces, No Favoured Direction

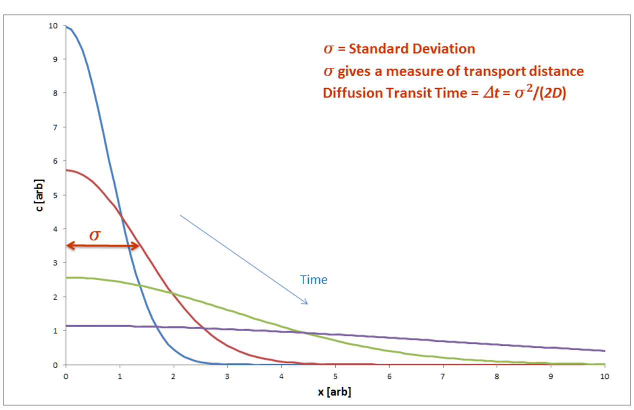


The diffusion from high to low concentration is due to random thermal motion.

It is mixing without stirring. And it's slow. Oh so slow!

1c. Introduction: Diffusion

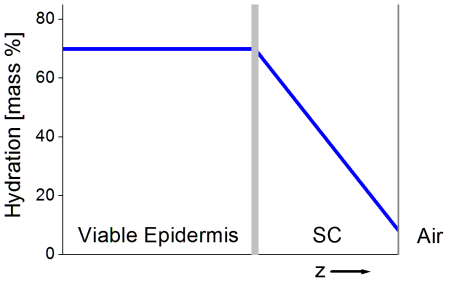
Fick's 2nd law: Diffusion Transit Time



The Diffusion Transit Time Δt gives a measure of the speed of diffusion.

1c. Introduction: Diffusion

Volar Forearm TEWL Transit Time



Quantity	Value	Units
TEWL	10	$gm^{-2}h^{-1}$
SC Thickness	10	μm
SC Base Hydration	700	kgm^{-3}
SC Surface Hydration	100	kgm^{-3}
Transit Time	**~17**	**min**

At that speed it would take about 1 month to get through a 1 inch thickness of SC!

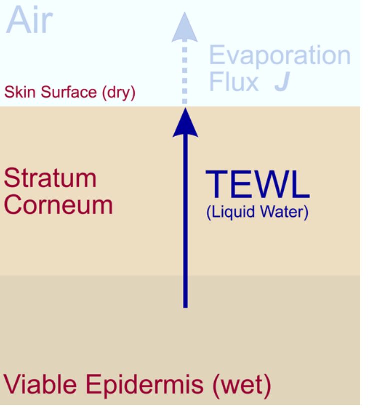
Therefore, TEWL is slow to change when external conditions change.

Presentation Plan

1. Introduction
   a) The Skin Water-loss Barrier
   b) TEWL
   c) Diffusion
2. **TEWL Measurement**
   a) How?
   b) Main Current Methods
   c) Performance
3. AquaFlux Guidelines
   a) Evaporation Flux & TEWL
   b) Study Preparation
   c) Quality Control
4. Summary

2a. TEWL Measurement: How?

TEWL and Evaporation Flux



TEWL (ie liquid water diffusing through the SC) cannot be measured directly.

Instead, we measure evaporation flux from the SC surface into the adjacent air.

Therefore

All TEWL instruments are Evaporimeters.

But

Not all evaporation flux is TEWL - more later.

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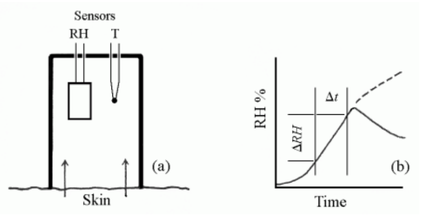
2b. TEWL Measurement: Main Current Methods

Unventilated-chamber Method



The evaporation flux is trapped in a closed chamber.

TEWL is determined from time-rate of humidity increase.

EF Wallihan. ***Modification and use of an Electric Hygrometer for Estimating Relative Stomatal Apertures***. Plant Physiol. 39: 86-90 (1964).

DL Miller, AM Brown & EJ Artz. ***Indirect Measures of Transepidermal Water Loss***. In: Bioengineering and the skin. (R Marks & PA Payne, eds). MTP Press, Lancaster (1981).

2b. TEWL Measurement: Main Current Methods

Commercial Instruments using the Unventilated-chamber Method

Vapometer

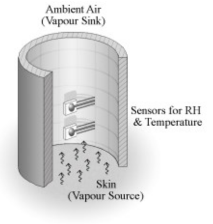
Delfin

gpskin

gpower

2b. TEWL Measurement: Main Current Methods

Open-chamber Method



The evaporation flux diffuses through the chamber into the ambient air.

The evaporation flux & the axial humidity gradient are proportional (Fick's 1st law).

It uses two RH&T sensors to measure this gradient and hence the flux.

TEWL is determined from evaporation flux vs time measurements.

This is Nilsson's diffusion gradient measurement principle.

GE Nilsson. ***Measurement of Water Exchange through Skin***. Med Biol Comput. 15: 209-18 (1977).

2b. TEWL Measurement: Main Current Methods

Commercial Instruments using the Open-chamber Method

Evaporimeter

Servomed

Tewameter

Courage & Khazaka

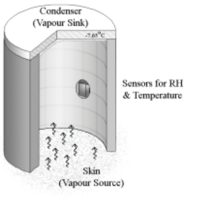
DermaLab

Cortex Technology

This is currently the most widely used method for TEWL measurement.

2b. TEWL Measurement: Main Current Methods

Condenser-chamber Method



The evaporation flux diffuses through the chamber and freezes onto the condenser.

The evaporation flux & the axial humidity gradient are proportional (Fick's 1st law).

It uses one RH&T sensor and the condenser T to measure this gradient and hence the flux.

TEWL is determined from evaporation flux vs time measurements.

This also uses Nilsson's diffusion gradient measurement principle.

RE Imhof. ***Method and Equipment for Measuring Water Vapor Flux from Surfaces***. USA Patent 6439028 (2000).

2b. TEWL Measurement: Main Current Methods

Commercial Instrument using the Condenser-chamber Method

AquaFlux

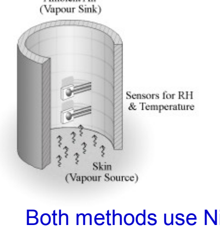
Biox

Presentation Plan

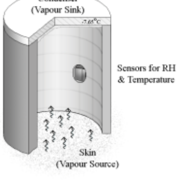
2c. TEWL Measurement: Performance

Open-chamber and Condenser-chamber Methods

Open-chamber



Condenser-chamber



Both methods use Nilsson's diffusion gradient measurement principle.

However

With the open-chamber, the ultra-still air needed for diffusion within the chamber is easily disturbed by ambient air movements. How easily?

2c. TEWL Measurement: Performance

How sensitive is the Open-chamber to Disturbance from Ambient Air Movements?

The diffusion transit time gives a clue:

Quantity	Value	Units
TEWL	10	$gm^{-2}h^{-1}$
Open-chamber Height	20	mm
Diffusion Coefficient D_{VA}	2.42×10^{-5}	m^2s^{-1}
Transit Time	**~8**	**sec**

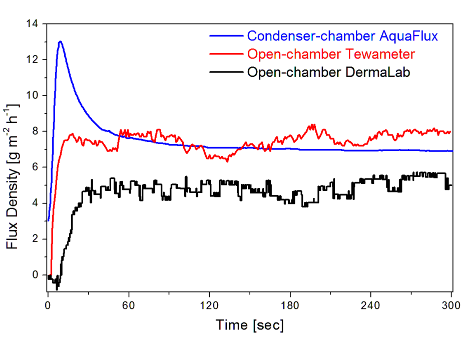
20mm in 8 seconds is equivalent to an air-flow speed of 0.005 miles/hour!
Very still indoor air moves at typically 0.7 miles/hour, ie >100 times faster [1].
Natural convection (Skin T ~30°C, Air T ~20°C) is >1000 times faster [1].

This gives a measure of how vulnerable open-chamber measurements are to disturbance by ambient air movements.

[1] AE Wheldon & JL Monteith. ***Performance of a Skin Evaporimeter***. Med Biol Comput. 18:201–5 (1980).

2c. TEWL Measurement: Performance

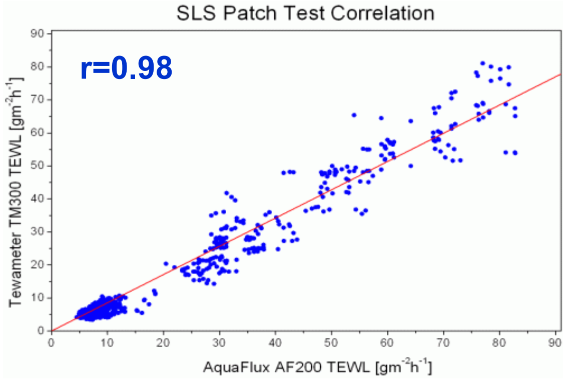
Fluctuations in Condenser-chamber and Open-chamber Flux Curves



Condenser-chamber flux curves have low fluctuations because the chamber is closed.

2c. TEWL Measurement: Performance

Ah, but do they Measure the same Thing?



I Angelova-Fischer, TW Fischer & D Zillikens. ***Die Kondensator-Kammer-Methode zur nicht-invasiven Beurteilung von irritativen Hautschäden und deren Regeneration: eine Pilotstudie***. Dermatol Beruf Umwelt. 57(3):125 (2009).

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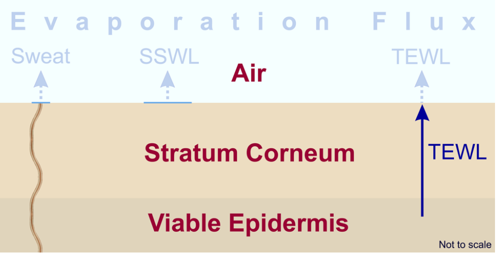
3a. AquaFlux Guidelines: Evaporation Flux & TEWL

Not all Evaporation Flux is TEWL!



Sweat is not TEWL. Skin Surface Water Loss (SSWL) is not TEWL.

Therefore, to measure TEWL by Evaporimetry,

TEWL must be THE ONLY SOURCE of evaporation flux!

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3b. AquaFlux Guidelines: Study Preparation

Preparation away from the Study Centre

The Guidelines below give detailed advice on how subjects should prepare themselves for measurement. In brief:-

Do not eat, consume caffeine-containing drinks or smoke (perspiration).
Do not perform vigorous physical exercise (perspiration).
Follow study-centre advice on the use of medicines (perspiration).

Follow study-centre advice on the use of topical products (occlusion, surface water).
Follow study-centre advice on washing (abrasion, surface water).

J Pinnagoda, RA Tupker, J Agner & J Serup. ***Guidelines for Transepidermal Water Loss (TEWL) Measurement. A Report from the Standardization Group of the European Society of Contact Dermatitis***. Contact Dermatitis. 22, 164-78 (1990).

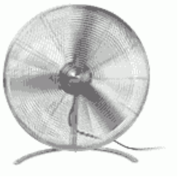
V Rogiers & the EEMCO Group. ***EEMCO Guidance for the Assessment of Transepidermal Water Loss in Cosmetic Sciences***. Skin Pharmacol Appl Skin Physiol. 14, 117-28 (2001).

J du Plessis, A Stefaniak, F Eloff, S John, T Agner, T-C Chou, R Nixon, M Steiner, A Franken, I Kudla & L Holness. ***International Guidelines for the In-vivo Assessment of Skin Properties in Non-clinical Settings: Part 2. Transepidermal Water Loss and Skin Hydration***. 19(3), 265-78 (2013).

3b. AquaFlux Guidelines: Study Preparation

Acclimatisation at the Study Centre

Acclimatisation Time: 15-30 minutes, longer is better.



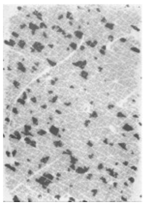
Ambient conditions for acclimatisation:

- Ambient Temperature: 20-22^{o}C.
- Ambient Humidity: Less than 60%. Lower is better.
- Use moving air to dry exposed skin sites (eg fan).

3b. AquaFlux Guidelines: Study Preparation

Skin Surface Water from Insensible Perspiration

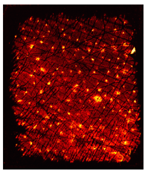
Capacitance contact imaging can be used to inspect skin sites prior to TEWL measurement.



1. L'Oreal Skin Chip [1]

Dark areas are more hydrated.

The black spots are surface water at sweat gland openings.



2. Biox Epsilon

Bright areas are more hydrated.

The yellow spots are surface water at sweat gland openings.

[1] E Xhauflaire-Uhoda, G Mayeux, P Quatresooz, A Scheen & GE Piérard. ***Facing up to the Imperceptible Perspiration. Modulatory Influences by Diabetic Neuropathy, Physical Exercise and Antiperspirant***. Skin Res Technol 17(4), 487-93 (2011).

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3c. AquaFlux Guidelines: Quality Control

Why and How ?

Preparation and acclimatisation are essential, but you can do more to make sure that the measurements are good.

Quality control can identify measurements spoilt by sweat gland activity.

Quality control can also identify measurements spoilt by operator error such as:
- The probe not sealing against the skin.
- The probe sliding over the skin.
- Premature probe lift-off.

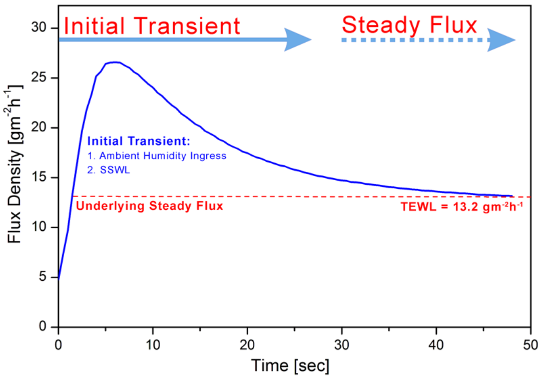
Bad measurements generally show up in the flux curves because the main causes of bad measurements are time-dependent, whereas TEWL is steady.

Looking for bad measurements in the flux curves is Quality Control

3c. AquaFlux Guidelines: Quality Control

The Flux Curves tell the Story

You determine TEWL from measurements of water vapour flux density against time.



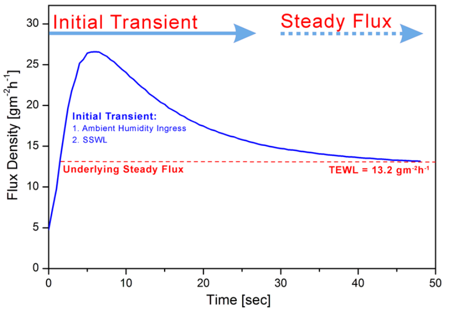
TEWL is the underlying steady flux density.

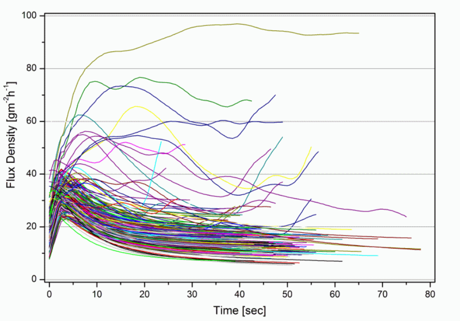
3c. AquaFlux Guidelines: Quality Control

Quality Control Criteria

The two main criteria for identifying bad measurements are:

1. Modulations in the flux curves.
2. Measurements that do not settle to a final steady flux.

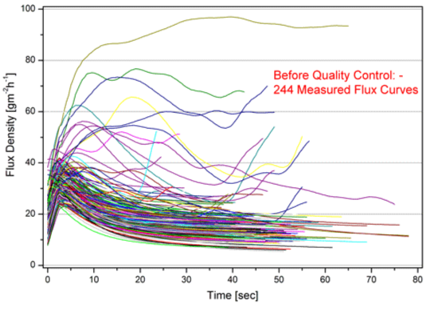


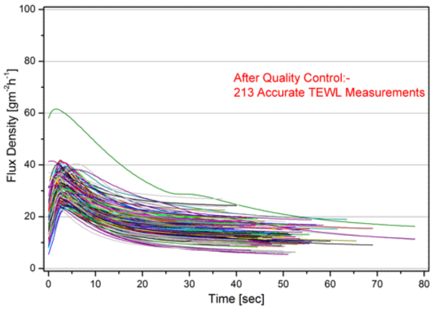


3c. AquaFlux Guidelines: Quality Control

Quality Control - Practical Example

In this case, 31 out of 244 (13%) of measurements were identified as bad and discarded. This improves the statistical significance of the remaining 213 good TEWL measurements.





You can also inspect flux curves during the study and immediately repeat bad measurements.

The flux curves are crucial for validating TEWL measurements!

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4. Summary

1. TEWL is an indicator of the quality of the skin water-loss barrier.
2. TEWL is measured by evaporimetry, but not all evaporation flux is TEWL.
3. TEWL diffuses through the SC very, very slowly.
4. Preparation & acclimatisation are important for good TEWL measurement.
5. The flux curves are important indicators of good TEWL measurements.
6. Quality Control is a powerful method for verifying TEWL measurements.