Climate change, air pollution, and allergic respiratory diseases: an update

Gennaro D'Amato[a,b], *Carolina Vitale*[c], *Maurizia Lanza*[d], *Antonio Molino*[d], *and Maria D'Amato*[d]

Purpose of review
The rising trend in prevalence of allergic respiratory disease and bronchial asthma, observed over the last decades, can be explained by changes occurring in the environment, with increasing presence of biologic, such as allergens, and chemical atmospheric trigger factors able to stimulate the sensitization and symptoms of these diseases.

Recent findings
Many studies have shown changes in production, dispersion, and allergen content of pollen and spores because of climate change with an increasing effect of aeroallergens on allergic patients.

Summary
Over the last 50 years, global earth's temperature has markedly risen likely because of growing emission of anthropogenic greenhouse gas concentrations. Major changes involving the atmosphere and the climate, including global warming induced by human activity, have a major impact on the biosphere and human environment.
Urbanization and high levels of vehicle emissions are correlated to an increase in the frequency of pollen-induced respiratory allergy prevalent in people who live in urban areas compared with those who live in rural areas. Measures of mitigation need to be applied for reducing future impacts of climate change on our planet, but until global emissions continue to rise, adaptation to the impacts of future climate variability will also be required.

Keywords
air pollution and respiratory diseases, airways hyperreactivity, climate change and asthma, climate change and respiratory allergy, thunderstorm asthma

INTRODUCTION

Over the last decades, a substantial increase in the prevalence of allergic respiratory disease and bronchial asthma has been observed. This rising trend cannot be explained only by genetic factors that play an important role in the development of asthma and allergic diseases, but by changes occurring in the environment, with increasing presence of biologic, such as allergens, and chemical atmospheric trigger factors able to stimulate the sensitization and symptoms of these diseases. Over the last 50 years, global earth's temperature has markedly risen [1,2,3▪,4] and most of this increase is very likely due to growing emission of anthropogenic greenhouse gas concentrations, as stated in the Working Group I Report of the Intergovernmental Panel on Climate Change [1]. Changes are occurring in the amount, intensity, frequency, and type of precipitation as well as in the increase of extreme events like heat waves, droughts, floods, thunderstorms, and hurricanes and these are a real and daunting problem [1,2,3▪,4–6,7▪,8].

The most important anthropogenic greenhouse gas is carbon dioxide (CO_2), whose atmospheric concentration has increased dramatically over the last century, especially during the last two decades [1,2,3▪,4–6,7▪,8].

[a]Division of Respiratory and Allergic Diseases, Department of Respiratory Diseases, High Specialty Hospital 'A. Cardarelli', Napoli, [b]School of Specialization in Respiratory Diseases, University of Naples Federico II, Naples, [c]Department of Medicine and Surgery, University of Salerno, Salerno and [d]Respiratory Department, High Speciality Hospital 'V. Monaldi' and University 'Federico II', Napoli, Italy

Correspondence to Gennaro D'Amato, University Professor of Respiratory Medicine, Division of Respiratory and Allergic Diseases, High Specialty Hospital 'A. Cardarelli', Via Rione Sirignano, 10, 80121 Napoli, Italy. Tel: +39 3355915589; e-mail: Gdamatomail@gmail.com

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KEY POINTS

- In the last 50 years, 50% of pluvial forests on the planet have been destroyed, and each year 13 million hectares of forest are being destroyed or deteriorated.
- Climate change affects the social and environmental determinants of health – clean air, safe drinking water, sufficient food, and secure shelter. The direct damage costs to health by the WHO is estimated to be between US$ 2 and 4 billion per year by the year 2030.
- Currently, it is mainly the vehicular pollution that degrades the quality of air in the cities of industrialized countries, whereas industrial pollution still constitutes the largest source of air pollution in countries undergoing industrialization.
- Exposure to air pollution has been linked to many signs of allergic respiratory diseases and asthma exacerbation, for example, increased bronchial hyperresponsiveness, increased medication use, visits to EDs, and hospital admissions.
- Asthma is a heterogeneous disease that is strongly influenced by environmental factors. Many of these factors are influenced by meteorological events and climate change that vary in type and intensity across the world.

About 75% of the anthropogenic CO_2 emissions into the atmosphere during the past 20 years resulted from fossil fuel burning by urbanization; most of the remaining ones resulted from changes in land use, especially deforestation [1,2,3▪,4–6,7▪,8]. Major changes involving the atmosphere and the climate, including global warming induced by human activity, have a major impact on the biosphere and human environment [1,2,3▪,4–6,7▪,8].

Current knowledge clarifies that air pollution and aeroallergens are critical in evaluating the possible effects of climate change on allergic respiratory diseases.

Epidemiological and experimental studies [9–23,24▪▪,25–35,36▪,37–52] have shown a positive correlation between climate change, air pollution, and allergic respiratory diseases. Climate changes affect air pollutant levels in several ways: the influence on regional weather may have an effect on severity and frequency of air pollution episodes and also on anthropogenic emissions (e.g. increase of energy demand for space heating or cooling); the enhancement of the urban heat island effect may increase some secondary pollutants (i.e. ozone – O_3), and it can indirectly increase natural sources of air pollutant emissions (e.g. decomposition of vegetation, soil erosion, and wildfires) [1,2,3▪,4–6,7▪,8]. Climate change appears to induce an increased concentration of all health-related air pollutants [1,2,3▪,4–6,7▪,8]. Of particular concern are potential changes in tropospheric O_3 and particulate matter.

These changes in climate and in air quality have a measurable impact not only on the morbidity but also on the mortality of patients with asthma and other respiratory diseases [1,2,3▪,4,5].

However, the relationship between air pollution, pollen exposure, and respiratory allergy is based on an individual's response to air pollution, which depends on the source and components of the pollution as well as on climatic agents and genetic constitution.

EFFECT OF AIR POLLUTION ON ALLERGIC RESPIRATORY DISEASES

Several studies [9–23,24▪▪,25–27] confirmed the negative effect of urban air pollution on human health and on allergic respiratory diseases. Epidemiologic studies [9–23,24▪▪,25–27] have demonstrated that urbanization, high levels of vehicle emissions, and westernized lifestyle are correlated to an increase in the frequency of pollen-induced respiratory allergy prevalent in people who live in urban areas compared with those who live in rural areas.

The most abundant components of air pollution in urban areas are nitrogen dioxide (NO_2), O_3, and particulate matter.

(1) NO_2 is a precursor of photochemical smog found in urban and industrial regions and is most often generated by cars and trucks exhausts, together with power plants. In conjunction with sunlight and hydrocarbons, NO_2 results in the production of O_3. Like O_3, NO_2 is an oxidizing pollutant, but with a lower chemical reactivity than O_3. NO_2 exposure is associated with increased emergency room visits, wheezing, and medication use among children with asthma [9]. Controlled exposure studies [7▪,8–12] on asthmatic patients have shown that NO_2 can enhance the allergic response to inhaled allergens and NO_2 concentrations in ambient air are also reportedly associated with cough, wheezing, and shortness of breath in atopic patients.

(2) O_3 is generated at ground level by photochemical reactions involving NO_2, hydrocarbons, and ultraviolet (UV) radiation. O_3 inhalation induces epithelial damage and consequent inflammatory responses in the upper and lower airways as shown by increased levels of inflammatory cells and mediators in nasal and

bronchoalveolar lavage [9]. Exposure to increased atmospheric levels of O_3 induces reduction of lung function, increased airway hyperreactivity to bronchoconstrictor agents, and is related to an increased risk of asthma exacerbations in asthmatic patients [9–15]. Epidemiologic studies have provided evidence that high ambient concentrations of this air pollutant are associated with an increased rate of asthma exacerbations, increased hospital admissions, and/or emergency department (ED) visits for respiratory diseases, including asthma. Furthermore, several studies [7▪,8–15] suggest that O_3 increases asthma morbidity by enhancing airway inflammation and epithelial permeability. It has been speculated for a long time that O_3 and other pollutants may render allergic-atopic patients more susceptible to the antigen they are sensitized [9–12]. Beck *et al.* [16] observed that high environmental O_3 levels enhance allergenicity of birch pollen with clinical relevance for susceptible individuals. The acute health effects of exposure to ambient O_3 have been examined in many geographical regions. Potential adverse effects include decrease in lung function, airway inflammation, symptoms of asthma, increases in hospitalization due to respiratory diseases, and excess mortality. O_3 exposure has both a priming effect on allergen-induced responses and an intrinsic proinflammatory action in the airways of allergic-atopic asthmatic patients [8–15]. In the long term, continuous exposure to high O_3 levels impairs respiratory function and causes or exacerbates airway inflammation in healthy patients and in asthma patients. At the population level, long-term exposure to O_3 may reduce lung function in schoolchildren and adults and increase the prevalence of asthma and asthmatic symptoms [14,15]. In addition, studies [8–10] have shown that asthma can be exacerbated by O_3, as measured by increased visits to EDs on days with higher levels of O_3 and other pollutants. Recently Malig *et al.* [17] explored ozone's connection to asthma and total respiratory ED visits. A multisite time-stratified case-crossover study [17] of O_3 exposures for approximately 3.7 million respiratory ED visits from 2005 through 2008 was conducted among California residents living within 20 km of an O_3 monitor. The result was that short-term O_3 exposures among California residents living near an O_3 monitor were positively associated with ED visits for asthma, acute respiratory infections, pneumonia, chronic obstructive pulmonary disease, and upper respiratory tract inflammation from 2005 through 2008. Those associations were typically larger and more consistent during the warm season [17].

(3) Particulate matter is a mixture of organic and inorganic solid and liquid particles of different origins, size, and composition. Ultrafine particulate matter (UFPM), with diameters of 0.1 μm or less, is a major component of vehicles' emissions. These particles accumulate into larger fine particulate matter with a diameter of ≤2.5 mm ($PM_{2.5}$, particulate matter with a diameter of 2.5 mm or less), within short distances from the point of release. PM_{10} consists of $PM_{2.5}$ and larger particles of mainly crustal or biological origin including many aeroallergens. On the basis of epidemiological and laboratory studies [18–21], $PM_{2.5}$ appears to be a more potent agent for the development of respiratory and cardiovascular disease compared with PM_{10}. PM_{10} can penetrate the lower airways, and $PM_{2.5}$ is thought to constitute a notable health risk because it can be inhaled more deeply into the lungs at the alveoli level. Although human lung parenchyma retains $PM_{2.5}$, particles larger than 5 μm and smaller than 10 μm reach the proximal airways only, wherein they are eliminated by mucociliary clearance if the airway mucosa is intact [8–10]. A large portion of urban particulate matter originates from diesel engines, as diesel exhaust particles (DEPs), which include other components such as polycyclic aromatic hydrocarbons (PAHs). DEPs account for up to 90% of airborne particulate matter in the world's largest cities and are composed of fine (2.5–0.1 μm) and ultrafine (0.1 μm) particles, which can also coalesce to form aggregates of varying sizes [21]. PM_{10} levels have been associated with early respiratory exacerbations in children with persistent asthma and with higher prevalence rates even after having considered the dispersion of the particles. Although there is compelling evidence that ambient air pollution exacerbates existing asthma, the link with the development of asthma syndrome is still less well established, as few studies provide extensive exposure data. Researches have elucidated the mechanisms whereby fine particles induce adverse effects; they appear to affect the balance between antioxidant pathways and airway inflammation. Gene polymorphisms involved in antioxidant pathways can modify responses to air pollution exposure. Acute exposure to diesel exhaust causes specific effects like irritation of nose and eyes, headache, lung function abnormalities, respiratory changes, fatigue, and

nausea, whereas chronic exposure is associated with cough, sputum production, and diminished lung function [18–21]. Studies [21–23] have demonstrated inflammation in the airways of healthy individuals after exposure to diesel exhaust and DEPs, and elevated expression and concentrations of inflammatory mediators have similarly been observed in the respiratory tract after diesel exhaust and DEP exposure.

Recently, Carlsten *et al.* [24▪▪] observed that inhalation of diesel exhaust at environmentally relevant concentrations augments allergen-induced allergic inflammation in the lower airways of atopic individuals. Particularly, diesel exhaust not only augmented the allergen-induced increase in airway eosinophils, interleukin-5 (IL-5), and eosinophil cationic protein (ECP) but also augmented markers of nonallergic inflammation and monocyte chemotactic protein (MCP)-1 and suppressed activity of macrophages and myeloid dendritic cells [24▪▪]. A large study [25] conducted on 5443 Korean children aged 6–14 years from 33 elementary schools in 10 cities during 2005–2006 has suggested that exposure to traffic-related air pollution may be associated with increased risk of asthma, allergic rhinitis, and allergic sensitization, and with reduced lung function in schoolchildren.

EFFECT OF CLIMATE CHANGE ON ALLERGIC RESPIRATORY DISEASES

Global warming affects the onset, duration, and intensity of the pollen season as well as the allergenicity of the pollen [1,2,3▪,4–6,7▪,8,9]. Studies on plant responses to elevated atmospheric levels of CO_2 indicate that plants exhibit enhanced photosynthesis and reproductive effects and produce more pollen. Moreover, the plants flower earlier in urban areas than in corresponding rural areas with earlier pollination of about 2–4 days.

Over the last decades, many studies [26–35] have shown changes in production, dispersion, and allergen content of pollen and spores and that nature of the changes may be different in different regions and species.

Current knowledge on the worldwide effects of climate change on respiratory allergic diseases is provided by several studies on the relationship between asthma and environmental factors, like meteorological variables, airborne allergens, and air pollution [1,2,3▪,4–6]. Published data suggest an increasing effect of aeroallergens on allergic patients, leading to a greater likelihood of development of an allergic respiratory disease in sensitized patients and an aggravation in patients already symptomatic [3▪,27,29–35,36▪,37–54].

Thunderstorm-related asthma

According to current climate change scenarios, there will be an increase in intensity and frequency of heavy rainfall episodes, including thunderstorms explained by the fact that warmer air carries more moisture, which means that rain falls in heavier bursts.

Thunderstorm asthma is a term used to describe an observed increase in acute bronchospasm cases following the occurrence of thunderstorms in the local vicinity [36▪].

Associations between thunderstorms and asthma morbidity have been identified in multiple locations around the world, predominantly in Europe and in Australia, during the pollen season and it is now recognized that thunderstorms are a risk factor for asthma attacks in patients suffering from pollen allergy [36▪,37–54].

One of the first observations of the link between thunderstorms and asthma outbreaks was at the East Birmingham Hospital (UK) in 1983 [42]. It was described as a remarkable increase in the number of asthma ED admissions during the hours of a thunderstorm. In a 36-h period, 26 asthma cases were treated in the ED, compared with a daily average of two or three cases in the days preceding the outbreak [42]. Successively, other asthma outbreaks during thunderstorms have been described in Italy, Australia, Canada, and USA [43–48]. However, the largest asthma outbreak ever recorded was in London, coinciding with a heavy thunderstorm on 24 June 1994 [49]. A large increase in the number of visits for asthma at the EDs of London and the south-west of England was observed. Several of the patients who experienced an asthma attack were not known to be asthmatic patients or were known to be sensitized to pollen and had been affected previously only by seasonal rhinitis [49]. During a 30-h period beginning 18:00 on 24 June 1994, 640 patients with asthma or other airways disease (283 of whom were not known to be asthmatic and 357 of whom were affected only by seasonal rhinitis) attended several EDs, nearly 10 times the expected number of 66 patients. In total, 104 patients were admitted, including five to an intensive care unit, 574 patients whose asthma was attributable to the thunderstorm [49].

Much remains to be discovered about the relationship between asthma attacks and thunderstorms, but there is reasonable evidence of a causal

relationship between the two in patients suffering from pollen allergy. Much of the evidence has shown that the asthma epidemics related to thunderstorms are limited to seasons when there are high atmospheric concentrations of airborne allergenic pollens.

To date, among pollens, only grass, *Parietaria*, and olive pollen have been suggested as possible triggers in thunderstorm-related asthma [50]. In the context of molds, *Alternaria* has been found at risk of inducing asthma connected with thunderstorm in sensitized patients [50,54]. Thunderstorms can concentrate pollen grains at ground level, which may release allergenic particles of respirable size into the atmosphere after their rupture by osmotic shock. During the first 20–30 min of a thunderstorm, patients suffering from pollen allergy may inhale a high concentration of the allergenic material that is dispersed into the atmosphere. This is due to dry updrafts that, during a thunderstorm, entrain whole pollens into the high humidity at the cloud base where they may rupture, followed by cold downdrafts that carry pollen fragments (pollen grains are too large to penetrate the deeper airways) to ground level where outflows distribute them. Because of strong electric fields that develop during thunderstorms, positive ions are released from the ground and could attach to particles and/or electric charge may enhance pollen rupture, thus, enhancing bronchial hyperresponsiveness [51]. This hypothesis was supported in a recent work that showed that in condition of higher humidity, more allergens, from pollen or smaller particles, are available in ambient air. These allergens can likely penetrate deeper into the lung, provoking more severe symptoms [35]. It has been suggested that cytoplasmatic components of some pollen grains such as starch granules are the most likely cause of associations between thunderstorms and asthma. Allergen-bearing starch granules obtained upon contact of pollen with water have been shown to create an inhalable allergenic aerosol capable of triggering an early asthmatic response in an experimental study. Starch granules were shown to be recognized by pollen-sensitized rat's sera and to trigger lymph node cell proliferation in these rats [52]. Because of their very small size (<5 mm), these microparticles can penetrate the lower airways inducing the occurrence of bronchial allergic symptoms (Table 1).

To better understand the association between thunderstorms and asthma attacks in patients suffering from pollen allergy, we used an epidemiological approach applying Hill's criteria of causality (Table 1), the criteria conditions necessary to provide adequate evidence of a causal relationship between a risk factor and a consequence [53]. Most of Hill's criteria support the hypothesis of a causal link of thunderstorms to asthma attacks through pollen exposure, but there is still some uncertainty (Table 2) [54]. Temporal relationship, strength, dose–response relationship, consistency, plausibility, consideration of alternate explanations, and specificity are fulfilled. Instead, there are only limited, in particular, experimental data, which challenge direct evidence on the intervention of pollen as well as the specificity criterion according to which a single putative cause produces a specific effect.

However, all patients affected by pollen allergy should be alerted to the danger of being outdoors during a thunderstorm in the pollen season, as such events may be an important cause of severe exacerbations. In light of these observations, it is useful to predict thunderstorms and thus minimize thunderstorm-related events [3▪].

CONCLUSION

Allergic respiratory diseases and asthma are a result of environmental and immunologic interaction. Climate change is modifying allergy and asthma in unpredictable ways.

An important advocacy tool on this topic is the last encyclics letter of Pope Francis: 'There is an urgent need to develop policies so that, in the next few years, the emission of CO_2 and other highly pollution gases can be drastically reduced, for

Table 1. Characteristics of described epidemics of thunderstorm-associated asthma

(1) The occurrence of epidemics is closely linked to thunderstorm
(2) The thunderstorm-related epidemics are limited to late spring and summer when there are high levels of airborne pollen grains
(3) There is a close temporal association between the arrival of the thunderstorm, a major rise in the concentration of pollen grains and the onset of epidemics
(4) Patients with pollen allergy, who stay indoors with windows closed during thunderstorm, are not involved
(5) There are no high levels of gaseous and particulate components of air pollution
(6) There is a major risk for patients who are not under antiasthma correct treatment
(7) Patients with allergic rhinitis and without previous asthma can experience severe bronchoconstriction

Table 2. Hill's criteria applied to thunderstorm-related asthma

Hill's criteria	Application to the thunderstorm-related asthma
Strength The stronger relationship between the independent variable and the dependent variable, the less likely it is that the relationship is due to an extraneous variable	Increased risk of asthma attacks in relation to thunderstorms
Specifity Causation is likely if a very specific population at a specific site and disease with no other likely explanation. The more specific an association between a factor and an effect is, the bigger the probability of a causal relationship [1]	Scantily demonstrated by experimental data (also sparse and eterogeneous)
Consistency Multiple observations, of an association, with different people under different circumstances and with different measurement instruments increase the credibility of a finding	Association between thunderstorm and asthma found in different studies and different populations
Temporality The effect has to occur after the cause	Thunderstorms can precede asthma attacks
Dose-response relationship There should be a direct relationship between the risk factor (i.e., the independent variable) and people's status on the disease variable (i.e., the dependent variable)	Increased amount of pollen and mould spores at the beginning of the thunderstorm associated with increased probability of asthma attacks in pollen allergic patients and other allergic patients
Plausibility It is easier to accept an association as causal when there is a rational and theoretical basis for such a conclusion	Evidence of biological plausibility at the basis of thunderstorm- related asthma through pollen exposure (allergens and starch granules in the cytoplasm or other paucimicronic cytoplasmic-components carrying allergens). Evidence to be estabilished in the case of mould spores
Coherence A cause-and-effect interpretation for an association is clearest when it does not conflict with what is known about the variables under study and when there are no plausible competing theories or rival hypotheses. In other words, the association must be coherent with other knowledge	Existing theory and knowledge support the existence of thunderstorm -related asthma
Experiment Any related research that is based on experiments will make a causal inference more plausible	Prevention is possible by avoiding exposure to thunderstorm (at is beginning) in pollen patients
Analogy The effect of similar factors may be considered	Alternate hypothesis involving chemical air pollution less explanatory than thunderstorm-related asthma

Modified from [36▪].

example, substituting for fossil fuels and developing sources of renewable energy' [55].

In conclusion, measures of mitigation need to be applied and are crucial for reducing future impacts of climate change on our planet, but until global emissions continue to rise, adaptation to the impacts of future climate variability will also be required.

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Conflicts of interest

There are no conflicts of interest.

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- ▪ of special interest
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Pollen allergy is frequently used to study the interrelationship between air pollution and respiratory allergic diseases such as rhinitis and bronchial asthma. Climatic factors (temperature, wind speed, humidity, thunderstorms, etc.) can affect both components (biological and chemical) of this interaction. Scientific societies should be involved in advocacy activities, such as those realized by the Global Alliance against chronic Respiratory Diseases (GARD).

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All patients affected by pollen allergy should be alerted to the danger of being outdoors during a thunderstorm in the pollen season, as such events may be an important cause of severe exacerbations of asthma and other allergic respiratory diseases. In the light of these observations, it is useful to predict thunderstorms and thus minimize thunderstorm-related events.

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