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Review

Climate change and atopic dermatitis: is there a link?

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Abstract

Atopic dermatitis (AD) is a chronic relapsing inflammatory skin disease with a growing health concern, because of its high prevalence and associated low quality of life. The etiology of AD is multifactorial with interaction between various factors such as genetic predisposition, immune, and importantly, environmental factors. Since climate change is associated with a profound shift in environmental factors, we suggest that AD is being influenced by climate change. This review highlights the effects of ultraviolet light, temperature, humidity, pollens, air pollutants, and their interaction between them contributing to the epidemiology and pathophysiology of AD.

Introduction

What are the changes associated with climate change? Climate includes patterns of temperature, humidity, precipitation, wind, and seasons, which play a fundamental role in shaping the natural ecosystem and human health. Our climate is rapidly changing, and the changes are progressing faster than any seen in the last thousand years.[1] This review examines how climate changes may affect atopic dermatitis (AD).

How climate change may affect atopic dermatitis

Epidemiology

Globally, the prevalence of AD has increased by 2-3 fold in the last half of the 20th century.[2] The epidemiology of AD is changing at the same time as climate change is occurring, raising the possibility that these are linked. While the prevalence of AD has previously been higher in the developed world, new evidence shows high prevalence in developing countries such as Africa, Asia, and Latin America.[3] In particular, adult-onset AD is more common than previously recognized, with a rate as high as 11-13% in some countries like Singapore, Malaysia, and Sweden.[4,5] The worldwide lifetime prevalence of AD is >20%–20% in children and 1–3% in adults, with higher incidence in developed countries.[2] The prevalence varies greatly throughout the world (Fig. 1), for example, in the school-aged children group 6 to 7, the prevalence of AD ranged from 0.9% in India, 4.8% in Eastern Mediterranean, 9.5% in Africa, 10.2% in Asia-Pacific, 17% in Oceania, to 22.5% in Ecuador; while in the group aged 13 to 14, the prevalence of AD ranged from 0.2% in China to 24.6% in Columbia.[3,4] It is particularly noteworthy that many epidemiological data in some developing countries such as Asia and Africa may certainly be underestimated due to the lack of trained dermatologists in accessing the disease epidemiology.

In conclusion, there are wide variations in prevalence in different regions and within countries, suggesting that environmental factors associated with climate change along with other factors play a role in the epidemiology of AD.

Pathophysiology

AD is a complex disease characterized by an underlying barrier defect associated with specific Th2 immune specific phenotypes.[6]

Filaggrin mutations

One of the key structural components of the epidermal barrier is filaggrin gene, which encodes for the filament aggregating protein (FLG). A deficiency of this protein is found in up to 60% of AD patients.[7] In AD children carrying the FLG mutations, AD occurs at areas of the body exposed to wind and cold.[8] Among Japanese AD patients with FLG mutations, the winter months were reported to be the worst months, when compared with those without FLG mutation.[9] Children living in a subtropical

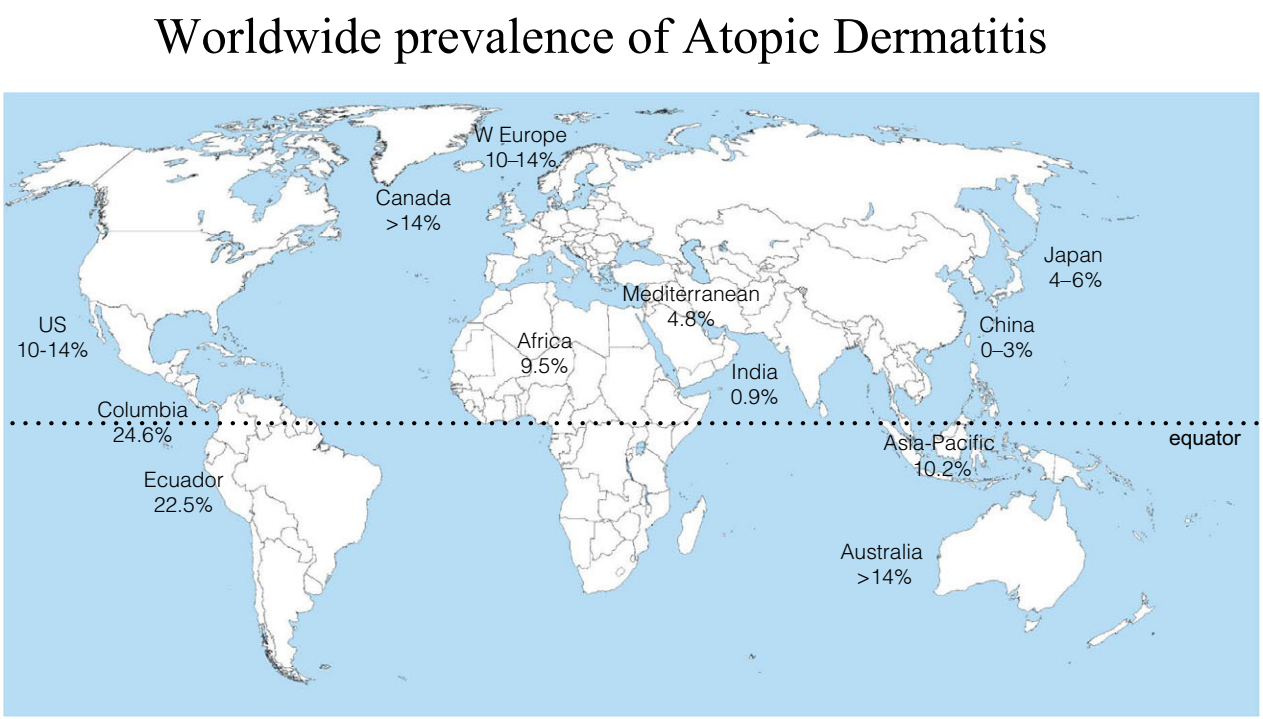

Figure 1 Worldwide prevalence of atopic dermatitis

climate had a lower prevalence of FLG mutation than those living in colder and drier parts of Japan.[10] Since only 44% of AD patients have heterozygous FLG mutations and 76% of homozygous patients suffer from AD, other factors such as the environment are likely to play a role in its pathogenesis.[11]

Effects of increased exposure to ultraviolet light

Ultraviolet (UV) radiation exerts immunosuppressive effects in AD patients.[12,13] Exposure of UVA/UVB has been shown to activate the expression of antimicrobial peptides, lipids, and skin barriers protein and decrease histamine release, providing a protective role in the development of AD.[12,13] Flohr *et al.* found UVA/B promotes the conversion of trans-urocanic acid, a byproduct of filaggrin, into its cis-urocanic acid that has immunosuppressive effect.[14] Numerous studies have revealed the local systemic immunosuppressive effects of UV on the human immune system such as UV exposure promotes Treg cells, leading to increase in Th2 cytokine productions.[15] In addition, UV reaction induces vitamin D production, leading to down regulation of cell-mediated immune function by enhancing Treg cells.[16] UVA/B also has a suppressive effect in *S. aureus* superantigen production, another common trigger for AD flare.[17] Therefore, phototherapy is generally used in patients with AD to relieve acute flares (UVA1) and chronic lesions (narrowband UVB).[18]

Global climate change could influence UV exposure via alternating the atmospheric conditions such as greenhouse gas and interaction between ozone layers. Factors that may increase ambient UV exposure are high altitude, duration and time spent in the sun, skin pigmentation, and the type of sun protective measurements. Supporting this hypothesis, there seems to be an increased incidence of AD during the winter months compared to summer months due to the reduced sun exposure seen in the winter;[19] downregulation however, other factors such as changed humidity and increased irritants with indoor time could also have played a role. AD was, also, more common among children born in the autumn and winter compared to the spring and summer.[20,21] Highest prevalence of AD was found in the Atlantic region, while the lowest incidence was in the Mediterranean region, which correlated with precipitation and humidity.[22] In American states, higher AD prevalence was found with low humidity, low UV exposure, and low outdoor temperature or the use of indoor heating.[23] Similar observations have been reported in Japan,[24] China,[25] India,[26] USA,[27] Finland,[28] and Australia.[29]

Effects of rising temperatures and increased humidity

Intriguingly, in contrast to the above hypothesis, several studies have suggested a strong trend toward a higher incidence of AD with an increase in latitude, suggesting that increased temperature exposure and humidity might lead to enhanced sweating, which has an irritant effect on the skin, thereby worsening AD.[30,31] Among German children, 18 of 39 had worsening AD symptoms during the summer months.[32] However, in the same study, the authors identified 20 patients who had worsening symptoms during the winter months.[32] An 8-year longitudinal study of AD patients in the US reported higher temperature and

increased sun exposure were associated with poorly-controlled eczema.[33]

Effect of increased temperatures and humidity on itching associated with atopic dermatitis

One of the hallmarks of AD is chronic and generalized pruritus. AD patients fare worst in dry climates as the skin barrier is derived of moisture (dry skin exacerbates itch). Pruriceptive itch originates when specific sensory nerve terminals located in the skin — slow conducting myelinated (Aδ) and unmyelinated (C) nerves fibers — are activated in response to noxious stimulation and temperature changes in the skin.[34] It has been reported that these nerve fibers are more active at high temperature.[35] However, increased itching was seen with low temperature, little sunshine, snowfall, and fog.[36] Furthermore, it is reported that children with AD who spent 4 weeks in a sunny, subtropical climate experienced a decrease in symptom severity and had a better life quality after their stay.[10] The disparate association between temperature and itch needs further study.

Effect of increased pollen and air pollutants

AD is characterized by a waxing and waning course. Multiple possible reasons for this have been advocated, including diet, stress, heat, sweating, damp, and external irritants. Pollen exposure and air pollutants are also factors that have been implicated.[37–40] Warmer temperatures can result in earlier and higher intensity of pollen, thereby triggering an eczema flare.[41] Air pollutants are ubiquitous and can originate from both indoor and outdoor sources.[42] A wide array of outdoor substances such as particulate matters, toluene, sulfuring particles, and formaldehyde, can aggravate skin symptoms of AD.[43–47]

Indoor substances such as tobacco smoke, stoves, construction materials, and dust mites can also contribute to AD flare.[48] Several studies with large patient cohorts revealed that air pollution increases the prevalence of AD.[49–51] The effects of air pollutants to AD could be due to an imbalance between oxidants and antioxidants, leading to oxidative stress damage to the skin barrier by external factors.[48] Therefore, changes in climate factors such as temperature, humidity, radiation, and air pollution could influence the response and symptoms of AD (Table 1).

Table 1 Summary of flare factors for atopic dermatitis

Factors	Positive effect	Negative effect
Climate		
UV	Protective (immunosuppressive)	
Season	Protective (summer)	Increased risk (summer)
Humidity	Protective (reduce sweating)	Increased risk (exacerbate itch)
Infection	Increased risk	
Air pollutants	Increased risk	
Stress	Increased risk	
Skin irritants	Increased risk	
Skin barrier defect	Increased risk	

Conclusion

Taken together, it seems the changing environment, attributable to climate change, is having a profound effect on the epidemiology of AD. Increased temperatures, increased humidity, increased pollen, and air pollution are all associated with changes in the epidemiology and severity of atopic dermatitis.

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