

REVIEW ARTICLE

The effect of environmental humidity and temperature on skin barrier function and dermatitis

K.A. Engebretsen,^{1*} J.D. Johansen,¹ S. Kezic,² A. Linneberg,^{3,4,5} J.P. Thyssen¹¹National Allergy Research Centre, Department of Dermato-Allergology, Gentofte University Hospital, University of Copenhagen, Hellerup, Denmark²Coronel Institute of Occupational Health, Academic Medical Centre, 1105 AZ, Amsterdam, The Netherlands³Research Centre for Prevention and Health, Glostrup, The Capital Region of Denmark, Copenhagen, Denmark⁴Department of Clinical Experimental Research, Glostrup University Hospital, Glostrup, Denmark⁵Department of Clinical Medicine, Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, Denmark

*Correspondence: K.A. Engebretsen. E-mail: kristiane.aasen.engebretsen.02@regionh.dk

Abstract

Physicians are aware that climatic conditions negatively affect the skin. In particular, people living in equator far countries such as the Northern parts of Europe and North America are exposed to harsh weather during the winter and may experience dry and itchy skin, or deterioration of already existing dermatoses. We searched the literature for studies that evaluated the mechanisms behind this phenomenon. Commonly used meteorological terms such as absolute humidity, relative humidity and dew point are explained. Furthermore, we review the negative effect of low humidity, low temperatures and different seasons on the skin barrier and on the risk of dermatitis. We conclude that low humidity and low temperatures lead to a general decrease in skin barrier function and increased susceptible towards mechanical stress. Since pro-inflammatory cytokines and cortisol are released by keratinocytes, and the number of dermal mast cells increases, the skin also becomes more reactive towards skin irritants and allergens. Collectively, published data show that cold and dry weather increase the prevalence and risk of flares in patients with atopic dermatitis.

Received: 6 February 2015; Accepted: 1 June 2015

Conflicts of interest

The authors have no conflict of interest to disclose.

Funding source

Supported by the COST Action TD1206 StanDerm. Jacob P. Thyssen and Kristiane Engebretsen are financially supported by an unrestricted grant from the Lundbeck Foundation. No involvement from the funders has taken place.

Introduction

The stratum corneum (SC) is a complex structure of anucleated cells, proteins and lipids that provides protection against invasion of microorganisms and allergens, but importantly also prevents excessive water loss. Intercellular hydrophobic lipids and osmolytic intracellular molecules such as amino acids, organic acids, urea and inorganic ions – collectively referred to as natural moisturizing factors (NMF) – are critical for adequate skin hydration together with SC thickness.^{1–3}

It is broadly accepted that skin barrier functions may be negatively affected by climatic conditions.^{4–8} Notably, the prevalence of atopic dermatitis (AD) appears to be latitude dependent with higher estimates in countries distant from the equator.⁹ While this could be explained by genetic differences, for example common filaggrin gene mutations, climatic effects on skin barrier

functions likely play a key role. This article reviews how climatic factors such as low humidity and cold temperatures negatively affect skin barrier functions and increase the risk of dermatitis.

Method and result

A systematic search in PubMed and Embase was performed in April 2015 where the following search terms were used; (atopic dermatitis OR atopic eczema OR dermatitis OR xerosis OR dry skin OR chapping OR skin barrier) AND (humidity OR weather OR climate OR temperature OR meteorological OR seasonal OR wind OR cold). No limit was set regarding the range of years. A total of 1025 articles were identified in PubMed and 315 articles in Embase. 53 articles were included. In addition, 46 articles were identified in reference lists of included articles and by the database function 'related articles' for selected publications,

resulting in 99 articles in total. Details of the search process and exclusion criteria are shown in Fig. 1.

Definition of humidity and dew point

Humidity is defined as the amount of water vapour in the air coming from terrestrial and oceanic water. Absolute humidity (AH) is defined as the mass of water vapour in a given volume of air, usually expressed in grams per cubic metre. Importantly, AH does not take temperature into consideration, and a change in temperature or air pressure will alter the AH.

Relative humidity (RH) is the actual amount of water vapour in the air divided by the amount of water vapour the air can hold, expressed as a percentage. RH depends on temperature, and warm air can hold more water than cold air. If air is cold, the same amount of water vapour produces a higher RH than the same amount of water vapour in warmer air.¹⁰ This explains why RH in polar region can be higher than RH at lower latitude.

Dew point is the temperature that air would have to be cooled down to for saturation to occur. When air is saturated, water condenses, and it is referred to as dew.⁵ A high dew point corresponds to high water vapour content and vice versa.

Residents on the northern hemisphere experience cold winters, and accordingly they heat their homes. Most do not have humidifiers, and when cold air is heated, the ability to hold water increases and the RH drops. For example, air with a tem-

perature of 0 °C and a RH of 85% will decrease to 22% if heated to 20 °C.¹⁰ As we will explore, a double negative influence on the skin barrier occurs in the winter; low indoor humidity and cold temperatures outside.

Low humidity negatively affects skin barrier functions

Animal studies

The breakdown of filaggrin proteins depends on environmental humidity. While late foetal rat skin shows accumulation of filaggrin throughout the whole SC,¹¹ postnatal observation shows that filaggrin is degraded when RH declines (Table 1).¹¹ Notably, breakdown can be prevented when covered with an occlusive patch to maintain 100% RH, mimicking the aqueous milieu *in utero*. This observation suggests that filaggrin proteolysis is controlled by SC water amount.

Hairless mice have been investigated for skin alteration when placed in a dry environment (RH ≤10%), either transferred from normal (RH 40–70%) or humid (RH >80–90%) conditions. After 12 h in a dry environment, skin conductance decreases and epidermal DNA synthesis increases.¹² The increased epidermal DNA synthesis can be inhibited by application of petrolatum, again suggesting that the water content in the SC may play a key role for compensatory epidermal recovery mechanisms.¹²

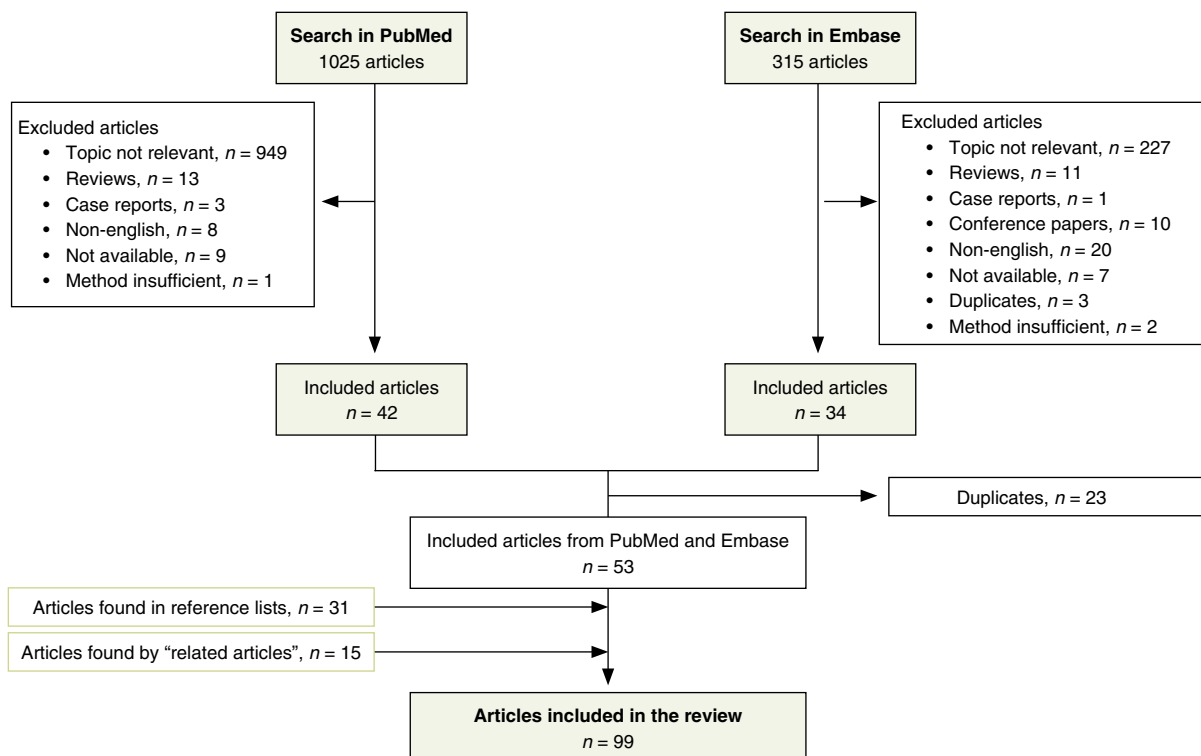


Figure 1 Flowchart of the systematic review selection procedure.

Table 1 Animal studies on the climatic effects on skin barrier

Climatic effect	First author	Reference	Year of publication	Animal	n	Exposure	End points	Main findings/conclusion
Low humidity	Scott and Harding	11	1986	Colworth-Wistar rats	–	Ambient humidity or 100% RH.	Flaggrin amount and distribution in SC and the amount of free amino acids	The proteolytically breakdown of flaggrin was prevented when newborn and adult rats were exposed to 100% RH, suggesting that flaggrin breakdown is dependent on the water activity of the environment.
Low humidity	Rawlings	17	1995	Skin from pigs	5	Dry (RH 44%) or humid (RH 80%) conditions for 7 days.	Desmosome degradation and extensibility of SC	Skin kept in dry conditions had decreased extensibility of SC and degradation of desmosomes compared to skin kept in humid conditions.
Low humidity	Sato	12	1998	Hairless mice (HR-1, Hoshino, Japan)	6–12	Dry (RH < 10%) or humid conditions (> 90%) for 12 h, application of petrolatum.	Epidermal DNA synthesis, skin conductance and TEWL	Mice kept in dry conditions had increased epidermal DNA synthesis and decreased skin conductance compared to mice kept in humid conditions. Application of petrolatum inhibited the increase in DNA synthesis.
Low humidity	Sato	7	1998	Hairless mice (HR-1, Hoshino, Japan)	3–8	Dry (RH < 10%) or humid conditions (RH > 80%) for 7 days	Skin surface appearance, water content, dry weight of SC, desmosomal protein and enzyme activity	Mice kept in dry conditions had more scaling, larger dry weight and thickness of SC. They also had decreased water content of SC and less effectively degraded desmosomes
Low humidity	Denda	21	1998	Hairless mice (HR-1, Hoshino, Japan)	3–20	Dry (RH < 10%) or humid conditions (RH > 80%) for 2 weeks, barrier disruption by acetone or tape stripping.	TEWL, lipid content in SC, epidermal morphology and thickness and recovery rate after barrier disruption	Mice kept in dry conditions had a lower TEWL, thicker epidermis and SC, more lamellar bodies and an accelerated barrier recovery rate.
Low humidity	Denda	8	1998	Hairless mice (HR-1, Hoshino, Japan)	4–12	Dry (RH < 10%) or humid conditions (RH > 80%), barrier disruption and switching between dry and humid conditions.	Epidermal DNA synthesis, hyperplasia and thickness and dermal mast cell hyperplasia and degranulation	Mice kept in dry conditions had increased epidermal DNA synthesis, but no epidermal hyperplasia. After barrier disruption they had a further increase in DNA synthesis and epidermal hyperplasia in addition to mast cell hyperplasia and degranulation.

Table 1 Continued

Climatic effect	First author	Reference	Year of publication	Animal	n	Exposure	End points	Main findings/conclusion
Low humidity	Hosoi	15	2000	Female mice (C57BL/6, Charles River Japan, Japan)	8–10	Dry (RH 10%) or humid conditions (RH 80%) for 0–7 days.	Activation of the skin immune system with induction of contact hypersensitivity, number of LC and allergen penetration	Mice kept in dry conditions had a greater reaction when contact hypersensitivity was elicited, more LC and a greater antigen penetration than mice kept in humid conditions.
Low humidity	Sato	16	2000	Hairless mice (HR-1, Hoshino, Japan)	4–16	Dry (RH < 10%) or humid conditions (RH > 80%) for 3 days.	Skin morphology	Mice kept in dry conditions had a significantly rougher skin surface compared to mice kept in humid conditions. Application of glycerol and immersion in water partly improved the roughness, suggesting that water content and thickness of SC is important for skin morphology.
Low humidity	Sato	18	2001	Hairless mice (HR-1, Hoshino, Japan)	5–12	Transfer after 2 weeks from normal (RH 40–70%) or humid (RH > 80%) conditions to dry conditions (RH < 10%) for 7 days.	Skin surface conductance and water-holding capacity, skin surface images and amino acid content in the SC	Mice transferred from humid conditions had rougher skin surface, less water-holding capacity, water content and amino acid content in SC compared to those transferred from normal conditions.
Low humidity	Denda	22	2001	Hairless mice (HR-1, Hoshino, Japan)	5–8	Transfer after 7 days from normal (RH 40–70%) to dry (RH 10%) or humid (80%) condition for various amount of time. Application and occlusion of 1% SDS 24 h before the mice were killed and analysed.	Epidermal hyperplasia, DNA synthesis and TEWL	The epidermal thickness and DNA synthesis 24 h after SDS treatment was increased in mice kept under low humidity for 2 days. No change was found for 1, 4 or 7 days. No significant change in TEWL up to 1 week, but after 2 weeks the TEWL decreased significantly in mice kept under low humidity and increased in those kept under high humidity.

Table 1 Continued

Climatic effect	First author	Reference	Year of publication	Animal	n	Exposure	End points	Main findings/conclusion
Low humidity	Ashida	13	2001	Hairless mice (HR-1, Hoshino, Japan)	3–12	Dry (RH<10%) or humid (>80%) conditions for 4 days.	Expression and release of epidermal IL-1 α	Mice kept in dry conditions had a higher expression of IL-1 α after 48 h compared to those kept in normal or humid conditions. The immediate release of IL-1 α after tape stripping was also significantly higher in mice kept in dry conditions.
Low humidity	Sato	19	2002	Hairless mice (HR-1, Hoshino, Japan)	12	Transfer after 2 weeks from normal (RH 40–70%) or humid (RH > 80%) conditions to dry (RH < 10%) for 7 days.	TEWL, SC hydration, pH, epidermal DNA synthesis and morphology of epidermis	Mice transferred from humid conditions had a transient defect in barrier function with increased TEWL, decreased hydration of SC, and a delayed increase in epidermal DNA synthesis compared to those transferred from normal conditions.
Low humidity	Ashida and Denda	14	2003	Hairless mice (HR-1, Hoshino, Japan)	5–16	Dry (RH<10%) or humid (>80%) conditions for 5 days.	Mast cell number in dermis and histamine content in epidermis and dermis	Mice kept in dry conditions had an increase in mast cells and histamine in dermis compared to those kept in humid conditions.
Low humidity	Katagiri	20	2003	Hairless mice (HR-1, Hoshino, Japan)	4–6	Transfer after 2 weeks from normal (RH 40–70%) or humid (RH > 80%) conditions to dry (RH < 10%) for 7 days.	Skin conductance, free amino acids and filaggrin expression in SC	Mice transferred from humid conditions had a decrease in skin conductance, free amino acids and filaggrin expression. They also lacked the ability to adapt to the dry environment as they did not have an increase in the production of filaggrin and free amino acids. Adaptation was seen in mice transferred from normal conditions.
Temperature	Denda	34	2006	Hairless mice (HR-1, Hoshino, Japan)	4–8	Exposure to a range in skin surface temperature from 32 °C to 42 °C after skin barrier disruption by tape stripping.	Barrier recovery	The barrier recovery rate was accelerated at temperatures between 36 and 40 °C compared with the area at 34 °C. Barrier recovery rate was delayed at 34 and 42 °C.

Table 1 Continued

Climatic effect	First author	Reference	Year of publication	Animal	n	Exposure	End points	Main findings/conclusion
Temperature	Middleton	35	1969	Skin from guinea pigs	–	Two different temperatures (25.0–26.0 vs. 33.5–37.0).	Extensibility of the SC	Skin kept at 33.5–37.0 °C had increased extensibility, independent of the water content of the SC compared to skin kept at a lower temperature (25.0–26.0 °C).
Temperature	Middleton	36	1973	Skin from guinea pigs	11–12	Two different temperature ranges (4–5 °C vs. 18–22 °C).	Extensibility of the SC	Skin kept at 4–5 °C had decreased extensibility independent of the water content of SC compared to skin kept at a higher temperature (18–22 °C).
Temperature	Halkier-Sørensen	37	1995	Hairless mice (HR/HR)	6	Barrier disruption with acetone and cooling from ice cubes.	TEWL, skin temperature, penetration of tracer through SC (lanthanum) and histology of epidermis	TEWL is misleadingly low after barrier disruption if the skin temperature is low, masking the barrier defect. When the temperature increases, TEWL also increases to levels above pre-exposure leading to dry skin. Cold exposure after barrier disruption also inhibits the formation of LBs and the tracer appears in the nucleated layers of epidermis and even in dermis. This suggests that exposure to cold after barrier disruption prevents barrier recovery.

–, not available; LB, lamellar bodies; LC, Langerhans cell; RH, relative humidity; SC, stratum corneum; SDS, sodium dodecyl sulphate; TEWL, transepidermal water loss.

Furthermore, the amount and release of IL-1 α , a pro-inflammatory cytokine that is highly abundant in the corneocytes, was higher in mice kept in a dry environment compared to those kept in a humid environment.¹³ Exposure to low humidity also induce dermal mast cell hypertrophy, degranulation and increased contact hypersensitivity reactions.^{14,15}

After 3 days exposure to low humidity, the mice showed clinical signs of xerosis with a rougher skin surface, more scaling, larger dry weight and increased thickness of SC.^{7,16} Skin roughness could be improved by application of glycerol or immersion in water.¹⁶ Since desmosome degradation is decreased, this may explain the impaired desquamation and scaling recognized from e.g. winter xerosis. Decreased desmosome degradation was also found in pig skin exposed to dry conditions (RH 44%) in addition to decreased extensibility.¹⁷

The effect of a dramatic change in humidity was investigated by transferring mice after 2 weeks from either normal (RH 40–70%) or humid (RH >80%) conditions to a dry environment (RH $\leq$ 10%).^{18–20} Those transferred from humid conditions developed a rougher and drier skin surface, increased transepidermal water loss (TEWL), reduced amino acid content and filaggrin expression compared to mice transferred from normal conditions. Collectively, a dry environment can influence the skin barrier by different mechanisms that likely make the skin more sensitive to physical or chemical stress and more prone to inflammation (Fig. 2).

In summary, it appears that the first 1–2 days in a dry environment provokes epidermal proliferation, a reduction in skin

hydration, a pro-inflammatory response and a transient barrier deficit. Next, there seems to be an adaption with increased thickness of SC and epidermis, synthesis of lamellar bodies and lipids and enhanced barrier function, indicated by a decrease in TEWL.^{21,22}

Human studies

Human skin that is exposed to low RH (32%) appears to be more susceptible to mechanical stress and fracture than skin in high RH (96%) (Table 2).²³ Also, healthy volunteers exposed to low RH (<10%) for 6 h had a decrease in skin hydration and it appeared clinically dry.²⁴ Similar results were found, when volunteers were transferred from, respectively, normal and high humidity to dry conditions in addition to increased TEWL.^{25,26} Those transferred from humid to dry conditions, also showed reduced skin elasticity.²⁶ Raman spectroscopy analysis shows that environmental humidity affects the level of partially bound and that unbound water increases with increasing RH. Optimal RH for lipids and protein organization is at 60%.²⁷

Factory workers in ultra-dry working conditions (RH 1–3%) and aircrew personnel are among those most heavily exposed to low humidity. Accordingly, factory workers report significantly more skin symptoms such as itch, contact dermatitis and AD compared to controls.^{28,29} They also have significantly lower TEWL and skin capacitance values.³⁰ The low TEWL might be due to compensatory mechanisms as seen in hairless mice exposed to dry air for longer periods.²¹ A large study comparing

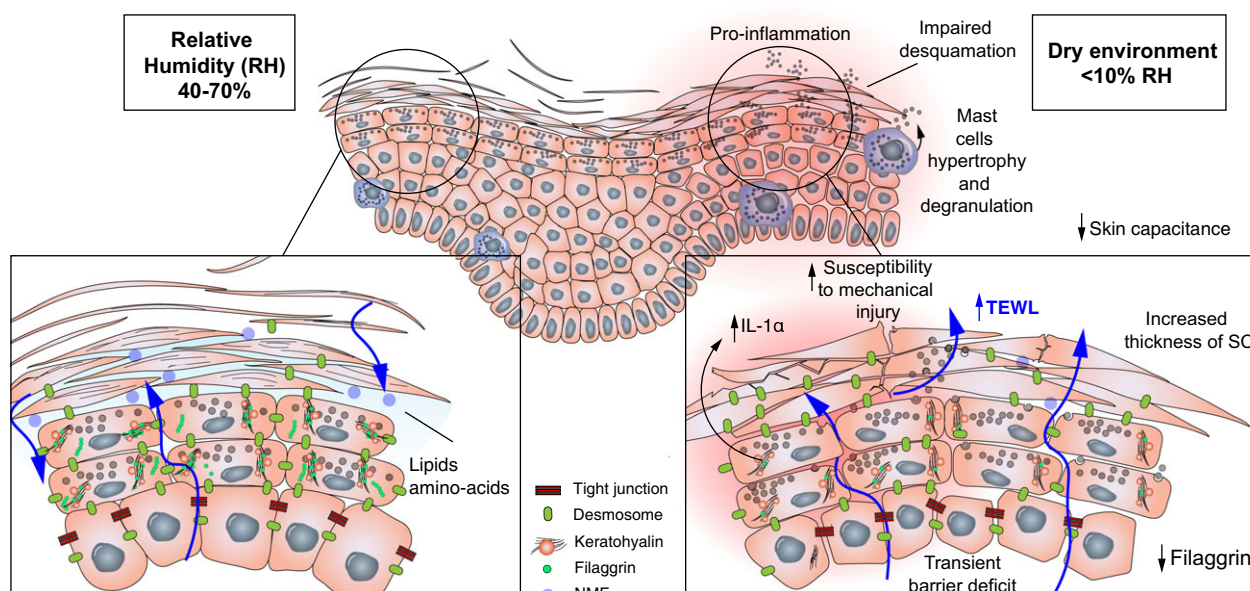


Figure 2 The short-term effect of dry environment (RH < 10%) on skin barrier function and composition.

Table 2 Human studies on the climatic effects on skin barrier

Climatic effect	First author	Reference	Year of publication	Country	Study subjects	n	Exposure	Age (years)	Female/ Male	End points	Main findings/conclusion
Low humidity	Wildnauer	23	1971	USA	Skin from healthy volunteers	15	RH of 32%, 76% or 98%.	20-44	–	The ability to withstand mechanical insults	The energy required to break SC increased with increasing RH. This suggests that skin kept in low RH are more fragile and susceptible to mechanical stress than skin kept in higher RH.
Low humidity	Reinikainen	32	1992	Finland	Office workers	290	Six-period cross-over trial where one wing of the building was operated with 30-40% humidification and the other wing had no air humidification (RH 20-30%), switching every week.	–	148/142	Self-reported questionnaire and change in dryness symptoms score (skin, eyes and pharyngeal symptoms)	The overall dryness score was significantly lower during the humidified phases, including symptoms from the skin (dryness, irritation, itching).
Low humidity	Lindgren	31	2002	Sweden	Commercial cabin crew and office workers from the same company	1681	Exposure to low RH (between 5-25%) (aircrew) and normal indoor environment (office workers).	Mean age 43 (±8)	891/790	Self-reported questionnaire on dermal symptoms	Aircrew reported significantly more skin symptoms from face (OR = 2.03) and hands (OR = 3.68) than office workers after adjustment for possible confounders.
Low humidity	Egawa	24	2002	Japan	Healthy volunteers	12	RH of 10% for 6 h	21-45	8/4	Skin hydration, TEWL and skin surface pattern	Significant decrease in TEWL, skin hydration in the upper layers of epidermis and changes in skin surface pattern resembling those of dry skin.
Low humidity	Sato	28	2003	Japan	Factory workers	155	Ultra-dry working conditions (RH 2.5%) or normal conditions.	22-66	22/133	Self-reported questionnaire on exposure symptoms, AD and asthma	Workers exposed to ultra-dry conditions reported significantly more skin symptoms and had more AD.
Low humidity	Chou	30	2005	Taiwan	Factory workers	49	Ultra-dry working conditions (RH 1.5%) for <0.5-20 months or normal conditions.	–	19/30	TEWL and skin capacitance	Workers exposed to ULH had a significantly decrease in TEWL and a non-significant decrease in skin capacitance compared to those working in normal conditions.
Low humidity	Sunwoo	25	2006	Japan	Healthy volunteers	16	Transfer from normal humidity (50%) to 3 different RH (10, 30 and 50%) for 180 min	–	0/16	TEWL and skin hydration	TEWL of the face increased and skin hydration decreased significantly in dry conditions (RH 10 and 30%) compared to normal conditions (RH 50%).
Low humidity	Tsukahara	26	2007	Japan	Healthy volunteers	20	Transfer from a room with high humidity (RH 70%) to a room with low humidity (RH 40%).	28-50	10/10	Water content of SC, skin elasticity and skin wrinkles and texture	Increased amount of fine wrinkles, decreased water content of SC and loss of elasticity after transfer from a room with high humidity to a room with low humidity.

Table 2 Continued

Climatic effect	First author	Reference	Year of publication	Country	Study subjects	n	Exposure	Age (years)	Female/Male	End points	Main findings/conclusion
Low humidity	Chou	29	2007	Taiwan	Factory workers	24	Ultra-dry working conditions (RH 1–3%) for 3 years (between 2000–2003).	–	24/0	Prevalence of itching at any site, winter eczema, contact dermatitis and urticarial.	Workers exposed to ULH had an 8-fold elevated risk of skin itch compared to the control group in 2000 and a 4-fold elevated risk in 2003. Further there was a large increase in risk of contact dermatitis after 3 years in ULH. No significant change was seen for winter eczema or urticaria.
Low humidity	Vyrmuhoore	27	2013	France	Human abdominal skin obtained from plastic surgery	5	Exposure to five different RH (4%, 28%, 44%, 60% and 75%) for 4 h.	40–50	5/0	Water distribution and organization of SC lipids and proteins.	The level of totally bound water did not vary with humidity. Partially bound water increased sharply between 28% and 60%. Unbound water increased slightly between 4% and 28% and more prominent between 44% and 75%. The organization of SC lipids and proteins were found to be optimal at RH 60%.
Temperature and humidity	Spencer	38	1975	USA	Skin from human cadavers	–	Four different temperatures (10 °C, 20 °C, 30 °C or 35 °C) at seven different levels of humidity (RH 30%, 40%, 60%, 75%, 83%, 93% or 96%).	–	–	Water content of SC	The water content of stratum corneum decreases with decreasing temperature. This dependence was stronger at RH below 60%.
Temperature and humidity	Cooper	42	1992	UK	Female volunteers	55	Seasonal differences in temperature, wind speed and absolute humidity.	18–58	55/0	The occurrence of dry facial skin	The scores for dry skin were higher with low temperature, high wind speed and low absolute humidity.
Temperature and humidity	Reinikainen	33	2003	Finland	Office workers	368	Six-week cross-over study was two separate wings of an office building was humidified with steam for 1 week each. A third wing was used as a non-humidified reference.	–	–	Self-reported questionnaire concerning symptoms of skin rash and skin dryness and continuous measurements of temperature and humidity in all three wings.	No significant association was found between temperature and skin symptoms, but high temperatures seemed to increase the sensation of dry skin. Skin symptoms were in general better with increasing absolute and relative humidity.
Temperature and humidity	Roure	43	2012	France	Female volunteers	12	Exposure to cold and dry wind for 15 min	53–70	12/0	Skin hydration and TEWL	After exposure to dry and cold wind there was a significant decrease in skin hydration, but no change in TEWL.
Temperature	Grice	40	1971	UK	Healthy volunteers	17	Skin temperatures ranging from 25–39 °C where sweating was inhibited.	–	–	TEWL	TEWL increased exponentially with increasing skin temperatures over the range 25 °–39 °C.
Temperature	Mathias	41	1981	USA	Skin from human cadavers	22	Five different skin surface temperatures.	>30	5/17	TEWL	Positive correlation between skin temperature and TEWL.

Table 2 Continued

Climatic effect	First author	Reference	Year of publication	Country	Study subjects	n	Exposure	Age (years)	Female/ Male	End points	Main findings/conclusion
Temperature	Halkier-Sørensen	44	1991	Denmark	Workers in the fish processing industry.	10	Exposure to iced fish during a whole working day.	19-55	10/0	TEWL, skin hydration, skin blood flow and skin temperature at the end of the workday and up to 1 h after work.	At the end of the work day TEWL, skin temperature and skin blood flow was low and hydration high. After 10 to 15 min, TEWL, skin temperature and skin blood flow increased to levels above normal and skin hydration to levels below normal (compared to controls). All values normalized after 1 h, except skin hydration which was still below normal.
Temperature	Halkier-Sørensen	45	1991	Denmark	Workers in the fish processing industry	143	Exposure to iced fish during a whole working day.	18-57	127/16	The relationship between skin surface temperature, TEWL and skin hydration.	A significant positive correlation was found between skin surface temperature and TEWL and a significant negative correlation was found between skin surface temperature and hydration and between skin hydration and TEWL.
Temperature	Fluhr	46	2005	Germany	Healthy volunteers	20	Exposure to cold and SLS or SLS alone.	21-50	10/10	TEWL and skin irritation (Chromameter and visual scoring)	Exposure to cold alone did not influence TEWL or cause skin irritation. SLS caused a significant increase in TEWL and an irritant skin reaction. If cold was applied together with the SLS, the increase in irritation and TEWL was lower, suggesting a protective effect of the cold.
Temperature	Cravello	39	2008	Italy	Healthy volunteers	6	Different environmental parameters in a climatic chamber (Temperature 20 °C, 25 °C or 30 °C, RH 25%, 45%, 65% or 85%).	25-34	6/0	Skin hydration and TEWL	No strong correlation between TEWL and RH, but a positive correlation between TEWL and skin temperature. Positively correlation between skin hydration, temperature and RH.
Temperature	Plab	47	2010	Germany	Male volunteers with and without AD	19	Application of histamine to induce skin itch and the exposure to two different temperatures (25 °C and 32 °C) modulated by a skin thermode.	Mean age 27.6 (±4.3)	0/19	Itch intensity judged by a visual analogue scale (0-100) and the Eppendorf and the Eppendorf Litch Questionnaire.	Mean itch intensity was generally higher during the low temperature. The scores were also higher for atopic skin than healthy skin and a significantly higher in lesional skin than non-lesional skin.

–, not available; AD, atopic dermatitis; FLG, filaggrin; RH, relative humidity; SC, stratum corneum; SLS, sodium lauryl sulfate; TEWL, transepidermal water loss; ULH, ultra-low humidity.

aircrew personnel and office workers in the same company showed that aircrew personnel reported significantly more skin symptoms from the face and hands than office workers.³¹ Furthermore, in an experimental study on the effect of air humidification, two different wings of an office building switched between air humidification (RH 30–40%) and (20–30%) over a 6-week period. Participants reported significantly less skin symptoms, during the periods a RH of 30–40%.³² In another similar cross-over study, skin symptoms also improved with increasing absolute and relative humidity.³³

Low temperature negatively affects skin barrier function

Animal studies

The barrier recovery rate in hairless mice has been found to be optimal between 36–40 °C, and temperatures below or above this delays the recovery (Table 1).³⁴ Experiments on skin from guinea pigs have shown that a reduction in temperature negatively affects the extensibility of the SC, independent of SC water content.^{35,36} Furthermore, exposure to low temperatures likely obscures a defect in skin barrier function as suggested by a study on hairless mice.³⁷ Immediately after barrier disruption on cooled skin (skin surface temperature 12 °C), TEWL was low, suggesting no defect in barrier function. However, just after cold exposure ceased (within 15 min) TEWL increased to levels above precold exposure and it took more than 5 h before it was normalized. Two observations in this study indicated a barrier deficiency; the increased TEWL and a higher percutaneous penetration rate of a tracer compound than at normal skin temperatures. Furthermore, after cooling, almost no lamellar bodies or lipids were present in the outer layer of the stratum granulosum.³⁷

Human studies

A study on human skin showed that the SC water content decreased together with temperature, and that the relationship was stronger with low RH (<60%) (Table 2).³⁸ In a study on healthy volunteers, a positive correlation between TEWL and skin temperature and between skin hydration, temperature and RH was observed.³⁹ Other studies have also confirmed a positive correlation between skin temperature and TEWL.^{4,40,41} A study on dry facial skin found a higher dryness score with low temperatures, high wind speed and low humidity,⁴² and as little as 15 min of cold and dry air has been proven to significantly decrease skin hydration.⁴³ These data suggest that a reduction in temperature leads to a decrease in skin hydration and TEWL, and that this effect is stronger when RH is low.

However, the decrease in TEWL might be misleading and indeed obscure a true skin barrier deficiency.³⁷ Employees in the fish processing industry had a low TEWL and a high skin hydration immediately after work, but when the skin tempera-

ture returned to normal (10–15 min), TEWL increased and skin hydration decreased to levels above and below normal, respectively.⁴⁴ A significant positive correlation was found between skin surface temperature and TEWL and a negative correlation between skin temperature and hydration.⁴⁵ However, in another study, cold alone for short periods of time (six cycles of 4 °C for 90 s) did not affect TEWL or skin irritation and cold was proved to have a protective effect on the irritation from SLS, suggesting that the duration of cold exposure might influence its effect on skin barrier function.⁴⁶ In addition, it has been proven that itch is perceived more intense if skin temperature is lowered.⁴⁷

Seasonal change significantly affects skin barrier function

Skin complaints during the winter are well-described, and common terms include 'winter itch', 'pruritus hiemalis' and 'frost itch'.^{48,49} The first article where meteorological conditions were observed in relation to skin complaints was published in 1894.⁵⁰ In the 1950s, a study on climatic conditions and skin chapping showed that the incidence of chapping peaked in periods with weather shifting from a high dew point and low barometric pressure to a low dew point and high barometric pressure; a typical transition during winter months.⁵ A plausible explanation is that during periods of high dew point, air holds more water and the skin get hydrated. A low barometric pressure allows water diffusion from the deeper layers of the skin to the epidermis, also increasing skin hydration. With a drop in dew point, the air becomes drier and water evaporates from the skin surface. A rise in the barometric pressure forces water out of epidermis. The skin therefore dries out, leaving it more susceptible to chapping.

Since then, several studies have investigated the influence of season on skin barrier function (Table 3). Briefly, during winter, a decrease in SC lipids and an increase in unsaturated fatty acids have been identified.^{4,51,52} A decrease in skin hydration as well as an increase in SC pH and stiffness was also observed in addition to lower levels of potassium, lactate, sodium and chlorine, components of the skin NMFs.^{53–56} Drier skin and increased reaction to skin irritants, suggest that the skin becomes more fragile and permeable during winter time.⁵⁷

During summer, TEWL and skin hydration increase, and sebum production is higher than during winter.^{4,58–63} Raman spectra of healthy skin showed a seasonal variation in skin surface hydration with highest values during summer. However, no seasonal variation was found for the depth water profile of the SC.⁶⁴ This suggests that the upper layer water content of the SC is more affected by environmental exposure than the deeper layers. Corneocyte number also increases during summer, they become smaller and display better desquamation.^{58,65} However, some studies could not confirm a seasonal variance in skin hydration⁶³ or TEWL⁶⁶ and another did not find any differences in skin surface lipids.⁵⁴

Table 3 Studies on the effects of seasonal changes on skin barrier

Seasonal change	First author	Reference	Year of publication	Country	n	Study subjects	Age	Female/ Male	Skin properties examined	Main findings
Summer vs. autumn vs. winter vs. spring	Abe	4	1980	Japan	24	Healthy volunteers	19–55	12/12	Skin temperature, pH, surface lipids and TEWL	TEWL and skin lipids are at their highest in July and lowest in January. A positive correlation between skin temperature and TEWL and an inverse correlation between skin pH and skin temperature.
Summer vs. autumn vs. winter vs. spring	Black	58	2000	France	24	Healthy female volunteers	18–35	24/0	Skin surface hydration, TEWL, corneocytes released during turbine stimulation and skin surface topography	Increased TEWL, amount of corneocytes and levels of skin hydration in July compared to spring and winter. This applied for the calf area and forearm, no seasonal variation was seen for the facial skin. No seasonal change was seen in surface topography.
Summer vs. autumn vs. winter vs. spring	Youn	61	2005	Korea	46	Healthy female volunteers	21–37	46/0	Facial sebum secretion	The sebum secretion was significantly higher during summer, compared to all other seasons.
Summer vs. autumn vs. winter vs. spring	Egawa	64	2008	Japan	45	Healthy volunteers	22–76	31/14	Water profile of the SC, amount of NMF, cholesterol and ceramide 3 evaluated by Raman spectra an skin capacitance in cheek and forearm	No significant seasonal changes in the depth profile of water content throughout the year. Hydration of the skin surface (skin capacitance) was highest during summer. Lactate, urea, cholesterol and ceramide 3 were also highest during summer in the cheek skin. Those 'feeling dry' had a significant lower amount of NMF in the cheek skin during autumn than those 'not feeling dry'.
Summer vs. autumn vs. winter vs. spring	Ishikawa	60	2013	Japan	10	Healthy volunteers	26–44	0/10	TEWL, skin capacitance and ceramide profile in different anatomical locations	The overall result of the study showed that the skin surface condition in summer is thought to be best for most body regions, judged by TEWL, skin capacitance and ceramide profile.

Table 3 Continued

Seasonal change	First author	Reference	Year of publication	Country	n	Study subjects	Age	Female/ Male	Skin properties examined	Main findings
Summer vs. autumn vs. winter vs. spring	Tsukahara	62	2013	Japan	32	Healthy volunteers	35–47	16/16	Intensity of wrinkles and skin hydration	No seasonal variation in the intensity of facial wrinkles was found in men or women. In men, the skin hydration was significantly lower in December and March compared to September. In women the lowest skin hydration was found in March.
Summer vs. winter	Herrmann	65	1983	Germany	40	Healthy young and old volunteers	–	20/20	Size of corneocytes	The size of the corneocytes was significantly smaller during summer than during winter in older males and females. Low corneocyte cell surface areas were associated with higher numbers of removable cells from the skin surface.
Summer vs. winter	Den Arend	66	1988	The Netherlands	26	Patients with AD and controls	–	–	TEWL and impedance	No seasonal influence on TEWL and impedance in atopics or non-atopics.
Summer vs. winter	Conti	51	1996	UK	10	Healthy female volunteers	18–25	10/0	SC lipids (ceramides, cholesterol and fatty acids)	A 40% reduction in ceramide and cholesterol from summer to winter and a 5% reduction in fatty acids. A greater amount of ceramide 1 linoleate was seen during winter than summer, and the levels could be reduced by application of a formula rich in linoleic acid over a period of 4 weeks.
Summer vs. winter	Rogers	52	1996	UK	26	Healthy female volunteers	21–60	26/0	SC lipids (ceramides, cholesterol and fatty acids)	A pronounced decline in all stratum corneum lipids from summer to spring and winter and more unsaturated fatty acids during winter time. All lipids declined to the same extent, leaving the relative proportions the same.

Table 3 Continued

Seasonal change	First author	Reference	Year of publication	Country	n	Study subjects	Age	Female/ Male	Skin properties examined	Main findings
Summer vs. winter	Kikuchi	54	2002	Japan	39	Healthy female volunteers	24–78	39/0	TEWL, skin surface lipids and hydration state of the SC	On the flexor forearm, skin hydration state decreased during winter compared to summer. No change was seen in facial skin. TEWL increased significantly at both the forearm and at the facial skin during winter compared to summer. No seasonal variation in skin surface lipids was found.
Summer vs. winter	Andersen	57	2004	USA	8	Women with dry and itchy skin during winter	63–78	8/0	Dry skin score, amount of skin scale removed by adhesive tape, skin hydration and response to a skin irritant (SLS) at the lower legs	Increased dry skin score, more removed skin scale and an increased reaction to a skin irritant was found during the winter than during the summer. No significant change in skin hydration. This suggest that the skin becomes loser and more permeable during the winter.
Summer vs. winter	Nakagawa	53	2004	Japan	40	Healthy male volunteers	27–55	0/40	SC hydration, elasticity of the skin, SC stiffness, pH, amount of NMF and their ionic composition	A significant decrease in SC hydration and increase in SC stiffness and pH during winter compared to the summer. The amino acid content was significantly higher during winter than summer and did not correlate with the physical properties of the SC. The levels of potassium, lactate, sodium and chloride were all significantly lower during winter than summer.
Summer vs. winter	Qiu	59	2011	China	354	Healthy female volunteers	18–80	354/0	Signs of ageing, skin tone, pigmentation, sebum production and skin hydration	Skin hydration and sebum production were higher during summer than winter. No signs of ageing during the 6 months between measurements.
Spring vs. winter	Devillers	55	2010	Belgium	40	Healthy female volunteers	52–59	40/0	The relationship between environmental dew point and the water-holding capacity of the skin	The water-holding capacity of the cheeks was significantly lower during winter than spring. No significant differences were found on the lips or on the back of the hand. A weak positive correlation was found between the water-holding capacity and environmental dew point.

Table 3 Continued

Seasonal change	First author	Reference	Year of publication	Country	n	Study subjects	Age	Female/ Male	Skin properties examined	Main findings
Summer vs. winter	Delvenne	56	2013	France	47	Postmenopausal female volunteers	–	47/0	Seasonal variation in skin hydration and flaky skin	During winter skin hydration decreased and the skin showed increased roughness and scaliness. The changes were less evident in women receiving hormonal replacement therapy (HRT).
Summer vs. winter	Nam	63	2015	Korea	89	Healthy female volunteers	20–38	89/0	Seasonal variation in skin hydration, sebum production, scaliness and elasticity	No clear variation in skin hydration during the different seasons. Sebum production was higher during summer than spring and winter. Skin elasticity in the winter was low compared to other seasons.

–, not available; AD, atopic dermatitis; NMF, natural moisturizing factors; SC, stratum corneum; SLS, sodium lauryl sulfate; TEWL, transepidermal water loss.

Effect of seasonal and climatic variations on the risk of dermatitis

Atopic dermatitis

Cold and dry weather increase the overall risk of flares in patients with AD and further increase its incidence and prevalence (Table 4).^{67–73} Accordingly, a higher prevalence of AD was found in American states with low humidity, low UV exposure, low outdoor temperature, use of indoor heating and frequent precipitation.⁷⁴ The AD prevalence was found to have a positive correlation with latitude and a negative correlation with mean outdoor temperature and indoor RH.⁷⁵ In Japan, a negative correlation between temperature and humidity and dermatological visits concerning AD has been found.⁷⁶ Supporting this observation, AD incidence has been found to peak in February and October,⁷⁷ and AD patients had decreased skin hydration, increased TEWL, a higher flare score, more irritation and dryness in November compared to July.⁷⁸ Children with AD who spent 4 weeks in a sunny, subtropical climate experienced a significant decrease in symptom severity and a better life quality after their stay and at the 3-month follow-up compared to baseline values.⁷⁹

It has been hypothesized that birth season might impact the development of atopic diseases. Studies from Japan, the UK and Sweden have indeed shown a higher prevalence of atopic diseases in children born during autumn and winter than spring and summer.^{80–84} The first months in dry and cold weather might explain this finding.^{13,24,42} Hence, during the first year of life, the skin's ability to store and transport water is decreased and infants have significantly lower levels of NMFs than adult skin, making it more vulnerable for external stressor such as low humidity and low temperatures.⁸⁵

It has been suggested that there exists two types of seasonal patterns in patients with AD. Some experience an aggravation during summer while others during winter.⁸⁶ The summer type has a worsening during periods with high grass pollen exposure and high outdoor temperatures, and the winter type with low outdoor temperatures, indicating different mechanisms. In school children with AD, 40% felt that hot weather worsened their symptoms, whereas 28% felt that cold weather worsened their disease.⁸⁷ Sudden changes in temperatures may also be perceived as a possible trigger for AD exacerbation.⁸⁸ In another study, the only significant association between environmental factors and flare of disease was damp weather.⁸⁹

A recent study also suggested a connection between loss-of-function mutations in the *FLG* and the susceptibility to climatic exposure in patients with AD. Children with AD and *FLG* mutations more often developed dermatitis at anatomical localizations exposed to wind and cold (extremities, cheeks, hands and feet).⁹⁰ Furthermore, children with AD living in a subtropical climate had a lower prevalence of *FLG* mutations compared to those living in colder and drier parts of Japan,⁹¹ suggesting that

Table 4 Studies on the effect of seasonal and climatic variations on the risk of dermatitis

Type of dermatitis	First author	Reference	Year of publication	Country	n	Study subjects	Age	Female/Male	Outcome	Main findings
Atopic dermatitis	Hellier	77	1940	UK	30 677	Patients seen at the Dermatological Department in Leeds between 1928–1938	–	–	Incidence of AD according to season.	The highest incidence of AD was found in February (high rise) and October (smaller rise).
Atopic dermatitis	Tupker	78	1995	The Netherlands	38	Patients with AD and healthy controls	17–53	–	The influence of season on irritant susceptibility and reactivity to i.c. injection of bioactive agents.	Both groups (AD and control group) had a higher TEWL, flare score, visual irritation and dryness score in November than in July and skin hydration was decreased.
Atopic dermatitis	Nilsson	80	1997	Sweden	209	Children	0–15	143/66	Prevalence of atopic disease according to season of birth (spring-summer vs. fall-winter).	Atopic disease was more common among children who were born in the autumn and winter compared to the spring and summer.
Atopic dermatitis	Remes	72	1998	Finland	11 607	School children	13–14	5874/5733	The prevalence of allergic rhinitis and AD in four regions of Finland.	The prevalence of AD was slightly higher in northern parts of Finland, most likely due to cold weather and low humidity.
Atopic dermatitis	Tariq	82	1998	UK	1456	Birth cohort	0–4	–	Risk factors for atopy in early childhood.	Atopic disease and allergen sensitization was significantly more common in children born during autumn and winter combined (14.0%) than those born during spring and summer combined (9.6%).
Atopic dermatitis	Aoki	84	1998	Japan	10 156	Patients diagnosed with AD at an outpatient clinic in Japan between 1989 and 1995	From 0 to >31 years	4641/5515	Seasonal variation in the month of first visit for AD patients.	For patients <1 year, there was a significant higher birth number during autumn and lower birth number during summer. Among children <1 year, there was a tendency of higher numbers of first visits during spring and smaller number of first visits during summer. There were no definite social reasons for the increase in first visits during the spring, suggesting that it might be a result of climatic effects.
Atopic dermatitis	Dhar	69	1998	India	672	Infants (0–1 years) and children with AD	0–12	288/384	Epidemiological factors and clinical patterns of AD.	Winter aggravation of AD symptoms were seen in 67.1% of the infants and 58.0% of the children compared to 23.4% and 32.9% who experienced aggravation during summer and 9.5% and 7.4% during spring.

Table 4 Continued

Type of dermatitis	First author	Reference	Year of publication	Country	n	Study subjects	Age	Female/Male	Outcome	Main findings
Atopic dermatitis	Williams	9	1999	Worldwide	715 033	A random sample of children in the two age groups 6–7 years and 13–14 years	6–14	–	Prevalence of AD.	The highest prevalence of AD was found in urban Africa, the Baltics, Australasia and Northern and Western Europe. Tendency of a latitude dependent variation in AD prevalence with low prevalence in low altitudes and high prevalence in Northern Europe and Australasia.
Atopic dermatitis	Kusunoki	81	1999	Japan	33 725	School children	7–15	–	Prevalence of AD according to month of birth.	Those born during autumn (October to December) showed the highest (7.5%, OR 1.22, 95% CI: 1.01–1.34) and those born during spring (April to June) showed the lowest (5.5%, OR 0.79, 95% CI: 0.71–0.88) prevalence of AD.
Atopic dermatitis	Uenishi	70	2001	Japan	682	Patients with AD	3–30	355/327	Seasonal aggravation of skin lesions.	66% of the patients experienced seasonal aggravation, winter being the most prevalent.
Atopic dermatitis	Vocks	67	2001	Switzerland	2106	Patients treated for AD at a Swiss clinic	16–74	1326/780	The severity of itching according to climatic conditions.	Increased itching was seen with low temperature, little sunshine, snowfall and fog. The most favourable weather conditions were a temperature around 20 °C, relative humidity around 70%, a fair amount of sunshine and moderate wind.
Atopic dermatitis	Williams	87	2004	UK	225	Schoolchildren with AD	8–14	–	Factors influencing disease activity.	In the group of children, 40.0% felt hot weather and 28.4% felt cold weather exacerbated their rash.
Atopic dermatitis	Hancox	73	2004	USA	296 168	Dermatological office visits from 1990 to 1998.	–	–	Seasonal variation in dermatologic disease in the USA.	Visits concerning atopic dermatitis showed a peak during winter. The trend was however not significant.

Table 4 Continued

Type of dermatitis	First author	Reference	Year of publication	Country	n	Study subjects	Age	Female/Male	Outcome	Main findings
Atopic dermatitis	Weiland	75	2004	Worldwide	721 601	A random sample of children in the two age groups 6–7 years and 13–14 years	6–14	–	Climatic influence on the prevalence of symptoms.	The prevalence of AD symptoms was positively correlated with latitude and negatively correlated with mean annual outdoor temperature both worldwide (6–7 year olds) and in Western Europe (both age groups). Worldwide there was a negative correlation between indoor relative humidity and AD symptoms for the 6–7 year olds.
Atopic dermatitis	Krämer	86	2005	Germany	39	Children with AD selected from a birth cohort	8–9	21/18	Seasonality of AD symptoms.	Two types of patterns; a summer type pattern with aggravation of symptoms during summer and a winter type pattern with aggravation of symptoms during winter. The winter type had worsening of symptoms with low temperatures and the summer type with high grass pollen exposure.
Atopic dermatitis	Langan	89	2006	Ireland	25	Children with AD	0–14	11/14	Association between environmental factors and flare of disease.	Heat, damp and stress was factors associated to disease flare, damp being the only significant
Atopic dermatitis	Byremo	79	2006	Norway	56	Children with severe AD	4–13	30/26	Improvement in SCORAD and CDLQI after 4 weeks in a sunny, subtropical climate and at the 3-month follow-up. Bacterial skin colonization with <i>S. Aureus</i> and use of local steroids.	The SCORAD and CDLQI in the index group declined significantly after 4 weeks and at the 3-month follow-up compared to baseline. The results were significantly better than in the control group. The index group also had a decrease in use of local steroids and bacteriological skin colonization after 4 weeks and at the 3-month follow-up, compared to baseline values.
Atopic dermatitis	Kuzume	83	2007	Japan	2136	Infants	0–1	1049/1087	Incidence of AD according to season of birth.	The incidence of AD was lowest (22.3%, OR 0.61, 95% CI: 0.49–0.76) in infants born during spring and highest (34.6%, 1.37, 95% CI: 1.11–1.69) in those born during autumn.

Table 4 Continued

Type of dermatitis	First author	Reference	Year of publication	Country	n	Study subjects	Age	Female/Male	Outcome	Main findings
Atopic dermatitis	Suárez-Varela	68	2008	Spain	28 394	School children	6–7	14 143/14 251	Prevalence of disease according to three different climatic regions in Spain.	The highest prevalence of AD was found in the Atlantic region (32.9%) and the lowest in the Mediterranean region (28.3%). The prevalence of AD symptoms were positively correlated with precipitation and humidity and negatively correlated with mean annual temperature and mean annual number of sunny hours.
Atopic dermatitis	Weiss	71	2008	USA	580	Patients with AD	–	–	Baseline ISGA score according to season of enrolment.	Among those recruited during winter, 70% had a baseline ISGA score of 3 or more compared to 50% of those recruited during spring. This shows a seasonal variation in AD severity.
Atopic dermatitis	Nemoto-Hasebe	92	2009	Japan	24	Patients with AD, 12 with <i>FLG</i> mutations and 12 without mutations	6–33	10/14	Seasonal aggravation of AD symptoms.	In AD patients with <i>FLG</i> mutations, 3/12 felt they had an aggravation of symptoms during winter. In AD patients without <i>FLG</i> mutations, 2/12 felt aggravation during winter and 4/12 felt aggravation during summer.
Atopic dermatitis	Furue	76	2011	Japan	67 448	Dermatological out- and inpatients of 170 clinics all over Japan	From 0 to >101	36 125/30 899 (424 undescribed)	Prevalence of dermatological disorders in Japan. Correlation with temperature and humidity.	The number of patients visiting due to AD (6733) was negatively correlated with temperature and humidity.
Atopic dermatitis	Carson	90	2012	Denmark	397	Children born to mothers with asthma (COPSAC)	0–7	–	The influence of <i>FLG</i> mutations on the anatomical localization, morphology and severity of AD.	Children with AD and <i>FLG</i> mutations had a higher severity score of their AD and more often dermatitis at anatomical localizations exposed to drying conditions (e.g. wind, cold, sun and radiation). This suggests that <i>FLG</i> mutations make children with AD more susceptible for climatic exposure than children without a <i>FLG</i> -mutation.

Table 4 Continued

Type of dermatitis	First author	Reference	Year of publication	Country	n	Study subjects	Age	Female/Male	Outcome	Main findings
Atopic dermatitis	Silverberg	74	2013	USA	91 642	Children living all over the USA	0-17	–	Association between climatic factors and prevalence of AD.	Increased AD prevalence with low humidity, low UV exposure, low outdoor temperature, indoor heating and increased precipitation. Decreased AD prevalence with high outdoor humidity, high UV exposure, high temperature, decreased precipitation.
Atopic dermatitis	Sasaki	91	2014	Japan	721	Children in a Japanese cohort (KIDs)	0-6	336/385	Prevalence of AD and FLG mutations in children with and without AD.	A lower prevalence of AD and FLG mutations in patients with AD among children living in a subtropical climate with high temperatures and high RH compared to those living in colder and drier parts of Japan. This suggests that FLG mutations are not a predisposing factor for AD in a subtropical climate.
Atopic dermatitis	Ortiz de Frutos	88	2014	Spain	241	Children and adults with moderate to severe AD	2-15 and >16	121/120	Triggers perceived by the patients to have the largest influence on exacerbations.	Among the adult patients 36.0% and among the children 42.2% associated sudden changes in temperature as a possible trigger for AD exacerbation.
Irritant dermatitis	Kavli and Førde	94	1984	Norway	14 667	Participants in a survey about coronary risk factors	20-54	7257/7410	Prevalence of hand dermatitis in northern parts of Norway compared the prevalence in a large Swedish health survey.	Higher prevalence of hand dermatitis in northern parts of Norway than in a large health survey from southern parts of Sweden. The climatic differences (less day-time sunshine hours, fewer clear days, lower average temperatures and low humidity) might explain the difference.
Irritant dermatitis	Agner	97	1989	Denmark	17	Healthy volunteers	25-38	7/10	Patch test reactions to SLS and non-anionic acid, TEWL.	Significantly stronger reactions to SLS (judged by TEWL value) during the winter than the summer.
Irritant dermatitis	Edman	102	1989	Sweden	3063	Patients patch tested between 1983-1987	–	–	Number of patients positive to the standard series according to season.	A peak of positive results in January (45%) and a low in June (24%). The author suggests that this might be due to UV radiation.

Table 4 Continued

Type of dermatitis	First author	Reference	Year of publication	Country	n	Study subjects	Age	Female/Male	Outcome	Main findings
Irritant dermatitis	Kränke	107	1996	Austria	11 516	Patients patch tested between 1992–1993	5–91	8234/3282	The influence of UV irradiation on patch test results.	The lowest outcome of positive or irritant/doubtful results was found in the summer months (June and August). For nickel and thimerosal, only ++ reactions showed a significantly lower peak in the summer months.
Irritant dermatitis	Basketter	98	1996	UK, China and Germany	100	Healthy volunteers	Adult	–	SDS dose response results, skin irritant scoring scale and seasonal variation in the dose response to SDS.	Higher rates of positive reactions when testing SDS during winter than summer. The German population (colder and drier weather conditions) appeared more sensitive to lower concentrations of SDS.
Irritant dermatitis	Uter	10	1998	Germany	1533	Hairdresser apprentices	–	–	Association between irritant skin changes and weather conditions.	Strong association between irritant skin changes, mean temperature and absolute humidity. Low temperatures and low absolute humidity increased the risk of irritant hand dermatitis.
Irritant dermatitis	Uter	103	2001	Germany	46 887	Patients patch tested between 1992–1997	–	30 523/16 364	Monthly variation in reaction to formaldehyde.	During cold and dry weather there was a twofold increase in weak positive reactions to formaldehyde compared to warm and humid periods.
Irritant dermatitis	Morris-Jones	93	2002	UK	335	Patients with dermatitis caused by physical irritants	1–78	148/187	Characterization of the materials and mechanisms behind the irritant dermatitis.	Low humidity due to air-conditioning was the most common cause of irritant dermatitis and was found in 32.7% of the cases.
Irritant dermatitis	Uter	99	2003	Germany	1600	Patients patch tested between 1996–2001	–	–	The influence of meteorological conditions on patch test results.	During cold weather and low absolute humidity, there is an approximately 50% increased chance of irritant reaction to 0.5% SLS. A significantly increased risk of doubtful/irritant reaction to a number of allergens was found with low temperature and dry air. For one allergen (potassium dichromate) the risk was decreased.

Table 4 Continued

Type of dermatitis	First author	Reference	Year of publication	Country	n	Study subjects	Age	Female/Male	Outcome	Main findings
Irritant dermatitis	Löffler	108	2003	Germany	487	Volunteers recruited from a dermatological outpatient clinic	18–60	281/206	The influence of meteorological conditions on TEWL and patch test results.	Basal TEWL values were unchanged over the year, but a sharp decrease in delta TEWL values from winter to summer was observed. The delta TEWL value was significantly correlated with temperature and absolute humidity, suggesting that the skin is more reactive during winter than summer.
Irritant dermatitis	Hancox	73	2004	USA	296 168	Dermatological office visits from 1990 to 1998.	–	–	Seasonal variation in dermatologic disease in the USA.	Visits concerning contact dermatitis showed a peak during winter. The trend was however not significant.
Irritant dermatitis	John	100	2005	Germany	554	Patients who had previously suffered from occupational skin disease	Mean male age was 42 and mean female age was 36	277/277	The influence of season on NaOH-induced skin irritation on the volar forearm and the back of the hand.	A strong association between low temperature and low absolute humidity and the reactivity to NaOH on the back of the hand. In cold and dry weather there was a fourfold increase in the chance of a positive reaction compared to warm and humid weather. No association between weather conditions and reactivity to NaOH was found on the volar forearm.
Irritant dermatitis	Jha	95	2006	Nepal	1746	New out-patients diagnosed with skin disease	–	953/793	Seasonal variation in skin disease.	Contact dermatitis showed a significant seasonal variation, winter being the most prevalent.
Irritant dermatitis	Trimble	101	2008	USA	442	Volunteers exposed to a 14-day cumulative irritation test protocol (0.1 % SLS as irritant and saline as control)	–	307/135	The influence of climatic conditions in three different study sites (dry/hot, humid/hot and dry/cold) on the patch test scores.	No statistical correlation between irritation scores and average temperature and RH, however, the dryer climate had a tendency to induce a higher overall irritation to 0.1 % SLS ($P = 0.071$).
Irritant dermatitis	Hegewald	105	2008	Germany and Austria	61 435	Patients patch tested between 1993–2001	Mean age 46	38 721/22 714	The influence of meteorological condition on patch test results.	The odds of irritant or doubtful reactions to nickel, cobalt and chromium and to weak allergic (positive) reactions to nickel and cobalt increased during cold/dry weather.

Table 4 Continued

Type of dermatitis	First author	Reference	Year of publication	Country	n	Study subjects	Age	Female/Male	Outcome	Main findings
Irritant dermatitis	Uter	106	2008	Germany and Austria	73 691	Patients patch tested between 1993–2001	–	46 499/27 192	The influence of meteorological conditions on patch test results with 12 standard series allergens.	For low temperatures and low humidity there was a significantly increased risk of irritant or doubtful reactions to 7 of 12 allergens. The risk of weak positive results was increased for four allergens, including formaldehyde, oil of turpentine, MDBGN + PE and fragrance mix.
Irritant dermatitis	Hegewald	104	2008	Germany and Austria	61 780	Patients patch tested between 1993–2001	Mean age 46	38 921/22 859	The influence of meteorological conditions on patch test results	The odds of irritant or doubtful reactions to three allergens (PPD, MCI/MI and formaldehyde) increased during cold and dry conditions. Two of them (PPD and formaldehyde) also showed a weak association between weak allergic reactions and weather conditions.
Irritant dermatitis	Callahan	96	2013	USA	90	Adult health care workers who washed their hands at least eight times a day.	Mean age 32 (± 9.6)	58/32	Association between the development and irritant hand dermatitis and different exposures.	A significant association between the development of irritant hand dermatitis and winter season, adjusted incidence rate ratio being 2.76 (95% CI; 1.35–5.65).

–, not available; AD, atopic dermatitis; CI, confidence interval; COPSAC, Copenhagen studies on asthma in childhood; FLG, filaggrin; ISGA, investigator static global assessment; MCI/MI, methylchloroisothiazolinone/methylisothiazolinone; MDBGN + PE, methyl/dibromo glutaronitrile + phenoxylethanol; NaOH, sodium hydroxide; OR, odds ratio; PPD, p-phenylenediamine; RH, relative humidity; SCORAD, scoring of atopic dermatitis; SD, standard deviation; SDS, sodium dodecyl sulfate; SLS, sodium lauryl sulfate; TEWL, transepidermal water loss; UV, ultraviolet.

FLG mutations are weaker risk factors for AD in a subtropical climate. For Japanese AD patients reporting a seasonal variation in AD severity, winter was the worst for those with *FLG* mutations whereas the summer was the worst for those without *FLG* mutations.⁹²

Irritant and allergic contact dermatitis

A strong association between irritant skin changes and climatic conditions has been established (Table 4). In hairdresser apprentices, low temperatures and low AH increased the risk of irritant skin changes,¹⁰ and in patients with dermatitis caused by physical irritants, low humidity was found to be the most common cause.⁹³ A higher prevalence of hand dermatitis was found in northern parts of Norway than in a similar survey from southern Sweden,⁹⁴ and contact dermatitis has been shown to be more prevalent during winter.⁹⁵ In health care workers, a significant association was also found between winter season and irritant hand dermatitis.⁹⁶ Similar, reactions to the known skin irritants sodium lauryl sulfate (SLS) and sodium hydroxide (NaOH) are significantly stronger during winter than summer, and the risk of doubtful/irritant reactions to 0.5% SLS was increased by 50% with low temperature and dry air.^{97–100} However, another study found no significant correlation between irritation scores, temperature and RH, although a dry climate had a tendency to induce higher overall irritation to 0.1% SLS.¹⁰¹

Also, there appears to be a seasonal effect on the outcome of patch testing. Hence, the number of patients with a positive patch test reaction peaks in January and drops in June.¹⁰² Moreover, an increase in irritant/doubtful and/or weak reactions has been shown for formaldehyde, fragrance mix I, oil of turpentine, nickel, cobalt, chromium, *p*-paraphenylenediamine, methyl-di-bromo glutaronitrile and methylchloroisothiazolinone/methylisothiazolinone during cold and dry weather when compared to warm and humid weather.^{103–106} The decrease in irritant/doubtful reactions during the summer season could be due to UV irradiation,¹⁰⁷ but the increase in delta TEWL values from summer to winter after patch testing suggests that the skin actually is more reactive during the winter.¹⁰⁸

The above seasonal affects may be biased by ultraviolet (UV) irradiation. While humans are predominantly exposed to UVB (280–320 nm) and UVA (320–400 nm), UVB photons primarily reach epidermis whereas UVA penetrates deeper and affects both epidermis and dermis.¹⁰⁹ Notably, *suberythemogenic* doses of narrowband UVA and UVB have a positive effect on skin barrier function and are therefore commonly applied in treatment of inflammatory skin conditions.¹¹⁰ Briefly, low doses of UVB irradiation activate the cutaneous vitamin D-system and increase the expression of antimicrobial peptides, lipids and skin barrier proteins including filaggrin and involucrin.¹¹¹ Moreover, UVA and UVB irradiation results in epidermal thickening¹¹² and reduced histamine release from mast cells.¹¹³ The absence of UV

exposure in winter therefore also affects the risk of skin barrier dysfunction and dermatitis. Nonetheless, available evidence clearly shows the detrimental effect of cold and dry environment on the skin, independent of UV exposure (Fig. 3).

Low humidity References	[Ref.]
Animal studies	
Decreased:	
Skin hydration	[7, 12, 18, 19, 20]
Desmosome degradation	[7, 17]
Skin extensibility	[17]
Amino acid content	[18, 20]
Filaggrin expression	[20]
TEWL (after prolonged exposure)	[21, 22]
Increased	
Epidermal DNA synthesis	[8, 12]
Synthesis and release of IL-1 α	[13]
Amount of dermal mast cells	[14]
Degranulation of mast cells	[14]
Contact sensitivity reactions	[15]
Roughness in skin surface	[16, 18]
Scaling	[7]
Dry weight of and thickness of SC	[7, 21]
TEWL (from humid to dry conditions)	[19]
Human studies	
Decreased:	
Skin hydration	[24, 25, 26, 27]
Elasticity of the skin	[26]
TEWL (prolonged exposure)	[24, 30]
Increased:	
Visual dryness of the skin	[24, 32]
Amount of fine wrinkles	[26]
Skin complaints (i.e. dryness, pruritus and irritation)	[28, 29, 31, 32]
Susceptibility to mechanical stress	[23]
TEWL (short exposure)	[25]
Low temperature	[Ref.]
Animal studies	
Decreased:	
Extensibility	[35, 36]
TEWL	[37]
Amount of lamellar bodies and lipids	[37]
Recovery rate after barrier disruption	[34]
Human studies	
Decreased	
Skin hydration	[27, 38, 43]
TEWL	[39, 40, 41, 44, 45]
Increased	
Dry skin	[42]
Sensation of itch	[47]

Figure 3 Climatic effects (low humidity and low temperature) and how they influence skin barrier function. Stratum corneum (SC), transepidermal water loss (TEWL).

References

- Angelova-Fischer I, Dapic I, Hoek AK *et al.* Skin barrier integrity and natural moisturising factor levels after cumulative dermal exposure to alkaline agents in atopic dermatitis. *Acta Derm Venereol* 2014; **94**: 640–644.
- Candi E, Schmidt R, Melino G. The cornified envelope: a model of cell death in the skin. *Nat Rev Mol Cell Biol* 2005; **6**: 328–340.
- Gabard B. Testing the efficacy of moisturizers. In Berardesca E, Maibach HI, Elsner P, eds. *Bioengineering of the Skin: Water and the Stratum Corneum*. CRC, Boca Raton, FL, 1994: 213.
- Abe T, Mayuzumi J, Kikuchi N *et al.* Seasonal variations in skin temperature, skin pH, evaporative water loss and skin surface lipid values on human skin. *Chem Pharm Bull (Tokyo)* 1980; **28**: 387–392.
- Gaul LE, Underwood GB. Relation of dew point and barometric pressure to chapping of normal skin. *J Invest Dermatol* 1952; **19**: 9–19.
- Jiang SJ, Chu AW, Lu ZF *et al.* Ultraviolet B-induced alterations of the skin barrier and epidermal calcium gradient. *Exp Dermatol* 2007; **16**: 985–992.
- Sato J, Denda M, Nakanishi J *et al.* Dry condition affects desquamation of stratum corneum in vivo. *J Dermatol Sci* 1998; **18**: 163–169.
- Denda M, Sato J, Tsuchiya T *et al.* Low humidity stimulates epidermal DNA synthesis and amplifies the hyperproliferative response to barrier disruption: implication for seasonal exacerbations of inflammatory dermatoses. *J Invest Dermatol* 1998; **111**: 873–878.
- Williams H, Robertson C, Stewart A *et al.* Worldwide variations in the prevalence of symptoms of atopic eczema in the International Study of Asthma and Allergies in Childhood. *J Allergy Clin Immunol* 1999; **103**: 125–138.
- Uter W, Gefeller O, Schwanitz HJ. An epidemiological study of the influence of season (cold and dry air) on the occurrence of irritant skin changes of the hands. *Br J Dermatol* 1998; **138**: 266–272.
- Scott IR, Harding CR. Filaggrin breakdown to water binding-compounds during development of the rat stratum-corneum is controlled by the water activity of the environment. *Dev Biol* 1986; **115**: 84–92.
- Sato J, Denda M, Ashida Y *et al.* Loss of water from the stratum corneum induces epidermal DNA synthesis in hairless mice. *Arch Dermatol Res* 1998; **290**: 634–637.
- Ashida Y, Ogo M, Denda M. Epidermal interleukin-1 α generation is amplified at low humidity: implications for the pathogenesis of inflammatory dermatoses. *Br J Dermatol* 2001; **144**: 238–243.
- Ashida Y, Denda M. Dry environment increases mast cell number and histamine content in dermis in hairless mice. *Br J Dermatol* 2003; **149**: 240–247.
- Hosoi J, Hariya T, Denda M *et al.* Regulation of the cutaneous allergic reaction by humidity. *Contact Dermatitis* 2000; **42**: 81–84.
- Sato J, Yanai M, Hirao T *et al.* Water content and thickness of the stratum corneum contribute to skin surface morphology. *Arch Dermatol Res* 2000; **292**: 412–417.
- Rawlings A, Sabin R, Harding C *et al.* The effect of glycerol and humidity on desmosome degradation in stratum corneum. *Arch Dermatol Res* 1995; **287**: 457–464.
- Sato J, Katagiri C, Nomura J *et al.* Drastic decrease in environmental humidity decreases water-holding capacity and free amino acid content of the stratum corneum. *Arch Dermatol Res* 2001; **293**: 477–480.
- Sato J, Denda M, Chang S *et al.* Abrupt decreases in environmental humidity induce abnormalities in permeability barrier homeostasis. *J Invest Dermatol* 2002; **119**: 900–904.
- Katagiri C, Sato J, Nomura J *et al.* Changes in environmental humidity affect the water-holding property of the stratum corneum and its free amino acid content, and the expression of filaggrin in the epidermis of hairless mice. *J Dermatol Sci* 2003; **31**: 29–35.
- Denda M, Sato J, Masuda Y *et al.* Exposure to a dry environment enhances epidermal permeability barrier function. *J Invest Dermatol* 1998; **111**: 858–863.
- Denda M. Epidermal proliferative response induced by sodium dodecyl sulphate varies with environmental humidity. *Br J Dermatol* 2001; **145**: 252–257.
- Wildnauer RH, Bothwell JW, Douglass AB. Stratum corneum biomechanical properties. I. Influence of relative humidity on normal and extracted human stratum corneum. *J Invest Dermatol* 1971; **56**: 72–78.
- Egawa M, Oguri M, Kuwahara T *et al.* Effect of exposure of human skin to a dry environment. *Skin Res Technol* 2002; **8**: 212–218.
- Sunwoo Y, Chou C, Takeshita J *et al.* Physiological and subjective responses to low relative humidity. *J Physiol Anthropol* 2006; **25**: 7–14.
- Tsukahara K, Hotta M, Fujimura T *et al.* Effect of room humidity on the formation of fine wrinkles in the facial skin of Japanese. *Skin Res Technol* 2007; **13**: 184–188.
- Vyumvuhore R, Tfayli A, Duplan H *et al.* Effects of atmospheric relative humidity on stratum corneum structure at the molecular level: ex vivo Raman spectroscopy analysis. *Analyst* 2013; **138**: 4103–4111.
- Sato M, Fukayo S, Yano E. Adverse environmental health effects of ultra-low relative humidity indoor air. *J Occup Health* 2003; **45**: 133–136.
- Chou TC, Lin KH, Sheu HM *et al.* Alterations in health examination items and skin symptoms from exposure to ultra-low humidity. *Int Arch Occup Environ Health* 2007; **80**: 290–297.
- Chou TC, Lin KH, Wang SM *et al.* Transepidermal water loss and skin capacitance alterations among workers in an ultra-low humidity environment. *Arch Dermatol Res* 2005; **296**: 489–495.
- Lindgren T, Andersson K, Dammstrom BG *et al.* Ocular, nasal, dermal and general symptoms among commercial airline crews. *Int Arch Occup Environ Health* 2002; **75**: 475–483.
- Reinikainen LM, Jaakkola JJK. The effect of air humidification on symptoms and perception of indoor air quality in office workers: a six-period cross-over trial. *Arch Environ Health* 1992; **47**: 8–15.
- Reinikainen LM, Jaakkola JJ. Significance of humidity and temperature on skin and upper airway symptoms. *Indoor Air* 2003; **13**: 344–352.
- Denda M, Sokabe T, Fukumi-Tominaga T *et al.* Effects of skin surface temperature on epidermal permeability barrier homeostasis. *J Invest Dermatol* 2006; **127**: 654–659.
- Middleton JD. The effect of temperature on extensibility of isolated corneum and its relation to skin chapping. *Br J Dermatol* 1969; **81**: 717–721.
- Middleton J, Allen B. The influence of temperature and humidity on stratum corneum and its relation to skin chapping. *J Soc Cosmet Chem* 1973; **24**: 239–243.
- Halkier-Sørensen L, Menon G, Elias P *et al.* Cutaneous barrier function after cold exposure in hairless mice: a model to demonstrate how cold interferes with barrier homeostasis among workers in the fish-processing industry. *Br J Dermatol* 1995; **132**: 391–401.
- Spencer TS, Linamen CE, Akers WA *et al.* Temperature dependence of water content of stratum corneum. *Br J Dermatol* 1975; **93**: 159–164.
- Cravetto B, Ferri A. Relationships between skin properties and environmental parameters. *Skin Res Technol* 2008; **14**: 180–186.
- Grice K, Sattar H, Sharratt M *et al.* Skin temperature and transepidermal water loss. *J Invest Dermatol* 1971; **57**: 108–110.
- Mathias CGT, Wilson DM, Maibach HI. Transepidermal water loss as a function of skin surface temperature. *J Invest Dermatol* 1981; **77**: 219–220.
- Cooper MD, Jardine H, Ferguson J. Seasonal influence on the occurrence of dry flaking facial skin. In Marks R and Plewig G, eds. *The Environmental Threat to the Skin*, Vol. 159. Martin Dunitz, London, 1992; 159–164.
- Roure R, Lanctin M, Nollent V *et al.* Methods to assess the protective efficacy of emollients against climatic and chemical aggressors. *Dermatol Res Pract* 2012; **2012**: 864734.
- Halkier-Sørensen L, Thestrup-Pedersen K. Skin physiological changes in employees in the fish processing industry immediately following work. A field study. *Contact Dermatitis* 1991; **25**: 19–24.

- 45 Halkier-Sorensen L, Thestrup-Pedersen K. The relationship between skin surface temperature, transepidermal water loss and electrical capacitance among workers in the fish processing industry: comparison with other occupations. A field study. *Contact Dermatitis* 1991; **24**: 345–355.
- 46 Fluhr JW, Bornkessel A, Akengin A et al. Sequential application of cold and sodium lauryl sulphate decreases irritation and barrier disruption in vivo in humans. *Br J Dermatol* 2005; **152**: 702–708.
- 47 Pfab F, Valet M, Sprenger T et al. Temperature modulated histamine-itch in lesional and nonlesional skin in atopic eczema – a combined psychophysical and neuroimaging study. *Allergy* 2010; **65**: 84–94.
- 48 Corlett WT. A clinical study of pruritus hiemalis, winter itch, frost itch, etc. *J Cut Genitourin Dis* 1891; **9**: 41–48.
- 49 Hutchinson J. Clinical Lecture on Winter Prurigo. *Br Med J*, 1875; **2**: 773–774.
- 50 Corlett W. Cold as an etiological factor in diseases of the skin. *J Cutaneous Genito-Urinary Diseases* 1894; **12**: 466.
- 51 Conti A, Rogers J, Verdejo P et al. Seasonal influences on stratum corneum ceramide 1 fatty acids and the influence of topical essential fatty acids. *Int J Cosmet Sci* 1996; **18**: 1–12.
- 52 Rogers J, Harding C, Mayo A et al. Stratum corneum lipids: the effect of ageing and the seasons. *Arch Dermatol Res* 1996; **288**: 765–770.
- 53 Nakagawa N, Sakai S, Matsumoto M et al. Relationship between NMF (lactate and potassium) content and the physical properties of the stratum corneum in healthy subjects. *J Invest Dermatol* 2004; **122**: 755–763.
- 54 Kikuchi K, Kobayashi H, Le Fur I et al. The winter season affects more severely the facial skin than the forearm skin: comparative biophysical studies conducted in the same Japanese females in later summer and winter. *Exog Dermatol* 2002; **1**: 32–38.
- 55 Devillers C, Pierard GE, Quatresooz P et al. Environmental dew point and skin and lip weathering. *J Eur Acad Dermatol Venereol* 2010; **24**: 513–517.
- 56 Delvenne M, Pierard-Franchimont C, Seidel L et al. The weather-beaten dorsal hand clinical rating, shadow casting optical profilometry, and skin capacitance mapping. *Biomed Res Int* 2013; **2013**: 913646.
- 57 Andersen F, Andersen K, Kligman A. Xerotic skin of the elderly: A summer versus winter comparison based on biophysical measurements. *Exog Dermatol* 2004; **2**: 190–194.
- 58 Black D, Del Pozo A, Lagarde JM et al. Seasonal variability in the biophysical properties of stratum corneum from different anatomical sites. *Skin Res Technol* 2000; **6**: 70–76.
- 59 Qiu H, Long X, Ye JC et al. Influence of season on some skin properties: winter vs. summer, as experienced by 354 Shanghai women of various ages. *Int J Cosmet Sci* 2011; **33**: 377–383.
- 60 Ishikawa J, Shimotoyodome Y, Ito S et al. Variations in the ceramide profile in different seasons and regions of the body contribute to stratum corneum functions. *Arch Dermatol Res* 2013; **305**: 151–162.
- 61 Youn SW, Na JJ, Choi SY et al. Regional and seasonal variations in facial sebum secretions: a proposal for the definition of combination skin type. *Skin Res Technol* 2005; **11**: 189–195.
- 62 Tsukahara K, Osanai O, Kitahara T et al. Seasonal and annual variation in the intensity of facial wrinkles. *Skin Res Technol* 2013; **19**: 279–287.
- 63 Nam GW, Baek JH, Koh JS et al. The seasonal variation in skin hydration, sebum, scaliness, brightness and elasticity in Korean females. *Skin Res Technol* 2015; **21**: 1–8.
- 64 Egawa M, Tagami H. Comparison of the depth profiles of water and water-binding substances in the stratum corneum determined in vivo by Raman spectroscopy between the cheek and volar forearm skin: effects of age, seasonal changes and artificial forced hydration. *Br J Dermatol* 2008; **158**: 251–260.
- 65 Herrmann S, Scheuber E, Plewig G. Exfoliative Cytology: Effects of the Seasons. In: Marks R, Plewig G, eds. *Stratum Corneum*. Springer, Berlin, Heidelberg, 1983: 181–185.
- 66 den Arend JA, de Haan AF, Malten KE. Seasonal transepidermal water loss and impedance of forearm skin in atopics and non-atopics. *Contact Dermatitis* 1988; **19**: 376–378.
- 67 Vocks E, Busch R, Frohlich C et al. Influence of weather and climate on subjective symptom intensity in atopic eczema. *Int J Biometeorol* 2001; **45**: 27–33.
- 68 Suarez-Varela MM, Garcia-Marcos Alvarez L, Kogan MD et al. Climate and prevalence of atopic eczema in 6- to 7-year-old school children in Spain. ISAAC phase III. *Int J Biometeorol* 2008; **52**: 833–840.
- 69 Dhar S, Kanwar AJ. Epidemiology and clinical pattern of atopic dermatitis in a North Indian pediatric population. *Pediatr Dermatol* 1998; **15**: 347.
- 70 Uenishi T, Sugiura H, Uehara M. Changes in the seasonal dependence of atopic dermatitis in Japan. *J Dermatol* 2001; **28**: 244–247.
- 71 Weiss SC, Rowell R, Krochmal L. Impact of seasonality on conducting clinical studies in dermatology. *Clin Dermatol* 2008; **26**: 565–569.
- 72 Remes ST, Korppi M, Kajosaari M et al. Prevalence of allergic rhinitis and atopic dermatitis among children in four regions of Finland. *Allergy* 1998; **53**: 682–689.
- 73 Hancox JG, Sheridan SC, Feldman SR et al. Seasonal variation of dermatologic disease in the USA: a study of office visits from 1990 to 1998. *Int J Dermatol* 2004; **43**: 6–11.
- 74 Silverberg JI, Hanifin J, Simpson EL. Climatic factors are associated with childhood eczema prevalence in the United States. *J Invest Dermatol* 2013; **133**: 1752–1759.
- 75 Weiland SK, Husing A, Strachan DP et al. Climate and the prevalence of symptoms of asthma, allergic rhinitis, and atopic eczema in children. *Occup Environ Med* 2004; **61**: 609–615.
- 76 Furue M, Yamazaki S, Jimbow K et al. Prevalence of dermatological disorders in Japan: a nationwide, cross-sectional, seasonal, multicenter, hospital-based study. *J Dermatol* 2011; **38**: 310–320.
- 77 Hellier FF. Environment and skin disease. *British J Dermatol Syphilis* 1940; **52**: 107–123.
- 78 Tupker RA, Coenraads PJ, Fidler V et al. Irritant susceptibility and weal and flare reactions to bioactive agents in atopic dermatitis. II. Influence of season. *Br J Dermatol* 1995; **133**: 365–370.
- 79 Byremo G, Rod G, Carlsen KH. Effect of climatic change in children with atopic eczema. *Allergy* 2006; **61**: 1403–1410.
- 80 Nilsson L, Bjorksten B, Hattevig G et al. Season of birth as predictor of atopic manifestations. *Arch Dis Child* 1997; **76**: 341–344.
- 81 Kusunoki T, Asai K, Harazaki M et al. Month of birth and prevalence of atopic dermatitis in schoolchildren: dry skin in early infancy as a possible etiologic factor. *J Allergy Clin Immunol* 1999; **103**: 1148–1152.
- 82 Tariq SM, Matthews SM, Hakim EA et al. The prevalence of and risk factors for atopy in early childhood: a whole population birth cohort study. *J Allergy Clin Immunol* 1998; **101**: 587–593.
- 83 Kuzume K, Kusu M. Before-birth climatologic data may play a role in the development of allergies in infants. *Pediatr Allergy Immunol* 2007; **18**: 281–287.
- 84 Aoki T, Kojima M, Adachi J et al. Seasonal variation in the month of first visit for atopic dermatitis patients. *Allergology Int* 1998; **47**: 137–142.
- 85 Nikolovski J, Stamatias 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.
- 86 Kramer U, Weidinger S, Darsow U et al. Seasonality in symptom severity influenced by temperature or grass pollen: results of a panel study in children with eczema. *J Invest Dermatol* 2005; **124**: 514–523.
- 87 Williams JR, Burr ML, Williams HC. Factors influencing atopic dermatitis—a questionnaire survey of schoolchildren's perceptions. *Br J Dermatol* 2004; **150**: 1154–1161.
- 88 Ortiz de Frutos FJ, Torrelo A, de Lucas R et al. Patient perspectives on triggers, adherence to medical recommendations, and disease control in atopic dermatitis: the DATOP study. *Actas Dermosifiliogr* 2014; **105**: 487–496.
- 89 Langan SM, Bourke JF, Silcocks P et al. An exploratory prospective observational study of environmental factors exacerbating atopic eczema in children. *Br J Dermatol* 2006; **154**: 979–980.

- 90 Carson CG, Rasmussen MA, Thyssen JP *et al.* Clinical presentation of atopic dermatitis by filaggrin gene mutation status during the first 7 years of life in a prospective cohort study. *PLoS One* 2012; **7**: e48678.
- 91 Sasaki T, Furusyo N, Shiohama A *et al.* Filaggrin loss-of-function mutations are not a predisposing factor for atopic dermatitis in an Ishigaki Island under subtropical climate. *J Dermatol Sci* 2014; **76**: 10–15.
- 92 Nemoto-Hasebe I, Akiyama M, Nomura T *et al.* Clinical severity correlates with impaired barrier in filaggrin-related eczema. *J Invest Dermatol* 2009; **129**: 682–689.
- 93 Morris-Jones R, Robertson SJ, Ross JS *et al.* Dermatitis caused by physical irritants. *Br J Dermatol* 2002; **147**: 270–275.
- 94 Kavli G, Forde OH. Hand dermatoses in Tromsø. *Contact Dermatitis* 1984; **10**: 174–177.
- 95 Jha AK, Gurung D. Seasonal variation of skin diseases in Nepal: a hospital based annual study of out-patient visits. *Nepal Med Coll J* 2006; **8**: 266–268.
- 96 Callahan A, Baron E, Fekedulegn D *et al.* Winter season, frequent hand washing, and irritant patch test reactions to detergents are associated with hand dermatitis in health care workers. *Dermatitis* 2013; **24**: 170–175.
- 97 Agner T, Serup J. Seasonal variation of skin resistance to irritants. *Br J Dermatol* 1989; **121**: 323–328.
- 98 Basketter DA, Griffiths HA, Wang XM *et al.* Individual, ethnic and seasonal variability in irritant susceptibility of skin: the implications for a predictive human patch test. *Contact Dermatitis* 1996; **35**: 208–213.
- 99 Uter W, Hegewald J, Pfahlberg A *et al.* The association between ambient air conditions (temperature and absolute humidity), irritant sodium lauryl sulfate patch test reactions and patch test reactivity to standard allergens. *Contact Dermatitis* 2003; **49**: 97–102.
- 100 John S, Uter W. Meteorological influence on NaOH irritation varies with body site. *Arch Dermatol Res* 2005; **296**: 320–326.
- 101 Trimble MW, Kaul N, Wild JE *et al.* The differences in human cumulative irritation responses to positive and negative irritant controls from three geographical locations. *Int J Cosmet Sci* 2008; **30**: 384.
- 102 Edman B. Seasonal influence on patch test results. *Contact Dermatitis* 1989; **20**: 226.
- 103 Uter W, Geier J, Land M *et al.* Another look at seasonal variation in patch test results – a multifactorial analysis of surveillance data of the IVDK. *Contact Dermatitis* 2001; **44**: 146–152.
- 104 Hegewald J, Uter W, Kranke B *et al.* Meteorological conditions and the diagnosis of occupationally related contact sensitizations. *Scand J Work Environ Health* 2008; **34**: 316–321.
- 105 Hegewald J, Uter W, Kranke B *et al.* Patch test results with metals and meteorological conditions. *Int Arch Allergy Immunol* 2008; **147**: 235–240.
- 106 Uter W, Hegewald J, Kranke B *et al.* The impact of meteorological conditions on patch test results with 12 standard series allergens (fragrances, biocides, topical ingredients). *Br J Dermatol* 2008; **158**: 734–739.
- 107 Kränke B, Aberer W. Seasonal influence on patch test results in Central Europe. *Contact Dermatitis* 1996; **34**: 215–231.
- 108 Löffler H, Happle R. Influence of climatic conditions on the irritant patch test with sodium lauryl sulphate. *Acta Derm Venereol* 2003; **83**: 338.
- 109 Hussein MR. Ultraviolet radiation and skin cancer: molecular mechanisms. *J Cutan Pathol* 2005; **32**: 191–205.
- 110 Wulf HC, Bech-Thomsen N. A UVB phototherapy protocol with very low dose increments as a treatment of atopic dermatitis. *Photodermatol Photoimmunol Photomed* 1998; **14**: 1–6.
- 111 Hong SP, Kim MJ, Jung MY *et al.* Biopositive effects of low-dose UVB on epidermis: coordinate upregulation of antimicrobial peptides and permeability barrier reinforcement. *J Invest Dermatol* 2008; **128**: 2880–2887.
- 112 Pearse AD, Gaskell SA, Marks R. Epidermal changes in human skin following irradiation with either UVB or UVA. *J Invest Dermatol* 1987; **88**: 83–87.
- 113 Hart PH, Grimbaldeston MA, Finlay-Jones JJ. Sunlight, immunosuppression and skin cancer: role of histamine and mast cells. *Clin Exp Pharmacol Physiol* 2001; **28**: 1–8.