

The impact of ambient humidity on healthy and diseased skin

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Abstract

Background: Temperature and ultraviolet radiation levels are known to have an impact on the skin's health and function. Several studies have examined the role of another variable climatic factor - humidity - on healthy and diseased skin in human and mouse subjects, with varying results.

Methods: An online literature search using key words was based around ambient relative humidity and its impact on skin health and function.

Results: Murine studies determine that low humidity causes a number of changes in the skin, including the impairment of the desquamation process, while studies in humans demonstrate changes in transepidermal water loss values (a measure of the integrity of the skins barrier function), water content in the stratum corneum, skin elasticity and roughness parameters. Further epidemiological studies indicate an association between common dermatoses and ambient humidity, while several studies support the hypothesis that changes in humidity levels can induce or exacerbate dry skin disorders.

Conclusion: Evidence suggests that humidity, and changes therein, can have an impact on a range of parameters involved in skin health. Further studies examining the effect of humidity on diseased skin and the associated biological mechanisms could provide evidence to support new treatment regimens for patients, helping to alleviate the burden of dry skin associated with many common skin disorders.

Keywords: Skin, Humidity, Dermatoses, Eczema, Mist

1. Introduction

Skin is sensitive to a number of climatic factors, such as temperature, ultraviolet light and humidity. This paper looks at the effect of ambient humidity on skin dryness, as well as skin disorders characterised by dry skin.* An online literature search through PubMed was conducted using combinations of the following keywords: skin, skin disease, humidity, dermatoses, eczema, mist. Publications included in this review were limited to studies in humans or animals, and showing relevance to the field of dermatology.

1.1. Humidity

Relative humidity, rather than absolute humidity, is the most common way of measuring the moisture content of the air. It is the amount of water vapour (moisture) in the air compared to the maximum amount that the air could hold at a given temperature and is expressed as a percentage. The hotter the air is, the more water it can contain, and for this reason outdoors humidity decreases in colder seasons and climates. Where the humidity is expressed as a percentage in this paper, this demonstrates that the relative, rather than the absolute, humidity is being studied, and unless otherwise specified, we will refer to relative humidity throughout. The American Society of Heating, Refrigerating and Air-Conditioning Engineers (ASHRAE) advises that a good range for relative humidity within the home is between 30 per cent and 60 per cent and this level of humidity minimizes the indoor growth of allergenic or pathogenic organisms such as dust mites and moulds¹. They further advise that a wider range of humidity levels, from a low of 25 per cent to a high of about 80 per cent, can be acceptable in terms of thermal comfort depending on the type of clothing worn and the level of physical activity¹.

1.2. The skin's barrier function

The skin is made up of three core layers: subcutaneous fat (lower layer), dermis (middle layer) and epidermis (outermost layer). The epidermis is itself comprised of four further layers: the lowest being the basal cell layer (stratum basale), followed by the spinous cell layer (stratum spinosum), granular cell layer (stratum granulosum) and finally the cornified layer (stratum corneum).

Ninety per cent of cells in the epidermis are keratinocytes, which multiply and migrate upwards from the basal cell layer. The stratum corneum is made

up of dead keratinocytes, called corneocytes, which provide a highly impermeable membrane. It is this layer that, in healthy skin, effectively provides the skin's barrier function, regulating water loss from tissue inside the body and preventing irritants and substances from the external environment from permeating the skin. The stratum corneum can be depicted as a thin, waterproof membrane tightly wrapping the enclosed fully water-saturated living skin tissue². Desmosomes are specialized junctions which allow corneocytes to adhere to one another. As the cells move upwards from the basal layer to the stratum corneum, the desmosome attachments gradually weaken. The older of the corneocytes are then shed from the skin surface, a process known as desquamation.

2. The dry versus the humid environment

Various studies using hairless mice, the skin of which provide a model (albeit not exact) for human skin, have examined the differences between skin that is exposed to either low or high environmental humidity, and furthermore the subsequent changes when skin is transferred from a normal or humid environment to a dry one. By comparing mice kept in conditions of low versus high humidity, one such study demonstrated that the desquamation process was impaired in skin exposed to dry air (low humidity)³. Dry air decreases the water content of the stratum corneum, which is responsible for disrupting the degradation of desmosomes, meaning there is failure of the cohesive bonds holding the skin cells together to adequately weaken. This impairs the desquamation process, as the corneocytes are unable to slough off from the skin surface, appearing instead as dry skin scales, a process which occurred within three days in exposed mice³. The implication here is that exposure to a dry environment could cause scaly skin.

Mouse skin does not provide an identical model for human skin, for example it is thinner. Therefore, caution must be exercised when using animal experiments to draw conclusions relating to human skin. While animal studies allow us to hypothesise that similar effects may be witnessed in human skin exposed to similar conditions, such indications must be supported by observations in human subjects.

An example is provided by a study exploring the effect of low relative humidity on healthy human skin⁴. The study used capacitance and conductance methods, which measure the water content of the stratum corneum, on the ventral forearm and the cheek before and after three or six-hour exposure

to low humidity. It also looked at transepidermal water loss which is a measurement of the quantity of water passing from within the body through the skin to the external environment. Increased transepidermal water loss can be a sign of skin barrier disruption, but it may also be influenced by water levels in the skin and environment.

Skin surface replicas were also taken before and after exposure and analysed for roughness parameters (which have previously been cited as an indication of skin dryness⁵).

The results demonstrated a significant decrease of water content of the stratum corneum at both test sites from the time points zero hours to three hours and six hours⁴. Interestingly, transepidermal water loss from the time point zero hours to six hours was also reduced due to unknown mechanisms. Changes of skin surface pattern on exposure to low humidity were observed through the roughness parameters measurements. Thus a short exposure of skin to a low humidity environment induced changes in the moisture content in the stratum corneum and skin surface pattern. This led the authors to consider that a dry environment in daily life might induce aggravation of skin texture and formation of fine wrinkles related to lack of water in the stratum corneum⁴.

Even a 30 per cent difference in relative humidity can affect skin properties in just 30 minutes, according to a study measuring skin conductance, elasticity and fine wrinkles on the eyelids of 20 volunteers, first after acclimatization for 30 minutes in a high humidity room (70 per cent relative humidity) and again after acclimatization for 30 minutes in a room with lower humidity (40 per cent)⁶. The temperature was maintained at 23C in both rooms. The study found significant decreases in skin surface conductance, signifying lower moisture levels, and decreases in elasticity, as well as significant increases in fine wrinkles, after acclimatisation to 40 per cent humidity compared with a high humidity environment.

Results from a Finnish study⁷, albeit based on self-reported data, seemingly support the link between dry skin and a dry environment in the general population. The study looked at the effect of air humidification on a range of self-reported symptoms, including dryness of the skin and mucosa. Two hundred and eleven workers were divided into two groups and located within two separate wings of an office building, identical but for one being operated with 30 to 40 per cent air humidification and the other receiving no humidification (relative humidity from natural conditions was 20 to 30 per cent). These were switched at one week intervals so that each group was exposed to three

periods of humidification and three non-humidification periods. Subjects recorded skin symptoms, defined as dryness, irritation and itching, in addition to non-dermatological symptoms during the study period. The mean of the dryness symptom score was lower during the humidified phase than during the non-humidified phase, reaching statistical significance.

A key implication for humidity regulation in human skin relates to pre-existing skin disease, and dry skin remains the most common characteristic of human skin disorders⁸, one example of which is eczema.

2.1. Case study: Eczema, a common skin disease

Atopic eczema is an extremely common inflammatory condition of the skin. It can start at any age but is most common in children, with a prevalence of up to 20 per cent in children in western populations⁹. The term atopic is used to describe a group of disorders which include asthma, eczema and hay-fever. These conditions are linked by an increased activity of the allergy component of the immune system¹⁰. In atopic eczema, a defect in the gene which is important for maintaining the skin barrier makes the skin in affected subjects much more susceptible to infection and irritation, and allows potentially allergy-inducing substances to enter the skin, with symptoms of itch and inflammation¹⁰.

Measurement of skin roughness has revealed a significant linear relationship with skin dryness⁵. Analysis of skin surface roughness in non-inflamed and non-scaling skin from 10 patients with atopic eczema and 10 controls with normal skin, revealed significant increases in the skin roughness parameters (meaning increased skin roughness and signifying increased dryness) in patients with atopic eczema, but not in the controls, after the being subjected to lower humidity (30 per cent) for three hours in a climatic chamber¹¹.

Data sourced from epidemiological studies assessing the impact of environmental factors, including humidity, on the prevalence and severity of atopic eczema, vary in quality. This is largely attributed to the absence of suitably sized cohorts to examine such factors, and difficulties with extricating the effects of confounding risk factors¹². A few recent studies have attempted to overcome these issues.

The International Study of Asthma and Allergies in Childhood (ISAAC) programme was developed in 1991, with one of its key aims being to measure the prevalence and severity of atopic diseases (including atopic eczema) in children at 155 study centres in over 50 countries. These data provide

a framework for further aetiological research into lifestyle, environmental, genetic and medical care factors affecting atopic diseases.

A study examining data taken from Phase One of ISAAC, involving children aged either 6-7 years or 13-14 years, looked specifically at the relationship between climate and atopic diseases. It reported a tendency toward a negative association between eczema symptoms and mean relative humidity indoors in children aged 6-7 years, implying a connection between low indoor humidity and the prevalence of the skin disorder in this age group¹³.

Contrariwise, a survey using ISAAC Phase III data of over 20,000 school children aged 6-7 years in three different climatic regions in Spain, found that the disease was in fact positively associated with precipitation and humidity (broadly meaning increased incidence in areas of high humidity)¹⁴. These findings are reflected by a study of 5,595 US children enrolled in the Pediatric Eczema Elective Registry between 2004 and 2012¹⁵. This study found that higher humidity was associated with poorly controlled disease, but the statistical significance of this association was lost in the multivariate analysis. Both studies looked specifically at outdoor humidity, therefore not including the impact of indoor humidity as might be affected by central heating and air conditioning.

Possibly the largest epidemiological investigation to look at the role of humidity in skin allergy prevalence alone, as opposed to atopic disease more broadly, emanates from the United States where data from 91,642 children aged 0-17 years included in the 2007 National Survey of Children's Health were cross referenced with the 2006-2007 National Climate Data Center and Weather Service measurements of relative humidity, indoor heating degree days, clear-sky UV indices, ozone levels, and outdoor air temperature¹⁶. However, the study did not look exclusively at atopic eczema, but rather a diagnosis of eczema or any other kind of skin allergy in the previous 12 months. The study revealed a reduced eczema / skin allergy prevalence in areas with high relative humidity, high UV index, high mean temperature, reduced precipitation and fewer days of central heating use. In addition to possibly demonstrating that higher outdoor humidity may reduce eczema prevalence, the US data around indoor heating degree days might reflect the ISAAC Phase One study findings of an association between low indoor humidity and eczema, given that central heating use is known to reduce humidity.

Low humidity may also be a risk factor for irritant eczema, another common form of the disorder, in which external irritants perturb the skin's barrier

function. This was highlighted by a study in which a substantially higher proportion of irritant responses (60.7 per cent) were diagnosed in hairdressing apprentices during a particularly cold January to February, compared to the same months the previous year (49.7 per cent) in which conditions were milder¹⁷. As occupational and constitutional factors could not explain this sharp increase in prevalence, dry, frosty weather was suspected as a likely cause. Prompted by this observation, the importance of several meteorological factors (day means of temperature, relative and absolute humidity) was assessed in extensive statistical analyses based on data of 742 participants, supplemented by meteorological information. Analysis including known determinants of irritant hand dermatitis in this setting, showed that low temperature and low relative humidity tended to be risk factors and also confirmed that absolute humidity significantly influenced the occurrence of irritant hand eczema.

2.2. Moving from humid to dry environments

Changes in environmental humidity are believed to contribute to the onset, aggravation or - conversely - the improvement of various dry skin disorders that involve barrier deficiency. Patients with the common skin disorders psoriasis and atopic eczema, for example, frequently report exacerbation of their symptoms during the winter months when ambient humidity is lower.

Looking at the barrier function, structure and lipid (protective oil) content of the stratum corneum in conditions of high (>80 per cent) versus low (<10 per cent) relative humidity, it has been suggested that barrier function is in fact improved in dry as opposed to humid conditions¹⁸. However, despite this suggested barrier improvement, evidence implies that low humidity can cause skin scaling in normal, otherwise healthy skin, and could worsen existing dry skin diseases^{19,20}. Studies examining changes to the skin following sudden shifts from environments with high humidity to low humidity, suggest that it is these significant fluctuations in air moisture, and a lack of regularity in the ambient humidity, that may be responsible for the exacerbation of dry skin disorders in winter when people move between dry, heated indoors environments and the outdoors.

“Modern buildings may be almost totally closed fully air-conditioned structures. This may cause drastic differences in the environmental humidity an individual is exposed to daily... [This] suggests that such alterations in our living and working conditions might

*alter skin function thus exposing our body to a harmful environment.”*²¹

When looking at groups of mice kept in either a humid (>80 per cent relative humidity) or normal environment (40 to 70 per cent relative humidity), then transferred to conditions of low humidity (<10 per cent relative humidity), those transferred from humid environments demonstrated a six to seven-fold increase in transepidermal water loss within two days of transfer, returning to normal within seven days²². No increase in transepidermal water loss occurred in response to a switch from a normal to a dry environment. Factors leading to barrier function abnormality in the humid to dry group were identified, including a decrease in lamellar bodies in the stratum granulosum as per previous studies²⁰, leading the authors to suggest that sudden changes from a high to a low humidity environment might result in abnormal barrier function.

Sudden changes in humidity have also been found to affect the water-holding property of the stratum corneum, as revealed by studying skin surface conductance, which measures the ease with which an electrical current passes between points on the skin and which is elevated with increased skin moisture. Using the same humidity thresholds as the above study, skin surface conductance in the stratum corneum of hairless mice three to seven days after transfer from a humid environment to a dry one, was significantly lower than that of the mice transferred from a normal environment to a dry environment, showing that their skin became more dry, despite having previously been exposed to higher humidity²³.

Free amino acid content is pivotal to correct skin function and repair, playing a crucial role as a natural moisturizing factor in the stratum corneum²¹. A decrease in free amino acids has been found in various dry, scaly skin types^{21,24,25,26}. In the above study, the free amino acid content in the stratum corneum significantly decreased 24 hours after transfer of the mice from a normal to a dry condition, then it recovered to the original level within three days, while the mice transferred from a humid to a dry condition still showed a significantly lower amino acid content seven days after the transfer. This suggests that a drastic decrease in the environmental humidity reduced the total free amino acid generation and consequently induced skin surface dryness in the stratum corneum²³.

For humans, in daily life, fluctuations in ambient humidity outlined by the above murine studies might relate to movement between overly humidified

rooms (perhaps the use in a bedroom of a humidifier that does not adapt moisture output to the ambient humidity, allowing for humidity levels of above the normal upper threshold of around 70 per cent) to dry rooms (such as centrally heated or air conditioned home or work environments).

2.3. Nanodroplets and skin hydration

Evidence also suggests that the mode of delivery of humidity into an indoors environment is important. As the authors of a study into water nanodroplets (mist) and skin hydration explain, humidifiers are used to improve air dryness, but this often induces excess humidity and thermal discomfort²⁷. They therefore analysed the effects of mist on skin under air conditioning, by measuring biophysical parameters, such as skin conductance, transepidermal water loss and sebum levels, in 12 healthy volunteers with normal skin. They also examined the biomechanical parameters of skin distension and retraction, which measure skin elasticity and viscosity, before and after suction at the forehead, lateral canthus (corner of the eye), and cheek. Two test conditions were employed: with mist and without mist (control), both under air conditioning.

Participants spent the first 60 minutes in an air conditioned test area without mist, maintained at 24C and 35 per cent relative humidity. At 60 minutes, biophysical and biomechanical measurements were taken and these were considered to be the initial values. At this point, there were no significant differences between the mist group and the control group (no mist) for each parameter.

The participants were then either maintained in the same conditions as the test area (control group), or else in the same conditions as the test area with the addition of mist (emitted at a rate of less than 1 mg/h), for an additional 120 minutes, with the biophysical and biomechanical parameters being measured at 90, 120, 150 and 180 minutes.

Transepidermal water loss values at the three skin sites were found to decrease in the control group, but not in the mist group, for which the values were maintained at the initial values throughout the test. Significant differences were found at all sites of the face between the mist and control groups ($P < 0.01$). In the control group, transepidermal water loss values significantly decreased at the forehead and at the lateral canthus at 120 minutes, and at the cheek at 90 minutes, compared with the initial values. A significant difference was also observed between the measurements at 150 minutes and 180 minutes at the cheek. In the mist group, however, transedpidermal

water loss values steadily maintained their initial levels at all measurement sites up to 180 minutes.

The precise reasons for the decrease in transepidermal water loss values in the control group are unclear. However, according to the authors, the findings relating to the mist group suggest that some of the mist was absorbed into the stratum corneum while some remained on the skin surface and evaporated as a part of the transepidermal water loss process, and the change in transepidermal water loss values in the mist group indicate that the mist supplies water to the stratum corneum. The authors suggest that the increase in water in the surface of the stratum corneum supplied by the mist, reduced the evaporation of internal stratum corneum water, which helps to preserve the skin water content.

There were no significant differences between the mist and control groups in terms of skin conductance or sebum levels. In terms of the biomechanical parameters, skin distension was significantly increased in the group with mist compared with that in the control group at the forehead and cheek. This suggests that the mist caused hydration of the stratum corneum and produced a subsequent softening effect.

“Conventional room humidifiers supply excess water droplets to the air to moisturize it, but this causes other problems including dew condensation in winter or thermal discomfort in summer. To address this issue, we examined the use of generated mist, which aimed to protect the skin from dryness without increasing humidity in the air. These data indicated that a mist of water nanodroplets played an important role in softening skin in an air-conditioned room without increasing excess humidity.”²⁷

3. Discussion

A review of evidence around major climate conditions on skin integrity and function found that under dry conditions, surface roughness increases, while conductance decreases, indicating increased skin dryness²⁸. The review outlined further changes indicative of increased dry skin disorder activity or barrier disruption, including epidermal proliferation, and that dermal mast cells hypertrophy and release histamine, and inflammatory cytokines, such as interleukin-1 (IL-1), are up-regulated.

In this paper, we have sought to explore some of the key evidence available around skin hydration and ambient humidity. Our findings go some way to confirming those of the above review, but also highlight some conflicting evidence regarding transepidermal water loss and ambient humidity.

The study by Egawa et al.⁴ looking at the effect of low humidity on healthy human skin before and after three or six-hour exposure to low humidity, reported decreased moisture content in the stratum corneum but also decreased transepidermal water loss in skin subjected to low humidity⁴. The authors of the mist study²⁷ also report decreases in transepidermal water loss in their control group, and compare their findings to the Egawa study above; however, it is worth noting the difference in relative humidity associated with the findings in each of these studies (10 per cent in the Egawa study⁴, versus 35 per cent in the Ohno study²⁷). This reflects the need for further research to explain the altered transepidermal water loss values and importantly how these correlate to skin dryness, and what the implications are for skin health.

In summary, the studies outlined demonstrate that low humidity may effect the skin in a number of ways, for example by decreasing the water content of the stratum corneum, causing dry skin scales, aggravating skin texture, reducing elasticity and causing fine wrinkles.

However, the sometimes contradictory results uncovered by this review indicate that further studies on the effects of humidity on normal and diseased skin and the biological mechanisms involved are a priority. Further evidence may support preliminary data indicating potentially promising new treatment regimens involving humidity for patients with dry skin diseases such as eczema.

4. Footnotes

*Dry skin is a subjective term, which may vary from a feeling of roughness of the skin surface to diseased skin featuring a damaged barrier function, and across the available evidence examined here, we do use a set definition for what constitutes dryness. Indeed, the term dry may be used when the skin feels rough but does not actually feature a lower water content, and this is a consideration when interpreting the evidence for use in a wider context.

5. References

¹ American Society of Heating, Refrigerating and Air-Conditioning Engineers: <https://www.ashrae.org/>

- ² Tagami, H (2014), Electrical measurement of the hydration state of the skin surface in vivo. *Br J Dermatol*, 171:2933.
- ³ Sato J, Denda M, Nakanishi J, Koyama J (1998), Dry condition affects desquamation of stratum corneum in vivo. *J Derm Sci*, 18(3):163169.
- ⁴ Egawa M, Oguri M, Kuwahara T, Takahashi M (2002), Effect of exposure of human skin to a dry environment. *Skin Res Technol*, 2002 Nov;8(4):212-8.
- ⁵ Eberlein-Knig B, Schfer T, Huss-Marp J, Darsow U, Mhrenschrager M, Herbert O, Abeck D, Kramer U, Behrendt H, Ring J (2000), Skin surface pH, stratum corneum hydration, trans-epidermal water loss and skin roughness related to atopic eczema and skin dryness in a population of primary school children. *Acta Derm Venereol*, 80:188191.
- ⁶ Tsukahara K, Hotta M, Fujimura T, Haketa K, Kitahara T (2007), Effect of room humidity on the formation of fine wrinkles in the facial skin of Japanese. *Skin Res Technol*, 13(2):184-8.
- ⁷ Reinikainen LM, Jaakkola JJ, Seppnen O (1992), 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*, 47(1):8-15.
- ⁸ Vyumvuhore R, Tfayli A, Duplan H, Delalleau A, Manfait M, Baillet-Guffroy A (2013), Effects of atmospheric relative humidity on Stratum Corneum structure at the molecular level: ex vivo Raman spectroscopy analysis. *Analyst*, 138(14):4103-11.
- ⁹ Kay J, Gawkrödger DJ, Mortimer MJ, Jaron A (1994), The prevalence of childhood atopic eczema in a general population. *J Am Acad Dermatol*, 30(1):35-9.
- ¹⁰ British Association of Dermatologists Patient Information Leaflet: Atopic Eczema, Produced August 2004, Updated April 2013, <http://www.bad.org.uk/for-the-public/patient-information-leaflets/atopic-eczema>, consulted 27 November 2014.
- ¹¹ Eberlein-Knig B, Spiegl A, Przybilla B (1996), Change of skin roughness due to lowering air humidity in climate chamber. *Acta Derm Venereol*, 76(6):447-9.
- ¹² Langan SM, Irvine AD (2013), Childhood Eczema and the Importance of the Physical Environment. *J Invest Dermatol*, 133(7): 17061709
- ¹³ Weiland SK, Hsing A, Strachan DP, Rzehak P, Pearce N (2004), Climate and the prevalence of symptoms of asthma, allergic rhinitis, and atopic eczema in children. ISAAC Phase One Study Group. *Occup Environ Med*, 61:609615.

¹⁴ Surez-Varela MM, Garca-Marcos Alvarez L, Kogan MD, Gonzlez AL, Gimeno AM, Aguinaga Ontoso I, Daz CG, Pena AA, Aurrecoechea BD, Monge RM, Quiros AB, Garrido JB, Canflanca IM, Varela AL (2008), Climate and prevalence of atopic eczema in 6- to 7-year-old school children in Spain. ISAAC phase III. *Int J Biometeorol*, 52(8):833-40.

¹⁵ Sargen MR, Hoffstad O, Margolis DJ (2013), Warm, humid, and high sun exposure climates are associated with poorly controlled eczema: PEER (Pediatric Eczema Elective Registry) cohort, 2004-2012. *J Invest Dermatol*, 134(1):51-7.

¹⁶ Silverberg JI, Hanifin J, Simpson EL (2013), Climatic factors are associated with childhood eczema prevalence in US. *J Invest Dermatol*, 133(7):1752-1759.

¹⁷ Uter, Gefeller, Schwanitz (1998), 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*, 138:266272.

¹⁸ Denda M, Sato J, Masuda Y, Tsuchiya T, Koyama J, Kuramoto M, Elias PM, Feingold KR (1998), Exposure to a dry environment enhances epidermal permeability barrier function. *J Invest Dermatol*, 111(5):858-63.

¹⁹ Sauer GC, Hall JC (1996), Seasonal skin diseases. In: SauerGC, Hall JC (eds) *Manual of skin diseases*. Lippincott-Raven, Philadelphia, 2328.

²⁰ Wilkinson J, Rycroft R (1982), Contact dermatitis. In: Champion Burton J, Ebling F (eds) *Textbook of dermatology*, 5th edn. Blackwell Scientific Publications, Oxford, 614615.

²¹ Sato J, Katagiri C, Nomura J, Denda M (2001), Drastic decrease in environmental humidity decreases water-holding capacity and free amino acid content of the stratum corneum. *Arch Dermatol Res* 293:477-480.

²² Sato J, Denda M, Chang S, Elias PM, Feingold KR (2002), Abrupt Decreases in Environmental Humidity Induce Abnormalities in Permeability Barrier Homeostasis. *Journal of Investigative Dermatology* 119:900904.

²³ Katagiri C, Sato J, Nomura J, Denda M (2003), 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* 31(1):29-35.

²⁴ Denda M, Hori J, Koyama J, Yoshida S, Nanba R, Takahashi M, Horii I, Yamamoto A (1992), Stratum corneum sphingolipids and free amino acids in experimentally-induced scaly skin. *Arch Dermatol Res* 284:363367.

²⁵ Tanaka M, Okada M, Zhen YX, Inamura N, Kitano T, Shirai S, Sakamoto K, Inamura T, Tagami H (1998), Decreased hydration state of the stratum

corneum and reduced amino acid content of the skin surface in patients with seasonal allergic rhinitis. *Br J Dermatol* 139:618-621.

²⁶ Takahashi M, Ikezawa Z (2000), Dry skin in atopic dermatitis and patients on hemodialysis. In: Loden M, Maibach HI (eds) *Dry skin and moisturizers: chemistry and function*. CRC Press, Boca Raton, pp 135-146.

²⁷ Ohno H, Nishimura N, Yamada K, Shimizu Y, Iwase S, Sugeno J, Sato M (2013), Effects of water nanodroplets on skin moisture and viscoelasticity during air-conditioning. *Skin Res Technol* 19(4):375-83.

²⁸ Singh B, Maibach H (2013), Climate and skin function: an overview. *Skin Res Technol* 19(3):207-12.