The effects of climate change on respiratory allergy and asthma induced by pollen and mold allergens

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Article type : Review

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This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/ALL.14476

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Key words: Respiratory allergy; Allergenic pollen; Climate change and allergy; Biodiversity and Allergy; Pollen allergy; Severe allergic asthma; Thunderstorm asthma; Seasonal allergy.

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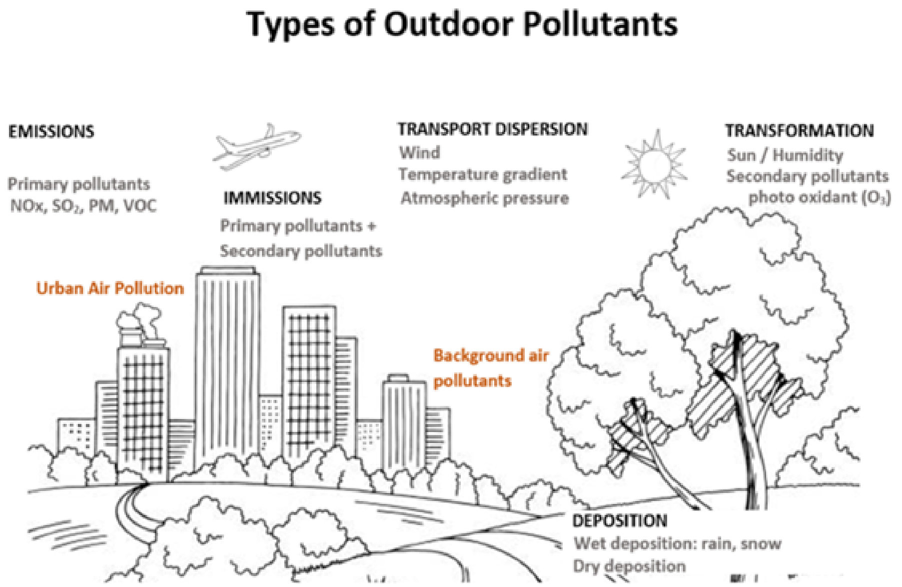
ABSTRACT

The impact of climate change on the environment, biosphere and biodiversity has become more evident in the recent years. Human activities have increased atmospheric concentrations of carbon dioxide (CO_2) and other greenhouse gases. Change in climate and the correlated global warming affects the quantity, intensity and frequency of precipitation type as well as the frequency of extreme events such as heat waves, droughts, thunderstorms, floods and hurricanes. Respiratory health can be particularly affected by climate change, which contributes to the development of allergic respiratory diseasesand asthma. Pollen and mold allergens are able to trigger the release of pro-inflammatory and immunomodulatory mediators that accelerate the onset the IgE-mediated sensitizationand of allergy. Allergy to pollen and pollen season at its beginning, in duration and intensity are altered by climatechange. Studies showed that plants exhibit enhanced photosynthesis and reproductive effects and produce more pollen as a response to high atmospheric levels of carbon dioxide (CO_2).Molds which proliferation is increased by floods and rainy storms are responsible for severe asthma. Pollen and mold allergy is generally used to evaluate the interrelation between air pollution and allergic respiratory diseases, such as rhinitis and asthma. Thunderstorms during pollen seasons can cause exacerbation of respiratory allergy and asthma in patients with hay fever. A similar phenomenon is observed for molds.Measures to reduce greenhouse gas emissions can have positive health benefits.

INTRODUCTION

Climate change affects human health and allergy appears to be at the front line of the sequelae of climate change in addition to infectious and cardiovascular diseases (1-11). Additional studies and research show that allergic respiratory diseases are affected by climate change and that climate change can be considered a threat to global health, affecting food supplies, water and air quality and climate. Present-day knowledge is taken from experimental and epidemiological studies on the relationship between allergic respiratory diseases, asthma and environmental factors, such as meteorological variables, airborne allergens, and air pollution while still lacking studies on respiratory allergy as effected by climate change (1,3,5-7). Urbanization with its high levels of vehicle emissions, and a westernized lifestyle are linked to the rising frequency of respiratory allergic diseases and bronchial asthma observed over recent decades in most industrialized countries (1,2,7,8-19). Climatic factors (thunderstorms, temperature, humidity, and wind speed) can affect both interaction components (chemical and biological) (1,3). The image 1 shows the types of outdoor air pollutants.

Image 1. Types of outdoor air pollutants



Source: Original elaboration making reference to: Penard-Morand, Annesi-Maesano. Breathe. 2005 (11).

By an increased carbon dioxide (CO_2) concentration, plant growth is affected in various ways leading to prolonged pollination periods (1,14). Due to environmental pollutant effects, which do not only act as irritants to skin and mucous membranes, allergen carriers such as pollen can be altered in the atmosphere and release allergens resulting in allergen-containing aerosols in the ambient air. Pollen has been demonstrated not only to be an allergen carrier, but also to release highly active lipid mediators (pollen-associated lipid mediators), which have proinflammatory and immunomodulating effects in allergy diseases (1).

Climate change, why and how?

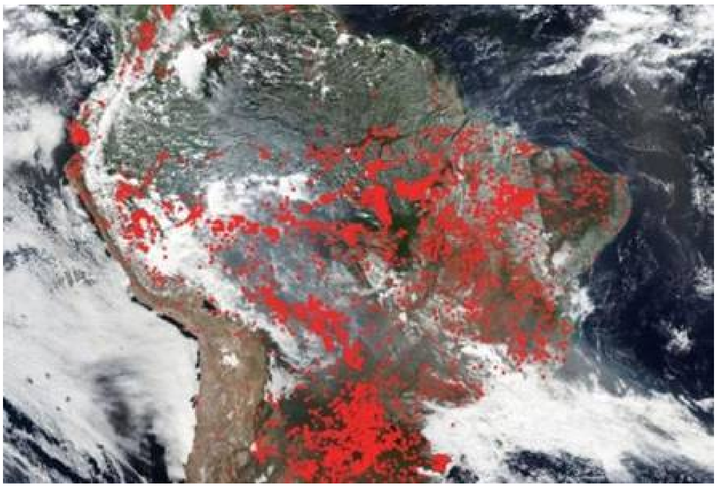
The climate change pattern will vary regionally depending on latitude, altitude, rainfall and storms, land-use patterns, urbanization, transportation, and energy production. The greatness of climate change and related increases in allergic diseases will be affected by how ambitiously greenhouse gas mitigation strategies are followed up on (5). CO_2, primarily emitted from burning fossil fuels, is the predominant greenhouse gas. Other greenhouse gasses include methane (CH4), nitrous oxide (NO2), and fluorinated gases (8).

Studies on plant responses to high atmospheric levels of CO2 demonstrate that plants exhibit enhanced photosynthesis, reproductive effects and produce more pollen (9).

Human activities have increased the natural concentration of carbon dioxide in our atmosphere, increasing Earth's natural greenhouse effect. In 1870, prior to the industrial revolution, Carbon dioxide was 280ppm and grew by 2.87 parts per million (ppm) at the mountain top observatory during 2018, shooting from an average of 407.05 ppm on Jan. 1, 2018, to 409.92 on Jan. 1, 2019, according to a new analysis of air samples collected by NOAA's Global Monitoring Division (GMD) (3,4).

As stipulated in the intergovernmental panel on climate change (IPCC) (6), it is important to reduce anthropogenic CO_2 emissions. Several measures to reduce greenhouse gas emissions can have positive health benefits (1, 3,4). Unfortunately, after CO_2 emissions are reduced and atmospheric concentrations stabilize, the surface air temperature will continue to rise for a period of a century or more (1, 19). This rise in temperature leads to an increase in the concentrations of ozone and particles at ground level (due to droughts, forest fires, desertification and a greater use of coal energy to produce energy to cool). Recently, at the end of 2019 and the beginning of 2020, two major forest fires were presented as a result of climate change, one of them in Brazil and another in Australia. Attached below are NASA satellite images of these natural disasters (Image 2 and 3)(16).

Image 2. Devastating fires in the Amazon (Br).

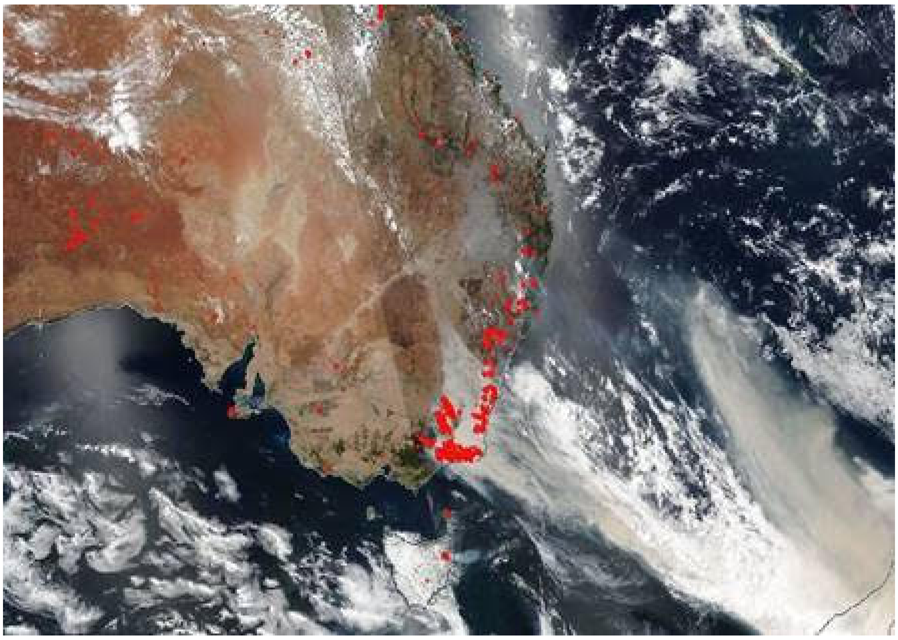


Source: NASA Earth Observatory. Aug. 15-22, 2019 (16).

In the report of European Environment Agency WHO Regional Office for Europe and Joint Research Centre of the European Commission On the Impacts of Europe's Changing Climate it is mentioned that increasing temperature, changing precipitation, rising sea level, more intense and frequent extreme weather events and melting glaciers, ice sheets and Arctic sea ice are some of the challenges already triggered by global climate change (1,3,4,6,19).

Over the past decades it has been demonstrated the positive role of tropical rainforests in capturing large amounts of atmospheric CO_2 In response to the increase in atmospheric CO_2 concentration, tropical forests act as a global carbon sink (17).

Image 3. Ferocious fires in Australia.



Source: NOAA-NASA's on Jan. 01, 2020 (16).

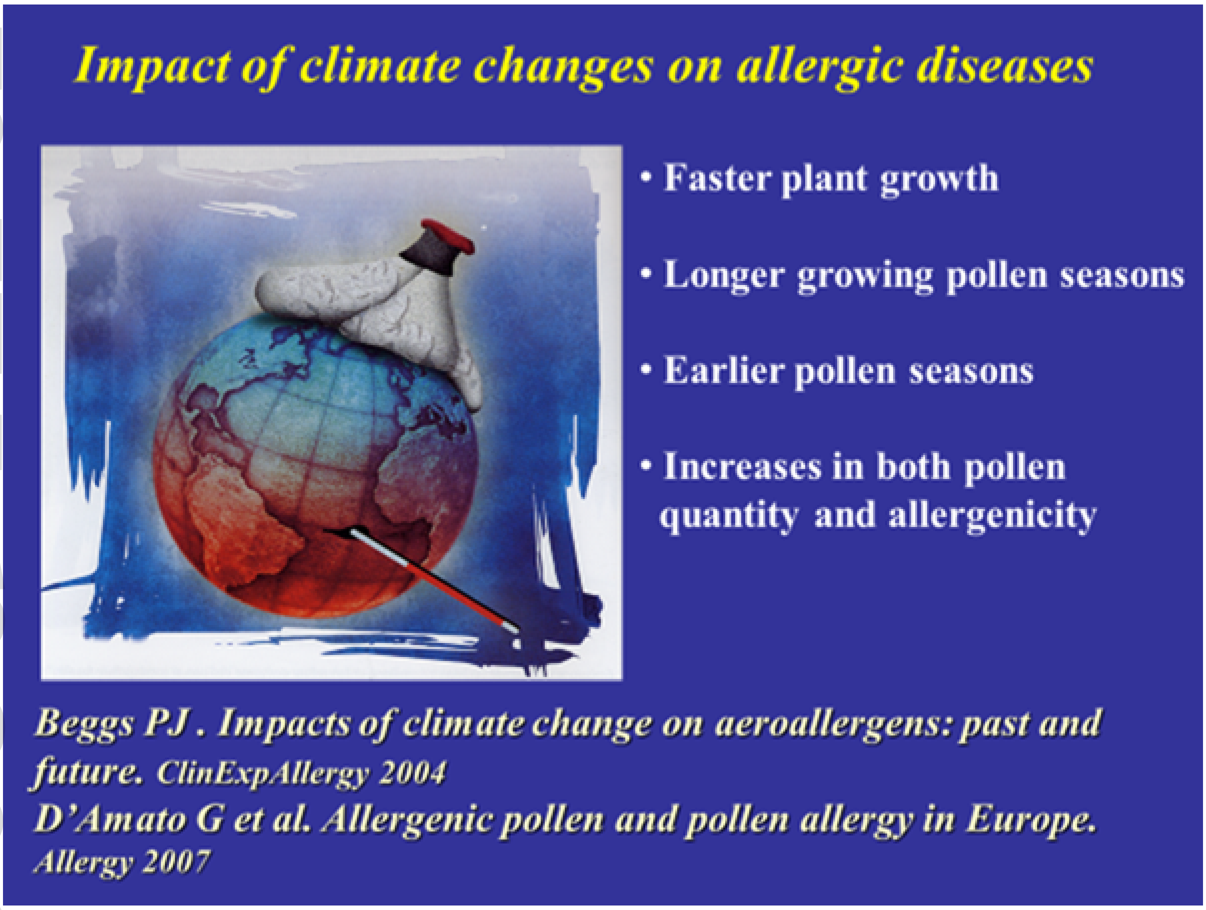
Effect of climate change on pollen allergens and allergy trigger

Changes in pollen allergens is correlated to climate change, due to an increasing concentration of CO2 in the atmosphere that is capable of inducing a faster and larger growth of plants,a rise in the potency of the pollen allergen and an increase in the intensity and time of flowering (1,5).

In addition, climate change produces greater exposure and sensitivity to subtropical grasses. An advance in the initiation of the pollen season and its peak are most pronounced in the species that bloom in early spring, and species that respond more to a warmer temperature. Likewise, species in urban areas flourish earlier than in rural areas, with an earlier pollination by approximately 2-4 days (6,13,14). Ziska et al,(20) showed that along the gradient, average daytime CO_2 concentration went up by 21% and maximum (daytime) and minimum (nighttime) daily temperatures went up by 1.6 and 3.3°C, respectively in an urban relative to a rural location. The urban-induced environmental changes that were seen were consistent with the majority of short-term (~50 year) global change scenarios regarding CO_2 concentration and air temperature. Productivity, defined as final above-ground biomass, and maximum plant height were positively affected by daytime and soil temperatures as well as enhancedCO_2 **,** increasing 60 and 115% for the suburban and urban sites, respectively, relative to the rural site (20). Singer et al.(10) demonstrated

that recent and projected increases in CO_2 could directly increase the allergenicity of ragweed pollen and consequently the prevalence and/or severity of seasonal allergic disease . Wayne et al. (14) observed that the doubling of the atmospheric concentration of CO_2 potentiated the production of pollen from ragweed by 61% more per plant. In addition, the ambrosia pollen collected along high traffic roads showed greater allergenicity than pollen in vegetative areas (14).

Image:4: Impact of climate changes on allergic diseases through the plants



As a result of climate change, the habitat patterns of the plants and the distribution of their species are likely to change (Image 4), with a gradual migration northwards in the northern hemisphere and further south in the southern hemisphere. Changes in land use also play an important role for some disseminated allergenic species, such as grasses (16,17).

Plants can be classified into two groups, these are C3 and C4 according to the metabolic differences related to carbon fixation. The members of the subfamily Pooideae are C3 grasses (temperate), while the subfamilies Chloridoideae and Panicoideae are C4 (subtropical) grasses (18). In seasonal climates when both grass types are present, C3 grasses increase in winter and bloom in spring, while C4 grasses grow and bloom in summer and early fall (19,20). Peaks for pollen of grasses in the air at the end of summer were observed at the same time as the flowering of subtropical grasses (21,22).The three subfamilies are well represented in the southern hemisphere in countries such as Brazil, Argentina, Australia and Uruguay, however, Pooideae are the most present (23,24). Research has shown an allergic sensitivity to subtropical pollen with climatic and geographic differences, especially in the southern hemisphere (25-29).

Studies on the response of plants to high levels of CO_2 in the atmosphere show that plants exhibit improved photosynthesis and reproductive effects and produce more pollen (29,30).

Currently, not only climate change is favoring the size of the population of subtropical grass and its expansion to areas where previously infrequent, but agriculture is also exerting a positive pressure (31-33). Australia and Argentina were the main countries in emerging organic agricultural lands (34).

A greater presentation of respiratory allergy caused by pollen in patients living in urban areas compared to those living in rural areas is linked to high levels of vehicle emissions, urbanization, and having a western lifestyle (35,36).

Anenberg et al, suggest that aeroallergens pose a substantial U.S. public health burden, that climate change could increase U.S. allergic disease incidence, and that mitigating climate change may have benefits from avoided pollen-related health impacts (37,38).

Effect of climate change on indoor and ambient molds exposures

The importance of climate change on indoor and outdoor mold has received little attention in comparison to other aeroallergens such as pollens (1,39-44). However, there is some evidence that climate change may increase the severity of indoor and atmospheric mold exposures. The climate change and its effects on the weather (frequent storms and heavy rainfall) and the rise in sea levels and the subsequent increased duration and frequency of floods will likely affect the number of buildings with damp and mold problems and exacerbate the defects in buildings that are already leaking. In addition to potential effects on outdoor mold growth and allergen release related to changing climate variables, there is also concern about indoor mold growth in association with rising air moisture after extreme storms, which can cause widespread indoor moisture problems from flooding and leaks in the building envelope (38-41). Nevertheless, the magnitude of the increase of houses affected by mold and their effects on respiratory health is unclear, in part because studies investigating the effect on indoor mold concentrations and respiratory symptoms due to flooding or water damage following severe storms are not common (39,40). The more important information available are from studies investigating mold exposure and health effects following hurricanes Katrina and Rita in the United States of America (39). These studies showed increased fungal growth in houses that were moderately to severely affected, and there was some suggestion that the composition of the microflora also changed after the hurricanes (39). Workers involved in renovation work immediately after the hurricanes were exposed to increased levels of fungal agents, but levels markedly decreased within the first year after the hurricanes (39,40). These studies show that increased exposure to mold following a flooding is likely, but exposure levels may return back to normal over time.

The effects on asthma are not clear with some reports suggesting an increased risk of respiratory symptoms in home occupants and renovation workers, and others showing no association (38,39).

Asthma and atmospheric mold exposures

Important studies have shown that increases in atmospheric fungal spore counts were associated with significantly more asthma admissions and emergency visits, and a positive associations have been observed for asthma medication, asthma symptoms, and peak flow variability (39,40,42,43). Most fungi are well adapted for wind spore dispersal. Species such as *Alternaria, Cladosporium and Aspergillus* have been associated in some but not all studies with a higher prevalence of asthma hospital admissions. Increased humidity along with higher winds speed can trigger spore production and dissemination (1,39-46). There is also evidence that increased atmospheric mold spore concentrations may play a role in thunderstorm asthma whit increase in asthma hospital emergency visits following this natural phenomenon (42). A Canadian study concludes that fungal spore counts doubled and pediatric asthma emergency admissions increased by more than 15 % on days with thunderstorms while no increases were found in the concentration of pollens (42). In addition to indoor sources of mold, atmospheric mold may also be a risk factor for asthma (exacerbations). *Alternaria alternata* sensitivity is a predictor of epidemic asthma in patients with seasonal asthma and is likely to be the important factor in thunderstorm-related asthma (43). Spores of Basidiospores and Ascospores molds as well as total pollen counts were associated with early wheeze among children under 24 months in a cohort study in California that involved children in an agricultural communities (44,45). We conclude that, with exposure of sufficient intensity and duration, the molds can produce asthma and exacerbate preexisting asthma (46).

Adaptation measures to reduce the impact of climate change on indoor molds

The adaptation measures are very important to minimize the effects of climate change on indoor mold and indoor dampness, and its associated respiratory health burden. These may involve a range of legislative and specific building design and construction measures to minimize the risks of leaks and surface flooding including (1,38,47-57):

1. Modification of regulations and building codes to better protect commercial and residential buildings from severe weather events and more stringent enforcement of existing and new regulations and building codes.
2. Restriction of building construction in flood-prone areas such as low-lying coastal and river areas.
3. Restriction of the use of flat roofs and installation of eaves to protect walls from getting wet from rain water.
4. The utilization of appropriate methods to ensure that buildings are watertight.
5. Installation of appropriate ventilation including in attic and crawl spaces to reduce the effects of indoor dampness.
6. Installation of vapor barriers in walls.
7. Improvement of control of rain and surface water through appropriate drainage including drainage of the building foundations.

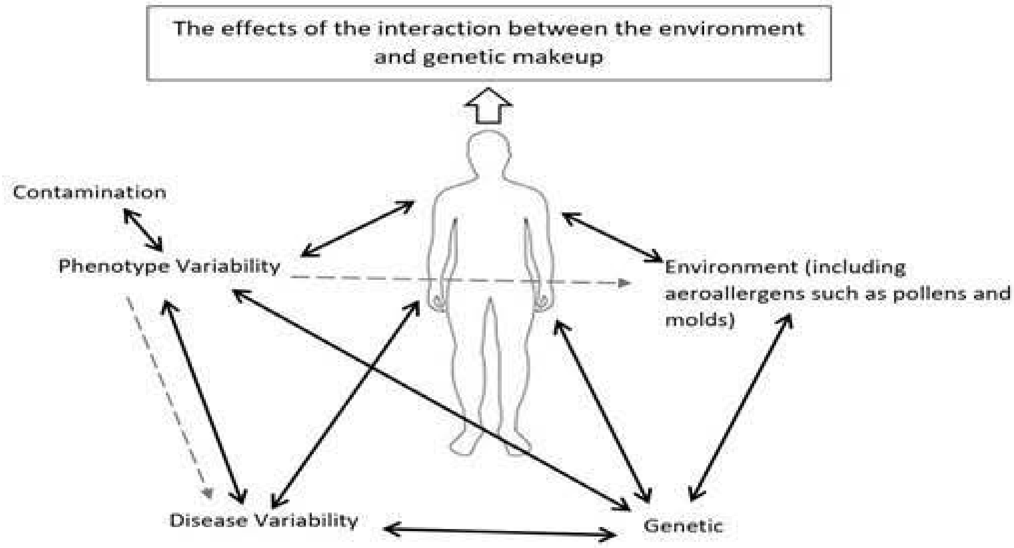
The consequences of climate change in winter due to fuel poverty (leading to increased risk of condensation and indoor dampness and respiratory symptoms) may be counteracted by the creation of incentives to introduce more fuel efficient heating sources (which in turn would contribute to lower green-house gas emissions).

Association between respiratory allergies, urban environmental pollution and climate change

Climate change together with exposure to environmental pollutants has been shown to have alarming consequences for human health and be responsible for some episodes of asthma exacerbations (47,48), and contribute to the onset and aggravation of allergic rhinitis and asthma (49).

The image 5 shows the interaction between genetic makeup and the environment, which gives rise to the different phenotypes of allergic respiratory disease.

Image 5. Interaction between genetic and the environment in the respiratory disease



Source: Original elaboration making reference to: De Marco R[1], Accordini S, Antonicelli L et al. The Gene-Environment Interactions in Respiratory Diseases (GEIRD) Project. 2010 (50).

Today, millions of tons of CO_2 are produced by burning thousands of hectares of forests around the world each year, which is an important factor in the greenhouse effect (51-53). The effects of ozone on the respiratory system are well known. Ozone inhalation has been associated with an acute decrease in lung function, an increase in airway responsiveness mediated by airway injury, inflammation, and systemic oxidative stress (54-57).

Gent et al (53) , analyzed the concomitant effects of fine particulate matter (PM 2.5) and ozone at levels below the standards of the EPA (United States Environmental Protection Agency) on the respiratory symptoms presented daily and the use of oral rescue or crisis medications in asthmatic children. In particular, the ozone was significantly associated with the presentation of respiratory symptoms and the need to use rescue medications in asthmatic children who use maintenance medications. A 1-hour increase of 50 parts per billion (ppb) of ozone was associated with the presence of wheezing (35%) and chest tightness (47%). Higher ozone levels (averages of 1-8 hours) were associated with increased dyspnea and the need for rescue or emergency medication (54).

Allergens derived from pollen or other parts of plants that reach the peripheral airways through inhaled air can induce asthma in patients withIgE-mediated hypersensitivity. Air pollution by ozone, particulate matter (PM) and diesel exhaust particles (DEP), nitrogen dioxide and sulfur dioxide increase the permeability of the respiratory tract, facilitate the penetration of allergens into mucous membranes and cause interaction with the cells of the immune system. As a result, air pollution plays an inflammatory role in the airways of predisposed patients (1,45).

Air pollutants adhere to the surface of pollen grains and paucimicronic-sized plant particles and change not only the morphology of these antigen-bearing agents, but also their allergenic potential (60). In addition, by producing airway inflammation increases the permeability of this pathway and pollutants overcome the mucosal barrier and could be responsible for enhancing the responses of pollinosis induced by allergens in atopic patients (58-60).

Published data suggest an increasing effect of aeroallergens in allergic patients, which generates a higher probability of developing an allergic respiratory disease in sensitized patients and an exacerbation in patients who are already symptomatic (60-67).

The effects of climate change on air pollution and allergenic pollen

The effect of climate change on changes in wind patterns, time and intensity of rainfall and temperature increase can affect the frequency and severity of air pollution episodes and also anthropogenic emissions such as increase in energy demand for space cooling or heating (1,47).

The urban heat island effect can increase some pollutants such as ozone and indirectly natural sources of air pollutant emissions (forest fires, vegetation breakdown, vehicle emission and soil erosion). The tropospheric ozone (O3) originates in the presence of bright sunlight due to the reaction between volatile organic compounds (VOC) and nitrogen oxides (NOx), emitted from natural and anthropogenic sources. Birch pollen exposed to higher levels of ozone induces larger wheals and erythema in the skin prick tests compared to pollen exposed to lower amounts of ozone, suggesting an allergenic effect of ozone (14,17).

Changes in precipitation and temperature can also increase the severity of forest fires which can lead to respiratory diseases. Higher temperatures can not only prolong the periods of time when ozone levels rise, but can also further aggravate maximum ozone concentrations and thus affect respiratory health.

Modifications in wind patterns can increase long-distance transport of pollutants and pollen grains, making this transport mechanism as important as the local one (16, 69).

The peculiarity of allergenic pollen and pollen allergy

The increasing prevalence of allergic respiratory symptoms due to the inhalation of pollen grains, and the associated increasing costs make pollen allergy a public health problem. From 10 to 35% of European young adults show serum IgE antibodies to grass pollen allergens (18). Changes in pollen patterns can result in an allergy that causes difficulty working, disabilities, medical consultations and medication requirements with a significant impact on the cost of health care (1,28-34).

In natural pollination, mature pollen grains dehydrate when they are released by the anthers at the time of dispersion and after coming into contact with a wet surface, the pollen grains absorb water and undergo a rapid metabolic change. Subsequently, when pollen grains penetrate the conjunctival, nasal or oral mucosa, the pollen allergens are released quickly, which induces symptoms of pollinosis in the ocular and respiratory mucous membranes of sensitized patients (2,14).

Under an osmotic shock pollen grains can explode, releasing cytoplasmic allergens into the atmosphere. In particular, fresh birch pollen can break under high humidity conditions and release an aerosol characterized by fragments of pollen cytoplasm in microdroplets (58). In this sense, Taylor et al (58,59) describe that approximately 65% of pollen grains grew in a pollen tube up to 300 µm long before rupture and that the release of their cytoplasmic content was under intense humidity.

The released particles, such as the cytoplasm of the fragmented pollen, form an ultrafine aerosol. Grass anthers are a pollen-breaking site and a source of fine particle aerosols containing pollen allergens (29,31-34). There are multiple associations between allergen exposure, inflammation of the upper and lower respiratory tract and clinical symptoms. In allergic patients, the severity of symptoms depends on the amount of allergenic pollen, however, other factors besides allergens seem to be involved. Although pollen grains penetrate the upper respiratory tract, they rarely reach the bronchi, since their size is always greater than 10 µm in diameter (1). Nevertheless, bronchial asthma and its equivalents, such as irritative cough, are not uncommon in patients who are allergic to pollen.

Although it is believed that rain removes pollen from the air, some studies have shown that allergens can be released from the pollen's surface in only a few seconds, when they come in contact with water. The hypothesis is that during thunderstorms and precipitation, pollen releases allergens that carry particles much smaller than pollen grains (paucimicronic particles). The paucimicronicparticles are small granules of 1-5 µm developed from anther tissues, loaded with allergens that may play a role in allergic asthma (1,60).

Severe asthma induced by extreme weather phenomenon of lightning thunderstorms during pollen seasons: a peculiar pollen allergy

Asthma related to thunderstorms is one of the phenomena that represents a threat to human health. Thunderstorms that occur during the pollen season have been observed to induce severe asthma attacks and also deaths in pollen allergic patients (61-74). Asthma by thunderstorm is a term used to describe an increase in cases of acute bronchospasm after the appearance of thunderstorms in an area. Exacerbations of asthma due to a thunderstorm are characterized, at the beginning of the storms, by a rapid increase in visits to the general practitioner or in the emergency services of hospitals due to asthma (70-74). Patients without asthma symptoms, but who suffer from seasonal rhinitis may have an asthma attack (70-74).

A possible explanation for asthma related to thunderstorms involves the role of rainwater promoting the release of inhalable particles. Thunderstorms occur at the end of spring and in the summer when there are high levels of pollen grains in the air.There is a strong association with the elevation of atmospheric concentrations of pollen grains, such as grasses or other species of allergenic plants. In the first 20 to 30 minutes of an thunderstorm, patients with pollen allergy can inhale a high concentration of allergens that disperse in the atmosphere (60-70). Exacerbations and asthma epidemics related to thunderstorms have been described in several cities, mainly in Europe (Birmingham and London in the United Kingdom and Naples in Italy) and Australia (Melbourne and Wagga Wagga) (61-74) **(Tables 1 and 2)** (74). Of note a similar phenomenon has been observed with molds (43,73,74).

CONCLUSION

Climate change has important effects related to environmental pollution and the origin of hypersensitivity and pollen allergy (1-5). This causes an increase in the production of pollens and a change in the characteristics that increase their allergenic properties. Through the effects of climate change in the future, plant growth can be altered so that the new pollens produced are modified and affect human health. As a consequence, the increase in the incidence of allergic diseases secondary to pollens is expected in the medium and long term.The education of the population and the emergence of governamentaldecisions to prevent environmental pollution and climate change are urgent measures to be dealt with throughout the world (1-5). Adaptation and mitigation measures can be undertaken to limit climate change impacts on air pollutioninduced by chemical agents, pollens and molds. Mitigation addresses the causes of climate change (accumulation of greenhouse gases in the atmosphere),whereas adaptation addresses the impacts of climate change. On the otherhand, adaptation will not be able to eliminate all negative impacts and mitigation is crucial to limit changes in the climate system. Extreme weather phenomena such as thunderstorms trigger exacerbations of asthma and severe asthma, with an important socio-economic impact (63,69,70). Patients with pollen allergy should be educated about the risk of asthma exacerbation and, especially, should be warned of the danger of staying outdoors without the proper treatment of their chronic rhinitis and asthma during a thunderstorm or pollen season (73,74).

Table 1. Storms associated with asthma exacerbations around the world (61-74)

Storms associated with asthma exacerbations around the world		
Year	**Country**	**Observations**
1983	United Kingdom (Birmingham)	26 unexpected cases of asthma crisis related to electrical storms.
1992	Australia (Melbourne)	Storms in late spring in Melbourne can trigger epidemics of asthma attacks (5 to 10 time-increase).
1994	United Kingdom (London)	Visits to the hospital for asthma or other diseases of the respiratory tract. 640 cases attended during a 30-hour period in June 1994, almost 10 times the expected number.
1992–2000	Canada	18970 hospital visits for asthma in children and young people between 2 and 15 years of age.
1993–2004	USA	215 832 consultations for asthma in the Emergency Department (ED); 24350 of these visits occurred on days following thunderstorms. Significant association between daily counts of asthma ED visits and thunderstorm occurrence. Asthma visits were 3% higher on days following thunderstorms.
2000	Australia	Asthma consultations in Australia during thunderstorms. The history of hay fever and rye allergy are strong predictors of asthma exacerbation during spring storms.
2001	Australia	The increase in hospital attendance due to asthma in late spring and summer was strongly

		related to the occurrence of storms.
2002	United Kingdom	A case-control study of 26 patients who arrived at the University Hospital of Cambridge with asthma after the storm. The sensitivity of Alternaria alternata is a convincing predictive factor of epidemic asthma in patients with seasonal asthma and allergy to grass pollen and is likely to be the important factor in asthma related to electrical storms.
2004	Italy (Naples)	7 cases of asthma related to electrical storms due to pollen (*Parietaria)*
2010	Italy (Barletta-Puglia)	20 cases of asthma related to electrical storms which were due to pollen (olive).
2010	Australia	"Storm asthma" epidemics that occurred in Melbourne during the spring of 2010. The approach of spring, along with the high rainfall in the winter in Melbourne and its surroundings announcing an intense pollen season, increases the risk of rhinitis allergic and asthma in people sensitive to pollen.
2016	Australia (Melbourne)	On Monday, November 21, 2016, associated with severe storms, hospitals were filled with patients with severe asthma attacks. There were more than 9000 patients with 10 patients who presented severe crises. There were thousands of calls to firefighters and police, as well as doctors and mid-level providers contacted by patients. As in previous epidemics, including the Naples event, many people had no history of asthma, only hay fever.

Sources: 61-74

Table 2. Characteristics of the described epidemics of asthma associated with thunderstormsSources 61-74

Characteristics of the described epidemics of asthma associated with thunderstorms
1. The occurrence of epidemics is closely linked to thunderstorms.
2. Epidemics related to thunderstorms are limited in late spring and summer when there are high levels of pollen grains in the air.
3. There is a close seasonal association between the arrival of the storm, a significant increase in the concentration of pollen grains and the onset of epidemics.
4. Patients with pollen allergy, who remain intramural with closed windows during thunderstorms, are not involved.
5. There is a great risk for patients who do not have a treatment for optimal asthma. Patients with allergic rhinitis induced by pollen and without a history of asthma may experience bronchoconstriction, which is also sometimes severe.

References

1. D'Amato G, Holgate ST, Pawankar R, et al. Meteorological conditions, climate change, new emerging factors, and asthma and related allergic disorders. A statement of the World Allergy Organization. World Allergy Organ J. 2015;8(1):25. Published 2015 Jul 14. doi:10.1186/s40413-015-0073-0.
2. Beggs PJ. Impacts of climate change on aeroallergens: past and future. Clin Exp Allergy. 2004;34:1507–13.
3. Haines A, Ebi K. The Imperative for Climate Action to Protect Health. N Engl J Med. 2019;380((3)):263–73. doi: 10.1056/NEJMra1807873.
4. Solomon CG, LaRocque RC. Climate Change — A Health Emergency. N Engl J Med. 2019;380((3)):209–11. doi: 10.1056/NEJMp1817067.
5. D'Amato G, Vitale C, Lanza M, Molino A, D'Amato M. Climate change, air pollution, and allergic respiratory diseases: an update. CurrOpin Allergy Clin Immunol. 2016 Oct;16(5):434-40. doi: 10.1097/ACI.0000000000000301.
6. Hegerl GC, Zwiers FW, Braconnot P, Gillett NP, Luo Y, Marengo JA, et al. Understanding and attributing climate change. In: Solomon S, Qin D, Manning M, Chen Z, Marquis M, Averyt KB, et al, editors. Climate change 2007: the physical science basis. Contribution of the Working Group I to the Fourth Assessment Report of the Intergovernamental Panel on Climate Change. Cambridge, UK and New York: Cambridge University Press.2007;p.663-746.
7. Bielory L, Lyons K,Goldberg R. Climate change and allergic disease Curr Allergy Asthma Rep 12:485-494. 2012.
8. Watts N, Amann M, Arnell N, Ayeb-Karlsson S, Belesova K, Berry H, et al. The 2018 report of the Lancet Countdown on health and climate change: shaping the health of nations for centuries to come. Lancet. 2018;392((10163)):2479–514. doi: 10.1016/S0140-6736(18)32594-7. .
9. Cecchi L, D’Amato G, Annesi-Maesano I. External exposome and allergic respiratory and skin diseases. J Allergy Clin Immunol. 2018;141((3)):846–57. doi: 10.1016/j.jaci.2018.01.016.
10. Singer BD, Ziska LH, Frenz DA, et al. Increasing Amb a 1 content in common ragweed (Ambrosia artemisiifolia) pollen as a function of rising atmospheric CO2 concentration. Func Plant Biol 2005; 32: 667–70.
11. Penard-Morand, Annesi-Maesano I. Air pollution: from sources of emissions to health

effects. Breathe. 2005. Volumen I, número 2. pp. 109-119.

12. De Marco R, Accordini S, Antonicelli L et al. The Gene-Environment Interactions in Respiratory Diseases (GEIRD) Project. 2010 (50).
13. United States Environmental Protection Agency (EPA). Overview of Greenhouse Gases. Accessed August 17, 2019.
14. Wayne P,FosterS,Connolly J, Bazzez F, Epstein P. Production of allergenic pollen by ragweed (Ambrosia artemisiifolia L) in increased CO2 enriched atmosphere. Ann Allergy Asthma Immunol 2002;88 (3) 279-82
15. National Oceanic and Atmospheric Administration. Global carbon dioxide growth in 2018 reached 4th highest in record. Accessed August 17, 2019.
16. The Eart Observatory from EOS Project Science Office at NASA Goddard Space Flight Center. https://earthobservatory.nasa.gov/. Accessed Jan 19, 2020.
17. Pan Y, Birdsey R, Fang Jingyun et al. A Large and Persistent Carbon Sink in the World's Forests.Science. 2011: Vol. 333, Issue 6045, pp. 988-993. DOI: 10.1126/science.1201609
18. D'Amato G, Cecchi L, Bonini S, et al. Allergenic pollen and pollen allergy in Europe. Allergy 2007; 62: 976–90.
19. Watts N, Amann M, Arnell N, Ayeb-Karlsson S, Belesova K, Berry H, et al. The 2018 report of the Lancet Countdown on health and climate change: shaping the health of nations for centuries to come. Lancet. 2018;392((10163)):2479–514. doi: 10.1016/S0140-6736(18)32594-7. .
20. Ziska LH, Bunce JA, Goins EW. Characterization of an urban-rural CO2/temperature gradient and associated changes in initial plant productivity during secondary succession. Oecologia.2004;139(3):454-8.
21. Bouchenak-Khelladi Y, Muasya AM, Linder HP. A revised evolutionary history of Poales: origins and diversification. Botanical Journal of the Linnean Society 2014; 175(1): 4-16.
22. Kellogg EA, Camara PE, Rudall PJ, Ladd P, Malcomber ST, Whipple C, et al. Early inflorescence development in the grasses (Poaceae). Frontiers in plant science 2013; 4: 250.
23. Kellogg EA. Flowering Plants. Monocots. Springer International Publishing, Switzerland, 2015.
24. Davies JM. Grass pollen allergens globally: the contribution of subtropical grasses to burden of allergic respiratory diseases. Clinical & Experimental Allergy 2014; 44(6): 790-801.
25. Osborne NJ, Alcock I, Wheeler BW, Hajat S, Sarran C, Clewlow Y, et al. Pollen exposure and hospitalization due to asthma exacerbations: daily time series in a European city. International journal of biometeorology 2017; 61(10): 1837-48

26. Biganzoli F and Zuloaga F. Analysis of Poaceae biodiversity in austral South America. Rodriguésia 2015:66(2): 337-51.
27. Soreng RJ, Peterson PM, Romaschenko K, Davidse G, Teisher JK, Clark LG, et al. A worldwide phylogenetic classification of the Poaceae (Gramineae) II: An update and a comparison of two 2015 classifications. Journal of Systematics and Evolution 2017; 55(4): 259-90.
28. Davies JM, Timbrell V, Reibelt L, Simmonds C, Solley G, Smith W, et al. Regional variation in allergic sensitivity to subtropical and temperate grass pollen allergens; outcomes of the multicenter cross-sectional Grass Pollen Allergy Survey (GPAS). European Journal of Immunology 2016; 46: 841.
29. Cherrez-Ojeda, I., Ramon, G. D., Barrionuevo, L. B., Arango, N., Long, M. A., &Viego, V. Prevalence of skin sensitivity to temperate and subtropical grasses in patients with seasonal allergic rhinitis in Bahía Blanca, Argentina. Journal of Allergy and Clinical Immunology, 2018. 141(2), AB128.
30. Rogers CA, Wayne PM, Macklin EA, Muilenberg ML, Wagner CJ, Epstein PR, Bazzaz FA.. Interaction of the Onset of Spring and Elevated Atmospheric Carbon Dioxide on Ragweed (Ambrosia artemisiifolia L.) Pollen Production. Environ. Health Perspect. 2006 114:865–869.
31. Albertine JM, Manning WJ, DaCosta M, Stinson KA, Muilenberg ML, Rogers CA. 2014. Projected Carbon Dioxide to Increase Grass Pollen and Allergen Exposure Despite Higher Ozone Levels. PLoS One 9.
32. Blumenthal DM, Kray JA, Ziska L, and Dukes J. Climate change, plant traits and invasion in natural and agricultural ecosystems. Invasive Species and Global Climate Change 2014; 4: 62.
33. Sorokin Y, Zelikova TJ, Blumenthal D, Williams DG, and Pendall E. Seasonally contrasting responses of evapotranspiration to warming and elevated CO2 in a semiarid grassland. Ecohydrology 2017; 10(7): e1880.
34. Augustine DJ, Derner JD, Milchunas D, Blumenthal D, and Porensky LM. Grazing moderates increases in C3 grass abundance over seven decades across a soil texture gradient in shortgrass steppe. Journal of Vegetation Science 2017; 28(3): 562-72.
35. Willer H and Lernoud Julia (Eds.) The World of Organic Agriculture. Statistics and Emerging Trends. 17 edition. Research Institute of Organic Agriculture FiBL and IFOAM Organics International, Frick and Bonn 2017.
36. D'Amato G, Cecchi L. Effects of climate change on environmental factors in respiratory

allergic diseases. Clin Exp Allergy. 2008;38:1264–74.
37. Anenberg S, Weinberger, Roman H et al. Impacts of oak pollen on allergic asthma in the United States and potential influence of future climate change. GeoHealth. 2017. Volume 1, Issue 3. Doi:10.1002/2017GH000055.
38. Kinney P.L. Climate Change, Air Quality, and Human Health. American Journal of Preventive Medicine. 2008, 35 (5) , pp. 459-467.
39. Rao CY, Riggs MA, Chew GL, Muilenberg ML, Thorne PS, Van Sickle D, et al. Characterization of airborne molds, endotoxins, and glucans in homes in New Orleans after Hurricanes Katrina and Rita. Appl Environ Microbiol. 2007;73:1630–4. doi: 10.1128/AEM.01973-06.
40. Rando RJ, Kwon CW, Lefante JJ. Exposures to thoracic particulate matter, endotoxin, and glucan during post-hurricane Katrina restoration work, New Orleans 2005–2012. J Occup Environ Hyg. 2014;11:9–18. doi: 10.1080/15459624.2013.839879.
41. Cecchi L, D'Amato, Avres J et al. Projections of the effects of climate change on allergic asthma: the contribution of aerobiology. Allergy. 2010. Sep;65(9):1073-81. doi.org/10.1111/j.1398-9995.2010.02423.x.
42. Dales RE, Cakmak S, Judek S, Dann T, Coates F, Brook JR, et al. The role of fungal spores in thunderstorm asthma. Chest. 2003;123:745–50. doi: 10.1378/chest.123.3.745.
43. Pulimood TB, Corden JM, Bryden C, Sharples L, Nasser SM. Epidemic asthma and the role of the fungal mold Alternaria alternata. J Allergy Clin Immunol. 2007 Sep;120(3):610-7. Epub 2007 Jul 10.
44. Harley KG, Macher JM, Lipsett M, et al. Fungi and pollen exposure in the first months of life and risk of early childhood wheezing. Thorax. 2009;64:353–358.
45. Sheffield PE, Weinberger KR, Kinney PL. Climate change, aeroallergens, and pediatric allergic disease. Mt Sinai J Med. 2011;78(1):78–84. doi:10.1002/msj.20232.
46. Michaels, Robert. Environmental Moisture, Molds, and Asthma—Emerging Fungal Risks in the Context of Climate Change. Environmental Claims Journal. 2017, 29. 171-93.
47. Shea KM, Truckner RT, Weber RW, Peden DB Climate change and allergic disease. J Allergy Clin Immunol. 2008 Sep;122(3):443-53; quiz 454-5. doi: 10.1016/j.jaci.2008.06.032.
48. Smith KR. National burden of disease in India from indoor air pollution. Proc Natl Acad Sci USA 2000; 97: 13286–13293.
49. Eguiluz-Gracia I., Mathioudakis AG., BartelS et al. The need for clean air: the way air pollution and climate change affect allergic rhinitis and asthma. Allergy. 2020 Jan 9. doi: 10.1111/all.14177.

50. De Marco R, Accordini S, Antonicelli L et al. The Gene-Environment Interactions in Respiratory Diseases (GEIRD) Project. Int Arch Allergy Immunol. 2010;152(3):255-63. doi: 10.1159/000283034. Epub 2010 Feb 11.
51. BBC News–In Pictures. Chile battles wildfires. Available at: www.bbc.co.uk/news/world-latin-america-16406681 [cited 2012 Jan 25]. 2012,
52. News BBC. Australia fires leave trail of devastation near Perth.. Available at: http://www.bbc.com/news/world-asia-pacific-12378717.2011
53. Gent JF, Triche EW, Holford TR, Belanger K, Bracken MB, Beckett WS. Leaderer BP. Association of low-level ozone and fine particles with respiratory symptoms in children with asthma. JAMA. 2003 ;290(14):1859-1867.
54. McConnell R, Berhane K, Gilliland F, et al. Asthma in exercising children exposed to ozone: a cohort study. Lancet. 2002;359:386-391.
55. Islam T, Gauderman WJ, Berhane K, et al. Relationship between air pollution, lung function and asthma in adolescents. Thorax. 2007;62:957-963.
56. Mayaux, P., Holmgren, P., Achard, F., Eva, H., Stibig, H. &Branthomme, A. Tropical forest cover change in the 1990s and options for future monitoring. Phil. Trans. R. Soc. B 360, 373–384. (doi:10.1098/rstb.2004.1590).2005
57. D'Amato G, Ortega OPM, Annesi-Maesano I,D'Amato M. Prevention of allergic asthma with allergen avoidance measures and the role of exposome. Curr Allergy Asthma Rep. 2020 Feb26;20(3):8. doi: 10.1007/s11882-020-0901-3.
58. Taylor PE, Flagan RC, Miguel AG, Valenta R., Glovsky MM. Birch pollen rupture and the release of aerosols of respirable allergens. Clin Exp Allergy 2004;34:1591-1596.
59. Taylor PE, Hagan R, Valenta R, Glovsky MM Release of allergens in respirable aerosols: a link between grass pollen and asthma. J Allergy Clin Immunol 2002;109:51-56.
60. Traidl-Hoffmann C, KascheA,MenzelA,Jakob T, Thiel M, Ring J, Behrendt H. Impact of pollen on human health: more than allergen carriers? Int Arch Allergy Immunol 2003;131:1-13.
61. Cecchi L, D 'Amato, Avres J et al. Projections of the effects of climate change on allergic asthma: the contribution of aerobiology. Allergy. 2010. Sep;65(9):1073-81. doi.org/10.1111/j.1398-9995.2010.02423.x.
62. Packe GE, Ayres JG. Asthma outbreak during a thunderstorm. Lancet. 1985;2:199-204
63. D'Amato G, Vitale C, D'Amato M, Cecchi L, Liccardi G, Molino A, Vatrella A, Sanduzzi A, Maesano C, Annesi-Maesano I. Thunderstorm-relatedasthma:whathappens and why. Clin Exp Allergy. 2016 Mar;46(3):390-6. doi: 10.1111/cea.12709.

64. Marks GB, Colquhoun JR, Girgis ST, et al. Thunderstorm outflows preceding epidemics of asthma during spring and summer. Thorax. 2001;56:468-471. 9
65. Venables KM, Allitt U, Collier CG, et al. Thunderstorm-related asthma – epidemic of 24-25 June 1994. Clin Exp Allergy. 1997;27:725-736
66. Andrew E, Nehme Z, Bernard Abramson MJ, Smith K Stormy. Weather: A retrospective analysis of demand for emergency medical services during epidemic thunderstorm asthma. BMJ 2017;359: j5636.
67. Lindstrom SJ, Silver JD, Sutherland MF. Thunderstormasthmaoutbreak of November2016: a naturaldisasterrequiring planning. Med J Aust2017;207:235-7.
68. Final Report: Literature review on thunderstorm asthma and its implications for public health advice. Queensland University of Technology. Brisbane, Australia. Contractedby: Department of Health and Human Services, Victorian State Government. May 19, 2017.
69. Thien F, Beggs PJ, Csutoros D, et al. The Melbourne epidemic thunderstorm asthma event 2016: an investigation of environmental triggers, effects on health services, and patient risk factors. Lancet Planet Health. 2018;2:255-263.
70. Hew M, Lee J, Susanto NH, et al. The 2016 Melbourne thunderstorm asthma epidemic: 1 risk factors for severe attacks requiring hospital admission. Allergy. 2018; https://doi.org/10.1111/all.13609.
71. Davies JM, Thien F, Hew M. Thunderstorm asthma: controlling (deadly) grass pollen allergy. BMJ. 2018;360:k43
72. Harun NS, Lachapelle P, Douglas J Thunderstorm-troggeredasthma:what we know so far. J Asthma Allergy 2019 May https://doi.org/10.2147/JAA.S175155
73. D'Amato G, Annesi-Maesano I, Vaghi A, Cecchi L, D'Amato M. How Do Storms Affect Asthma?. Curr Allergy Asthma Rep. 2018;18(4):24. Published 2018 Mar 24. doi:10.1007/s11882-018-0775-9
74. D'Amato G, Annesi-Maesano I, Cecchi L, D'Amato M . Latest news on relationship between thunderstorms and respiratory allergy, severe asthma, and deaths for asthma. Allergy. 2019 Jan;74(1):9-11. doi: 10.1111/all.13616

Conflict of Interest statement:

Dr. Ansotegui reports personal fees from Mundipharma, personal fees from Roxall, personal fees from Sanofi, personal fees from MSD, personal fees from Faes Farma, personal fees from Hikma, personal fees from UCB, personal fees from Astra Zeneca, personal fees from Stallergenes, personal fees from Abbott, personal fees from Bial, outside the submitted work. Dr. Haahtela reports personal fees from GSK, personal fees from Mundipharma, personal fees from OrionPharma, outside the submitted work. All the authors have nothing to disclose.