Impact of Climate Change–Related Environmental Factors on Allergen Production and the Epidemiology and Severity of Allergic Diseases

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Abstract

Background: Allergic disease affects up to 40% of the adult population worldwide. This percentage is increasing as a result of environmental changes related to global warming.
Methods: We undertook a systematic review of the literature to identify and evaluate current evidence on the impact of climate change–related environmental factors on allergen production and the epidemiology and severity of allergic diseases. We applied the Population, Exposure, Comparison, Outcome (PECO) criteria to guide our literature searches of the PubMed and Cochrane databases (January 1, 2016 to December 31, 2021). Study outcomes were categorized and grouped to facilitate data synthesis. Outcomes were classified as significant ($P<.05$), nonsignificant ($P>.05$), or undetermined (P value not reported). Study quality was assessed using the Mixed Methods Appraisal Tool.
Results: Of 195 studies, 40 were considered relevant, and 9 provided data that could be included in the quantitative data synthesis. Environmental factors, including the presence of pollutants, temperature, and drought influenced the type, volume, and timing of exposure to local aeroallergens. The most relevant environmental factor was the presence of environmental pollutants, of which tropospheric ozone was the most frequently associated with changes in allergen production and prevalence and severity of allergic disease. Several publications also demonstrated the impact of environmental factors on health care burden.
Conclusions: Climate change–related environmental factors worsened allergic disease in terms of prevalence, severity, and health care burden owing to alterations in allergen exposure (volume and type), with the presence of pollutants such as ozone being the most common drivers of this increase.

Key words: Allergen. Environment. Allergy. Pollutant. Epidemiology. Climate change.

Resumen

Antecedentes: Las enfermedades alérgicas afectan hasta el 40% de la población adulta mundial, una proporción que se incrementa con los cambios ambientales relacionados con el calentamiento global.
Métodos: Realizamos una revisión sistemática de la literatura para identificar y evaluar la evidencia actual del impacto de los factores ambientales relacionados con el cambio climático en la producción de alérgenos y en la epidemiología y gravedad de las patologías alérgicas. Se establecieron criterios PECO que guiaron las búsquedas bibliográficas en las bases de datos de PubMed y Cochrane (del 1 de enero de 2016 al 31 de diciembre de 2021). Los resultados de los estudios fueron categorizados y agrupados para facilitar la síntesis de datos. Los resultados se clasificaron como significativos (significación estadística $p<0,05$), no significativos ($p>0,05$) o indeterminados (valor de p no proporcionado). La calidad del estudio se evaluó utilizando el análisis MMAT.

Resultados: De 195 registros, se consideraron relevantes 40, y 9 publicaciones proporcionaron datos que fueron incluidos en la síntesis cuantitativa de datos. Factores ambientales, como la presencia de contaminantes, la temperatura y la sequía, influyeron en el tipo, volumen y momento de exposición a los aeroalérgenos locales. El factor ambiental más relevante fue la presencia de contaminantes ambientales, entre los cuales el ozono troposférico fue el más frecuentemente asociado a cambios en la producción de alérgenos, prevalencia y gravedad de las enfermedades alérgicas. Adicionalmente varias publicaciones demostraron el impacto de factores medioambientales sobre la presión asistencial.
Conclusiones: Los factores ambientales relacionados con el cambio climático incrementan la prevalencia, gravedad y presión asistencial de las enfermedades alérgicas debido a alteraciones en la exposición a alérgenos (volumen y tipo). El ozono es el contaminante más implicado en este incremento.

Palabras clave: Alérgeno. Medio ambiente. Alergia. Contaminante. Epidemiología. Cambio climático.

Introduction

Allergic disease has been estimated to affect up to 40% of the global population, imposing a substantial burden on individuals, communities, and health care systems [1-3]. The prevalence of allergic disease has increased sharply in recent decades, most notably in developed countries [2,4]. Industrialization, urbanization, and changing lifestyles may have contributed to this increase through changes in exposure to environmental allergens in terms of both volume and type [3-6].

The precise effect of environmental factors on allergic diseases remains controversial owing, in part, to the complex etiological mechanisms driving the emergence and severity of these diseases [2,4,7]. Epidemiological research on air pollution as a potential risk factor for allergic disease has gained attention in recent years. For example, in Spain, numerous studies have reported associations between pollen count and allergic diseases, including respiratory diseases such as asthma and allergic rhinitis, as well as conditions such as allergic sensitization [8-14]. More accurate results have been reported for other environmental factors, such as traffic-related air pollution, and their association with respiratory diseases (allergic or not) [15]. Results are discrepant. One cohort study found an increase in the prevalence of eczema in adults related to exposure to traffic-related air pollution [16], whereas another found no such effect [2]. Similarly, conflicting results have been reported for the association between air pollution and childhood eczema and the association between exposure to particulate matter less than 2.5 μm in diameter (PM2.5) and allergic rhinitis [17]. These disparate results point to a complex relationship between environmental factors and the range of allergic diseases.

The impact of climate change–related environmental factors, such as drought, flooding, and temperature (eg, heat waves), on allergic disease has also begun to receive more attention in recent years [18,19]. Such factors may have both direct effects on allergic disease and indirect effects by changing local and regional ecosystems, including pollen volume and type, exposure to molds in damp housing, local air pollution, and heat stress [18-22]. Of critical importance in mitigating the future burden on individuals and health care systems is an understanding of the modifiable factors associated with climate change that influence the prevalence and severity of allergic disease. Indeed, the United Nations, through the 2015 Paris Agreement and subsequent versions, continues to emphasise the effect of climate change on human health and allergic disease and to call for global understanding and cooperation to mitigate these impacts [23].

The objectives of this systematic literature review were to identify and evaluate current evidence on the impact of climate change–related environmental factors on the expression, prevalence, and nature of allergens and on the incidence, prevalence, and severity of allergic diseases, particularly rhinitis/conjunctivitis, asthma, food allergy, and atopic dermatitis.

Methods

We undertook a systematic review of the literature following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement, published in 2009 [24].

Search Strategy

The Population, Exposure, Comparison, Outcome (PECO) criteria were applied to guide the literature search and review. In our case, *Population* referred to adults with allergic disease, Exposure referred to climate change–related environmental factors (eg, climate factors, air quality), *Comparison* was not applicable, and *Outcomes* referred to the expression, prevalence, and nature of allergens and the incidence, prevalence, and severity of allergic diseases.

The research questions to be addressed were as follows: "*Do climate change and air quality modify the expression, prevalence, or nature of different allergens, turning them into more aggressive allergens?, "Do climate change and air quality have a direct and significant impact on the incidence, prevalence, or severity of allergic diseases?*", and "*What is the impact of climate change and air quality specifically on rhinitis, conjunctivitis, asthma, food allergy, and atopic dermatitis?*"

The literature search was conducted in the PubMed and the Cochrane databases of systematic reviews for the period January 1, 2016 to December 31, 2021 and was restricted to publications in English or Spanish for which an abstract was available. Search terms were defined as follows: (climate change[Title/Abstract]) OR (greenhouse gas*[Title/Abstract])) AND ((airway diseases [Title/Abstract] OR airway pathology

[Title/Abstract] OR Respiratory diseases [Title/Abstract] OR Respiratory pathology [Title/Abstract] OR allergic diseases [Title/Abstract] OR asthma [Title/Abstract] OR conjunctivitis [Title/Abstract] OR rhinitis [Title/Abstract] OR "food allergy" [Title/Abstract] OR "Atopic dermatitis" [Title/Abstract] OR eczema)[Title/Abstract])) AND ((inciden* OR prevalen* OR sever* OR epidemiol* OR allergenicity) OR ("house dust mites" OR pollen OR alternaria)) ("2016/01/01"[Date - Publication] : "3000"[Date - Publication]).

Inclusion Criteria and Screening Process

All types of original studies (randomized clinical trials [RCTs], nonrandomized trials, post hoc analyses of RCTs, and observational studies) and systematic reviews (with or without meta-analyses) were searched for. Studies were included in the systematic review if they presented quantitative data related to the impact of climate change–related environmental factors on the expression, prevalence, or nature of allergens or the incidence, prevalence, or severity of allergic diseases. We excluded studies dealing with diseases other than rhinitis/conjunctivitis, asthma, food allergy, and atopic dermatitis (Supplementary material 1).

Publications in languages other than English or Spanish were identified but are not included in the PRISMA flowchart (Figure). Publications without an abstract and unpublished studies were also excluded. The full texts of all the studies fulfilling the selection criteria (Supplementary material 2) were retrieved. The titles and abstracts of all identified studies were independently screened for relevance by 2 reviewers (Gloria González and Sara García, both of whom are educated to degree level in biology and chemistry), and duplicates were removed. The full text of potential studies for inclusion were then interrogated for relevance with regard to the PECO questions. Disagreements in study selection between the 2 lead reviewers were resolved by a third reviewer. An additional reviewer (Maite Artés) double-checked the selection criteria of a random sample of 15% of the records.

The publications that were excluded and the reasons why are provided in Supplementary material 3.

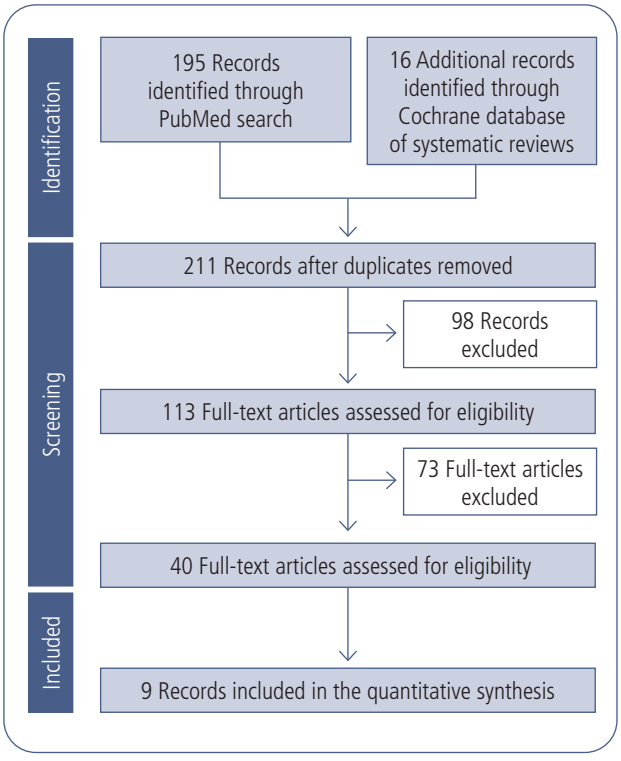

Figure. PRISMA flowchart for the systematic literature review.

Data Synthesis

Reported study outcomes were categorized and grouped to facilitate data synthesis. Given the heterogeneity of the type of outcomes found, data were classified as significant ($P<.05$) and nonsignificant ($P>.05$). In publications with no direct comparison, when a P value was not provided, or when data were descriptive, the results were considered undetermined.

Quality Assessment

Study quality was assessed using the Mixed Methods Appraisal Tool (MMAT) [25], which enables evaluation of the quality of qualitative, quantitative, and mixed-methods studies focusing on methodological criteria.

Results

A total of 195 studies were identified and reviewed, 40 studies were considered initially eligible, and 9 reports provided relevant quantitative data related to the PECO criteria and were finally included in the data synthesis (Figure). Of these 9 reports, 8 had an MMAT score >60%.

Impact of Climate Change–Related Environmental Factors on Allergens

The 9 studies included in the data synthesis provided information on the impact of climate change–related environmental factors on allergenicity (8 outcomes from 2 different studies [26,27]), changes in allergen production (alteration of time/quantity of allergen production, 25 outcomes from 7 different studies [26,28-33]), and epitope modification (2 outcomes from 1 study [34]).

Climate change–related environmental factors reported as causing adverse changes in the volume or type of allergens included the presence of pollutants (up to 11 study outcomes were provided by 5 different studies, indicating a relationship between pollutants and increased allergenicity and changes in the production of allergens). Increases in temperature due to climate change were related to allergenicity and epitope modification, as reported by Choi et al [26]. Droughts were related to increases in ambient dust levels (PM2.5/PM 2.5-10) due to changes in aridity, as reported by Achakulwisut et al [28] (for 3 outcomes), and other weather conditions were related to changes in the production of allergens (pollen and house dust mites) [30] (for 2 outcomes) (Table 1). Three studies [29,31,34] reported a statistically significant association between the presence of environmental pollutants and a change in the production or type of allergens (for 7 outcomes).

The environmental pollutants contributing to changes in the volume or type of allergens included black carbon, carbon dioxide, PM2.5, tropospheric ozone, and various (including a combination of traffic-related pollutants and others described above) (Table 2). The association between the presence of black carbon and changes in local allergen production reached statistical significance in 1 study [31] (for 1 outcome). The association between PM2.5 and the change in allergen production reached statistical significance in 1 study [29] (for 2 outcomes). The association between tropospheric ozone and the

Table 1. Environmental Factors Causing Alterations in Allergen Parameters.

Environmental factor (exposure factor)	Impact on allergen (outcome)			
	Allergenicity	Change in production (time/quantity)	Epitope modification	Total
Drought	–	3 [28]	–	3
Other weather conditions (pollen and house dust mites)	–	2 [30]	–	2
Pollutant[a]	3 [26,27]	7* [29,31,34] 1 [30]	–	11
Temperature	3 [26]	–	1 [26]	4
Various[b]	2 [26]	12 [26,30,32,33]	1 [26]	15
Total	8	25	2	35

Study design; location; period of study
[26] Review; NA; NA
[27] Review; North America, Europe and Asia countries; NA
[28] Epidemiological study; United States; projections for up to 2090
[29] Time-stratified case-crossover study; Philadelphia (United States); 2011-2014
[30] Review; Asia; last 20 years
[31] Observational study; New York (United States); 24 hours over a 6-day sampling period
[32] Epidemiological study; United States; projections for up to 2090
[33] Ex vivo and in vitro assay; NA
[34] Time-stratified case-crossover study; Belgium; 2017-2018 Jan-May (pollen season)

Abbreviation: NA, not available, not applicable.
*Indicates a statistically significant association.
[a]Black carbon, carbon dioxide, PM2.5, tropospheric ozone.
[b]The category "various" refers to a combination of the previous factors without specifying the individual contribution of each factor.

Table 2. Environmental Pollutants Causing Alterations in Allergen Parameters.

Environmental pollutant (exposition factor)	Impact on allergen (outcome)			
	Allergenicity	Change in production (time/quantity)	Epitope modification	Total
Black carbon	–	1* [31]	–	1
Carbon dioxide	–	1 [31]	–	1
PM2.5	1 [27]	2 [29]	–	3
Tropospheric ozone	–	4* [29,34]	–	4
Various[a]	2 [26]	–	–	2
Total	3	8		11

Study design; location; period of study
[26] Review; NA; NA
[27] Review; North America, Europe and Asia; NA
[29] Time-stratified case-crossover study; Philadelphia (United States); 2011-2014
[31] Observational study; New York (United States); 24 hours over a 6-day sampling period
[34] Time-stratified case-crossover study; Belgium; 2017-2018 Jan-May (pollen season)

Abbreviation: NA, not available, not applicable.
*Indicates a statistically significant association.
[a]The category "various" refers to a combination of the previous factors without specifying the individual contribution of each factor.

Table 3. Impact of Allergen Alteration on Allergic Diseases.

Allergen alteration (exposure factor)	Impact on allergic disease (outcome)				
	Asthma	Respiratory disease	Sensitization	Various[a]	Total
Allergenicity	–	1 [26]	–	3 [26]	4
Change in production (time/quantity)	3* [29] 2 [32]	4* [31,34] 2 [33]	4 [30]	4 [26]	19
Epitope modification	–	–	–	1 [26]	1
Total	5	7	4	8	24

Study design; location; period of study
[26] Review; NA; NA
[29] Time-stratified case-crossover study; Philadelphia (United States); 2011-2014
[30] Review; Asia; last 20 years
[31] Observational study; New York (United States); 24 hours over a 6-day sampling period
[32] Epidemiological study; United States; projections for up to 2090
[33] Ex vivo and in vitro assay; NA
[34] Time-stratified case-crossover study; Belgium; 2017-2018 Jan-May (pollen season)

Abbreviation: NA, not available, not applicable.
*Indicates a statistically significant association.
[a]The category "various" refers to a combination of the previous allergy disease without specifying the individual contribution of each factor.

Table 4. Impact of Pollutants on Allergic Diseases.

Environmental pollutant (exposure factor)	Impact on allergic disease (outcome)				
	Asthma	Respiratory disease	Sensitization	Other	Total
Black carbon	–	1* [31]	–	–	1
Carbon dioxide	–	–	1 [30]	–	1
PM2.5	2* [29]	–	–	–	2
Tropospheric ozone	1 [29]	3* [34]	–	–	4
Various[a]	–	1 [26]	–	1 [26]	2
Total	3	5	1	1	10

Study design; location; period of study
[26] Review; NA; NA
[29] Time-stratified case-crossover study; Philadelphia (United States); 2011-2014
[30] Review; Asia; last 20 years
[31] Observational study; New York (United States); 24 hours over a 6-day sampling period
[34] Time-stratified case-crossover study; Belgium; 2017-2018 Jan-May (pollen season)

Abbreviation: NA, not available, not applicable.
*Indicates a statistically significant association.
[a]The category "various" refers to a combination of the previous factors without specifying the individual contribution of each factor.

change in allergen production reached statistical significance in 2 studies [29,34] (for 4 outcomes).

Impact of Allergen Alterations on Allergic Diseases

Studies reporting associations between changes in allergen production and allergic disease were explored (Table 3). Associations were reported for asthma, respiratory diseases, sensitization, and various other allergic diseases. One study reported a statistically significant association between the change in allergen production and asthma [29]. For respiratory diseases in general, statistically significant associations were reported for 4 outcomes related to a change in allergen production [31,34].

The environmental pollutants most frequently associated with allergic diseases were tropospheric ozone (associated with respiratory disease in general in 1 study [34] for 3 outcomes) and PM2.5 (associated with asthma in 1 study [29] for 2 outcomes) (Table 4).

Associations were noted between changes in allergen production and the epidemiology and health care burden of allergic diseases. A statistically significant association was reported for the association between changes in allergen production and the epidemiology of allergic disease (for 3

Table 5. Impact of Allergen Alteration on Allergic Diseases.

Allergen alterations (exposure factor)	Impact (outcome)					
	Epidemiology	Prevalence	Severity	Health care burden	Other[a]	Total
Allergenicity	3 [26]	–	3 [26]	–	1 [27]	7
Change in production (time/quantity)	3* [34] 6 [26,28,33]	4 [26,30,33]	3* [34] 1 [34]	5 [26,28,32]	1* [31] 1 [26]	24
Epitope modification	–	–	–	–	–	–
Total	12	4	7	5	3	31

Study design; location; period of study
[26] Review; NA; NA
[27] Review; North America, Europe and Asia; NA
[28] Epidemiological study; United States; projections for up to 2090
[30] Review; Asia; last 20 years
[31] Observational study; New York (United States); 24 hours over a 6-day sampling period
[32] Epidemiological study; United States; projections for up to 2090
[33] Ex vivo and in vitro assay; NA
[34] Time-stratified case-crossover study; Belgium; 2017-2018 Jan-May (pollen season)

Abbreviation: NA, not available, not applicable.
*Indicates a statistically significant association.
[a]Other (general adverse health effects).

Table 6. Impact of Environmental Factors on Epidemiology and Burden of Allergic Diseases.

Environmental factor (exposure factor)	Impact (outcome)			
	Epidemiology	Health care burden	Other[a]	Total
Drought	–	1 [28]	–	1
Unspecified weather conditions	1 [28]	–	–	1
Pollutant[b]	3* [34] 3 [26]	–	1* [31] 1 [27]	8
Various[c]	5 [26]	4 [26,32]	–	9
Total	12	5	2	19

Study design; location; period of study
[26] Review; NA; NA
[27] Review; North America, Europe and Asia; NA
[28] Epidemiological study; United States; projections for up to 2090
[31] Observational study; New York (United States); 24 hours over a 6-day sampling period
[32] Epidemiological study; United States; projections for up to 2090
[34] Time-stratified case-crossover study; Belgium; 2017-2018 Jan-May (pollen season)

Abbreviation: NA, not available, not applicable.
*Indicates a statistically significant association.
[a]The category "other" refers to general adverse health effects.
[b]Black carbon, carbon dioxide, PM2.5, tropospheric ozone, various others.
[c]Pollen and house dust mite.

outcomes) and the severity of allergic disease (for 3 outcomes) in 1 study [34] (Table 5).

Several studies highlighted the impact of environmental factors on the epidemiology and health care burden of allergic disease (Table 6). One study [34] reported a statistically significant association between the presence of environmental pollutants and the epidemiology of allergic diseases (for 3 outcomes) (Table 7).

Discussion

We undertook a systematic review of the literature to evaluate current scientific evidence on the impact of climate change–related environmental factors on allergen production and on the epidemiology and severity of allergic diseases. Our analysis of the current literature base supports an adverse impact of environmental factors, including those driven by

Table 7. Impact of Environmental Pollutants on the Epidemiology of Allergic Disease.

Environmental factor (exposure factor)	Impact (outcome)		
	Epidemiology	Other[a]	Total
Black carbon	–	1* [31]	1
Carbon dioxide	1 [30]	–	1
PM2.5	–	1 [27]	1
Tropospheric ozone	3* [34]	–	3
Various[b]	2 [26]	–	2
Total	6	2	8

Study design; location; period of study
[26] Review; NA; NA
[27] Review; North America, Europe and Asia; NA
[30] Review; Asia; last 20 years
[31] Observational study; New York (United States); 24 hours over a 6-day sampling period
[34] Time-stratified case-crossover study; Belgium; 2017-2018 Jan-May (pollen season)

Abbreviation: NA, not available, not applicable.
*Indicates a statistically significant association.
[a]Pollen and house dust mite
[b]The category "various" refers to a combination of the previous factors without specifying the individual contribution of each factor.

global climate change, on the volume and type of allergens to which local populations are exposed. These changes impact the type, prevalence, and burden of allergic disease in both developed and developing countries.

Environmental factors, including the presence of pollutants, temperature, and drought, influence the type (allergenicity, epitope modifications), volume (production and pollen count), and timing of exposure to local aeroallergens [26-34]. The most relevant environmental factor was the presence of environmental pollutants, of which tropospheric ozone was the most frequently reported [26,27,29-31,34]. Other environmental pollutants, including black carbon [31], carbon dioxide [30], and PM2.5 [27,29], were also identified as factors driving adverse exposure to aeroallergens.

The changes in production of allergens (in terms of time and quantity) had an impact on both allergic sensitization and allergic diseases, including respiratory diseases such as asthma [26-34]. Increases in the prevalence or severity of allergic diseases [26,30,33,34] and associated increases in the health care burden [26,28,32] were the principal effects reported. These effects were influenced by changes in allergen production, with changes in tropospheric ozone being the most frequently reported environmental factor [26,29-34]. A more recent study, published since our literature search was performed, indicates that exposure to particulate matter levels lower than current recommendations can have adverse effects for individuals with allergic respiratory diseases such as asthma, increasing the risk for potentially fatal exacerbations [35]. In relation to the impact of pressurized metered dose inhalers (pMDIs) prescribed for any indication on total value of CO_2 eq/year, we previously reported that the use of pMDIs accounts for 0.0909% of total emissions in Spain [36]. Furthermore, we showed that a switch of all pMDIs to dry-powder inhalers, other than for the delivery of rescue medications, would cut the associated CO_2 emissions from pMDIs to 0.0579% of the total emissions in Spain. However, the potential impact on asthma control and patient outcomes was not well defined, and, pending further research, inhalers should be selected based on patients' clinical criteria rather than on environmental considerations [36].

The strengths of the current systematic literature review include well-defined PECO questions to guide the literature search and subsequent data extraction and analysis and the evaluation of the quality of the studies included using MMAT criteria. In addition, our findings can be generalized to international level, as there were no exclusion criteria according to geographical area and all environmental pollutants and allergic diseases were considered.

Our findings are also subject to limitations. Only publications in English and Spanish were included, and the search was conducted solely in the Cochrane and PubMed databases for the 5 years before 2021. However, although only 1 publication was ruled out for language reasons, this limit on eligible literature did not compromise the validity or generalizability of the analysis presented herein. A potential limitation concerning the nonmitigation of impacts was that studies with no statistically significant results might not have been published. Finally, there was considerable heterogeneity in study design and outcome definitions, as the studies included in the current analysis were performed in many different countries and using different methodological approaches. While the heterogeneity in study design precluded formal statistical analyses and pooling of the reported results, it does not compromise the external validity of the review.

Climate change and increased levels and types of environmental pollution are among the greatest threats to human health in both developed and developing regions of the world [37,38]. Weather-related changes such as heat waves, thunderstorms, and changes in precipitation patterns will continue to alter and increase allergen exposure [39,40], as will

increasing levels of environmental pollution [41]. Geopolitical factors such as health of the population, health inequalities, poverty, famine, education, political instability, and conflict will continue to amplify the adverse effects of climate change on allergen exposure and the course and consequences of allergic disease [37]. Climate change and the consequences for human health necessitate urgent action to diminish impacts for future generations. In addition, it is important to develop novel approaches that help us understand the complex associated interrelationships and enable us to mitigate the resulting deleterious effects [42,43].

Conclusions

Climate change–related environmental factors affect allergic diseases by increasing prevalence, severity, and health care burden. This effect occurs owing to alterations in the allergen (mainly change in production) caused by various environmental factors, including the presence of pollutants such as ozone. The effect of environmental pollution was observed for multiple allergic diseases, including allergic respiratory diseases such as asthma. Specifically, exposure to lower concentrations of particulate matter than those currently recommended can have adverse effects for individuals with allergic respiratory diseases such as asthma. Further research based on homogenously designed studies is of paramount importance.

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Conflicts of Interest

Montoro J. Grants, SEAIC; consulting fees, Chiesi, Astra Zeneca, and Sanofi; speaker's fees, Astra Zeneca, GSK, Faes, Sanofi, and Novartis.

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