Urban Air Pollution and Climate Change as Environmental Risk Factors of Respiratory Allergy: An Update

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Abstract

The incidence of allergic respiratory diseases and bronchial asthma appears to be increasing worldwide, and people living in urban areas more frequently experience these conditions than those living in rural areas. One of the several causes of the rise in morbidity associated with allergic respiratory diseases is the increased presence of outdoor air pollutants resulting from more intense energy consumption and exhaust emissions from cars and other vehicles. Urban air pollution is now a serious public health hazard.

Laboratory studies confirm epidemiologic evidence that air pollution adversely affects lung function in asthmatics. Damage to airway mucous membranes and impaired mucociliary clearance caused by air pollution may facilitate access of inhaled allergens to the cells of the immune system, thus promoting sensitization of the airway. Consequently, a more severe immunoglobulin (Ig) E–mediated response to aeroallergens and airway inflammation could account for increasing prevalence of allergic respiratory diseases in polluted urban areas.

The most abundant components of urban air pollution in urban areas with high levels of vehicle traffic are airborne particulate matter, nitrogen dioxide, and ozone. In addition, the earth's temperature is increasing, mainly as a result of anthropogenic factors (eg, fossil fuel combustion and greenhouse gas emissions from energy supply, transport, industry, and agriculture), and climate change alters the concentration and distribution of air pollutants and interferes with the seasonal presence of allergenic pollens in the atmosphere by prolonging these periods.

Key words: Air pollution. Allergy. Allergic asthma. Bronchial asthma. Climate change. Environmental diseases. Airway hyperreactivity. Pollen allergy. Respiratory allergy. Urban air pollution. Hypersensitivity.

Resumen

La incidencia de enfermedades alérgicas respiratorias y asma bronquial parece que está aumentando en todo el mundo, y las personas que viven en zonas urbanas experimentan estas afecciones con mayor frecuencia que las que viven en zonas rurales. Una de las diversas causas del incremento de la morbilidad asociada a las enfermedades alérgicas respiratorias es la mayor presencia de contaminantes atmosféricos en el exterior, originada por un consumo energético más elevado y por las emisiones de los coches y otros vehículos. Actualmente, la contaminación atmosférica en las ciudades supone un riesgo grave para la salud pública.

Estudios analíticos confirman las evidencias epidemiológicas de que la contaminación atmosférica afecta de forma adversa a la función pulmonar de las personas asmáticas. Los daños en las mucosas de las vías respiratorias y la alteración del aclaramiento mucociliar a causa de la contaminación atmosférica pueden facilitar el acceso de los alérgenos inhalados a las células del sistema inmunitario y favorecer la sensibilización de las vías respiratorias. Por consiguiente, el aumento de la respuesta mediada por la inmunoglobulina (Ig) E frente a los aeroalérgenos y la inflamación de las vías respiratorias podría explicar el incremento de la prevalencia de enfermedades alérgicas respiratorias en las zonas urbanas con contaminación.

Los componentes que más abundan en la contaminación atmosférica en las zonas urbanas con altos niveles de tráfico rodado son las partículas en el aire, el dióxido de nitrógeno y el ozono. Además, la temperatura de la tierra está aumentando, principalmente como consecuencia de factores antropogénicos (p. ej., combustión de carburantes fósiles y emisiones de gases de efecto invernadero procedentes del consumo energético, el transporte, la industria y la agricultura), y el cambio climático altera la concentración y la distribución de los contaminantes atmosféricos e interfiere en la presencia estacional de pólenes alergénicos en la atmósfera al prolongar estos períodos.

Palabras clave: Contaminación atmosférica. Alergia. Asma alérgica. Asma bronquial. Cambio climático. Enfermedades ambientales. Hiperreactividad de las vías respiratorias. Alergia al polen. Alergia respiratoria. Contaminación atmosférica en zonas urbanas. Hipersensibilidad.

Introduction

A dramatic increase in the prevalence of allergic respiratory diseases such as rhinosinusitis and bronchial asthma has been observed during the last 3 decades in industrialized countries [1-6].

The key feature of bronchial asthma is the development of airway inflammation and bronchial hyperresponsiveness in the form of a heightened bronchoconstrictor response, not only to allergens to which an individual is sensitized, but also to a range of nonspecific stimuli, such as air pollutants and cold air [7-14]. There is some evidence to indicate that high levels of vehicle emissions in cities and an urban lifestyle are correlated with the rising trend in allergic respiratory diseases [7-12]. The adverse effect of air pollution on respiratory health has a quantifiable impact, not only on the morbidity but also on the mortality of respiratory diseases [15-17]. One commonly proposed explanation for the recent increase in morbidity associated with allergic respiratory diseases is the continuous degradation of air quality as a result of increasing levels of outdoor air pollutants such as vehicle emissions [7-20].

An understanding of the interplay between genetic background and environmental pollution may lead to interventions that can prevent the progression of asthma, the onset of airway inflammation with bronchial hyperresponsiveness to various specific and nonspecific stimuli, and the development of irreversible changes in airway function.

It is not easy to evaluate the impact of air pollution on the timing of asthma exacerbations or on the prevalence of asthma in general, since atmospheric concentrations of airborne allergens and air pollutants frequently increase simultaneously. However, some trials have evaluated the role of exposure to air pollution in reducing the threshold concentration of aeroallergens able to induce airway responsiveness to a specific bronchial challenge in sensitized subjects [7,9,10]. Factors such as type of air pollution, climate, plant species, degree of airway sensitization, and hyperresponsiveness of exposed individuals can influence this interaction.

Positive associations have been observed between urban air pollution and respiratory symptoms in children, and the literature contains many reports of a relation between motor vehicle exhausts and acute or chronic respiratory symptoms in children living near traffic [17-58]. Air pollution can negatively influence lung development in children and adolescents [38,40,44,45].

Outdoor Air Pollution in Urban Areas and Allergic Respiratory Diseases

In most industrialized countries, people who live in urban areas tend to be more affected by allergic respiratory diseases than those who live in rural areas. With its particulate and gaseous emissions, road traffic is the main contributor to air pollution in most urban areas, and there is evidence that living near high-traffic roads is associated with impaired respiratory health [23,24,26,29,43]. Air pollution is associated with asthma exacerbations, which are characterized by greater bronchial hyperresponsiveness, increased medication use, and more frequent visits to the emergency department and hospital admissions [7-10]. The effect of air pollutants on lung function depends on the type of pollutant and its environmental concentration, the duration of exposure, the total ventilation of exposed individuals, and the interaction between air pollution and aeroallergens such as pollens and fungal spores [7-12].

Studies on vehicle emissions have focused on roadways with dense truck and automobile traffic as the source of air pollution and have been conducted primarily among schoolchildren. The results suggest that the distance from and type of traffic are more significant risk factors than traffic volume for wheezing in early infancy. Infants living near stop-and-go bus and truck traffic had a significantly higher prevalence of wheezing than nonexposed infants [23,24,26-29].

Components of Air Pollution in Urban Areas

The massive increase in emissions of air pollutants due to economic and industrial growth in the last century has made air quality an important environmental problem throughout the world.

The most abundant components of air pollution in urban areas are nitrogen dioxide, ozone, and particulate matter. Sulfur dioxide is particularly abundant in industrial areas. Aeroallergens are carried and delivered by fungal spores or by plant-derived particles (pollen grains and microscopic components, such as soya bean dust and *Ricinus*) [7,9,10,55].

It is estimated that more than 50% of the population of the United States live in areas whose levels of ozone, nitrogen dioxide, sulfur dioxide, and particulates exceed current National Ambient Quality Standards, as monitored by the United States Environmental Protection Agency [8,14,17].

Particulate Matter

Particulate matter is a mixture of organic and inorganic solid and liquid particles of different origins, size, and composition. It is a major component of urban air pollution and has the greatest effect on health. Penetration of the tracheobronchial tract is related to particle size and the efficiency of airway defense mechanisms. Inhalable particulate matter that can reach the lower airways is classified in 3 sizes: PM_{10}, $PM_{2.5}$, and PM_{1} [7,16,55].

Particles with a diameter less than 10 μm (PM_{10}) can penetrate the lower airways, and fine particulate, that is, particles with an aerodynamic diameter ≤2.5 μm ($PM_{2.5}$), is thought to constitute a notable health risk, since it can be inhaled more deeply into the lungs. Particulate matter has been significantly associated with emergency department visits due to asthma, wheezing, bronchitis, and lower respiratory tract symptoms, as well as with the use of anti-asthma medication and physician visits for asthma [7,8,10,16,47,58,59,61].

While human lung parenchyma retains $PM_{2.5}$, particles

larger than 5 μm and <10 μm only reach the proximal airways, where they are eliminated by mucociliary clearance if the airway mucosa is intact [8,10,58]. Some studies also show a significant association between daily mortality from respiratory and cardiovascular diseases and particulate air pollution [15-17]. It has been hypothesized that urban fine particulate matter can penetrate deep into the airways and induce alveolar inflammation, which is responsible for variation in blood coagulability and release of mediators favoring acute episodes of respiratory and cardiovascular diseases [15-17]. Particulate levels are associated with early asthma exacerbations in children with persistent disease [56]. McConnell et al [56] observed that the incidence of new diagnoses of asthma in children is associated with physical exercise in areas with high concentrations of ozone and particulate matter. Consequently, air pollution and outdoor exercise could contribute to the development of asthma in children. Nevertheless, although there is extensive evidence that ambient air pollution exacerbates existing asthma, the link with the development of asthma is less well established, as few studies provide extensive exposure data. In the past few years, some reports have supported an association between air pollution and incidence of asthma [8,10,12,56].

Diesel Exhaust Particles

Much research is now being carried out on diesel exhaust particles (DEPs) and their components (eg, polycyclic aromatic hydrocarbons [PAH]), since a large part of urban particulate matter originates from diesel engines. This area is particularly important, given the increase in the number of new cars with diesel engines in industrialized countries [59-63].

DEPs account for most airborne particulate matter (up to 90%) in the world's largest cities [59,62], and are composed of fine particles (2.5-0.1 μm) and ultrafine (<0.1 μm) particles, although these primary DEPs can coalesce to form aggregates of varying sizes.

DEPs exert their effect through chemical agents such as PAHs. The particles are deposited on the mucosa of the airways and their hydrophobic nature mean that the PAHs allow them to diffuse easily through cell membranes and bind to the cytosolic receptor complex. Through subsequent nuclear activity, PAHs can modify cell growth and differentiation programs.

Acute exposure to diesel exhaust causes irritation of the nose and eyes, headache, lung function abnormalities, fatigue, and nausea, while chronic exposure is associated with cough, sputum production, and diminished lung function [60-62]. Experimental studies have shown that DEP-PAHs can modify the immune response in predisposed animals and humans and modulate the inflammatory process in the airway. In other words, DEPs seem to exert an adjuvant immunological effect on IgE synthesis in atopic subjects, thereby influencing sensitization to airborne allergens [63]. DEPs also cause respiratory symptoms and modify the immune response in atopic subjects [62,63]. In addition, DEPs can interact with aeroallergens to enhance antigen-induced responses, with the result that allergen-specific IgE levels are up to 50-fold greater in allergic patients stimulated with DEPs and allergens than in patients treated with allergen alone [7,63]. Combined challenge with DEPs and ragweed allergen markedly increases the expression of human nasal ragweed-specific IgE in vivo and skews cytokine production to a type 2 helper T-cell pattern [63].

Walking for 2 hours on a main street such as Oxford Street (London, UK) results in an asymptomatic but consistent reduction in forced expiratory volume in 1 second of up to 9.1% and in forced vital capacity of up to 5.4% [61]. The effects are greater in patients with moderate asthma than in those with mild asthma. These changes are accompanied by increases in levels of biomarkers of neutrophilic inflammation.

Nitrogen Dioxide

Automobile exhaust is the most significant source of outdoor nitrogen dioxide, which is a precursor of photochemical smog found in outdoor air in urban and industrial regions and, in conjunction with sunlight and hydrocarbons, results in the production of ozone. Like ozone, nitrogen dioxide is an oxidant pollutant, although it is less chemically reactive and thus less likely to induce airway inflammation [7,8,29,48,64].

Ozone

Ozone is the component of air pollution that has received most attention as an inducer of bronchial inflammation [64-70]. This agent is generated at ground level by photochemical reactions involving nitrogen dioxide, hydrocarbons, and UV radiation. Ozone inhalation induces epithelial damage and consequent inflammatory responses in the upper and lower airways, as witnessed by an increase in levels of neutrophils, eosinophils, mononuclear cells, fibronectin, granulocyte-macrophage colony-stimulating factor, interleukin (IL) 6, IL-8, and prostaglandin E in nasal and bronchoalveolar lavage fluids [7-10,65,66].

High ozone levels seem to be linked to asthma and asthma-like symptoms in both the short term and the long term. In the long term, continuous exposure to high ozone levels impairs respiratory function [8,10,68,69] and airway inflammation in atopic asthmatics. Moreover, there could be an interaction between pollution and climatic factors, so that a particular climate could elicit a pollution effect on health [7,9,10,64]. One possible explanation for the association between asthma prevalence and milder climatic areas could be the ozone concentration in the atmosphere; ozone is known to reach higher levels at higher temperatures. Chronic exposure to ambient ozone may increase the risk of asthma exacerbations among children [65,66,68].

The acute health effects of exposure to ambient ozone have been examined in many geographical regions. Potential adverse effects include diminished lung function, airway inflammation, symptoms of asthma, increases in hospitalization due to respiratory diseases, and excess mortality. Ozone exposure has both a priming effect on allergen-induced responses and an intrinsic inflammatory action in the airways of allergic asthmatics [64-69]. Studies have reported that long-term

exposure to ozone may reduce lung function in schoolchildren and adults and increase the prevalence of asthma and asthmatic symptoms [65-67].

Aeroallergens and Atopic Asthma

Aeroallergens have a significant impact on the development of asthma, and atopy is an important risk factor for the development of allergic asthma. The increasing frequency of allergic disease over time has not been adequately explained. It might imply a corresponding increase in associated sensitizing aeroallergens, although conclusive data to explain this hypothesis are not available. Several studies suggest that air pollution helps facilitate allergic sensitization of the airways in predisposed individuals [7,9,10,12,31], and the increase in allergic respiratory diseases appears to be paralleled by increasing atmospheric concentrations of gases and respirable particulate matter (Table 1).

Table 1. Possible Relationship Between Components of Air Pollution and Allergens in Inducing respiratory Allergy

Air pollution may be responsible for the following:

- Interaction with pollen grains, leading to increased release of allergens characterized by modified antigenicity.
- Interaction with microscopic allergen-carrying particles released by plants. These particles are able to reach the lower airways in inhaled air, inducing asthma in predisposed individuals.
- An inflammatory effect on the airways of susceptible individuals, with increased epithelial permeability, easier penetration of pollen allergens in the mucosa, and easier interaction with cells of the immune system. There is also evidence that predisposed individuals have increased airway reactivity induced by air pollution and increased bronchial responsiveness to inhaled pollen allergens.
- An adjuvant immunologic effect on IgE synthesis in atopic individuals, as already shown with diesel exhaust particles.

The major air pollutants that are toxic for plants, especially after long-term exposure, are ozone, sulfur dioxide, nitrogen dioxide, and particulate matter. Aeroallergens, such as those derived from pollen grains, lead to bronchial obstruction in predisposed individuals, and pollen allergy is one of the models most frequently used to study the relationship between air pollution and respiratory allergic disease [7,9,10]. It is not clear what percentage of cases of asthma each year can be attributed to aeroallergens, and no corresponding increase in aeroallergen levels that might account for the increase in asthma prevalence has been observed. However, while the prevalence of allergic rhinitis and allergic asthma is increasing in some European cities, the atmospheric concentration of grass pollen is falling [71-76]. This decrease has been attributed to substantial reductions in grassland over large areas of Europe. In fact, during the last 30 years, grassland in Western Europe has decreased by more than 20%. As a consequence, the increase in the number of cases of allergic rhinitis and asthma induced by grass pollen is probably related, among other factors, to increased air pollution.

Elevated atmospheric carbon dioxide concentrations and higher temperatures have been observed to induce increasing photosynthesis and reproductive effort in plants. In other words, biological aerosols such as pollen grains or their microscopic allergenic components can act as air pollutants in producing these effects [71-75]. The most frequent interaction is the synergistic proinflammatory action of airborne biological and chemical (gaseous or particulate) pollutants on the airway mucosa. Impaired mucociliary clearance induced by chemical pollutants may facilitate access of inhaled allergens to the cells of the immune system [8-10,77-79].

Although there is evidence suggesting that exposure to pollen allergens can induce asthma, overall sensitization to pollen remains a low risk factor for asthma development, with the exception of grains such as those of *Parietaria*, a member of the Urticaceae family, which is abundant in the southern Mediterranean area [7,9,10].

People who live in urban areas tend to be more affected by pollen-induced respiratory allergy than those living in rural areas, where individuals who are exposed to traffic usually experience a higher frequency of allergic respiratory diseases than those who are less exposed. An urban lifestyle has been found to be associated with a greater risk of allergic sensitization, including pollen allergy [77,79].

Global Warming and Climate Change

The role of weather (pressure, temperature, humidity) on the initiation and/or exacerbations of respiratory allergic symptoms in predisposed individuals is still poorly understood. Weather affects asthma directly, by acting on the airways, or indirectly, through airborne allergens and pollutant levels. The association between atmospheric factors and asthma raises the question of how increasing levels of greenhouse gases and concomitant climate change influence the frequency and severity of respiratory allergy.

Global warming induced by human activity has an impact on the biosphere and the environment [79-90]. The fourth synthesis report of the Intergovernmental Panel on Climate Change issued in February 2007 concludes that global temperature has risen markedly over the last 30 years due to increased greenhouse gas emissions, largely from anthropogenic sources [78]. Global greenhouse gas emissions due to human activity have been growing for several years, with an increase of 70% between 1970 and 2004. The list of greenhouse gases includes several components of air pollution. In this regard, the Intergovernmental Panel on Climate Change 2007 document stated that "most of the observed increase in globally averaged temperatures since the mid-20th century is very likely due to the observed increase in anthropogenic greenhouse gas concentrations" [78].

Carbon dioxide is the most important anthropogenic greenhouse gas, and emissions increased by approximately 80% between 1970 and 2004 [78]. Climate change resulting

from greenhouse gas emissions affects human health through increased frequency of respiratory and cardiovascular diseases due to higher concentrations of ground-level ozone, changes in the frequency of respiratory diseases from long-range (cross-border) air pollution, and the altered spatial and temporal distribution of allergens and some infectious disease vectors. These changes will affect not only patients with respiratory disease, but may also alter the incidence and prevalence of respiratory conditions [79-86].

The WHO has also warned that "there is now strong scientific consensus that global warming will affect, in profoundly adverse ways, some of the most fundamental determinants of health: food, air and water" [89]. The Italian Study of Asthma in Young Adults (ISAYA) [86], an extensive epidemiological survey comparing prevalence rates in different regions of Italy, showed that the prevalence of asthma seems to be significantly affected by climate: asthma-like symptoms were more common in urban areas with a Mediterranean climate (central-southern Italy) than in areas with a continental climate (northern Italy) [86].

The effects of climate change on respiratory allergy are still unclear, and studies addressing this topic are lacking. Global warming is expected to affect the start, duration, and intensity of the pollen season on the one hand, and the rate of asthma exacerbations due to respiratory infections and/or cold air inhalation on the other [7,9,80,81].

Knowledge of a plant's geographical distribution and its flowering period and possible variations induced by climate change is of great importance. The climate changes projected during the next century will influence plant and fungal reproductive systems and alter the timing, production, and distribution of aeroallergens. Increased exposure to allergens as a result of global warming, combined with exposure to pollutants that act synergistically to intensify the allergic response, could point to increased respiratory problems in the future. In fact, climate change is likely to influence vegetation, with consequent changes in growth and reproductive cycles and in the production of allergenic pollen (seasonal period and intensity). In addition, weed species are expected to proliferate. These changes can vary from one region to another, since some areas receive greater amounts of UV radiation and/or rainfall, than others. Moreover, UV radiation in a polluted urban atmosphere favors the formation of ozone, which is affected mostly by elevated daytime temperatures, low wind speeds, and clear skies (conditions observed in regions such as the Mediterranean, California, and Central and South America, all of which have high levels of traffic).

Extreme Weather Events and Thunderstorms

In recent years, the frequency of extreme weather events, such as heat waves, heavy rainfall, and thunderstorms, has increased [79-82]. There have been reports of heat-related incidence of hospitalization and mortality due to cardiovascular and respiratory disease [91-94].

Evidence exists that thunderstorms during the pollen season are associated with allergic asthma epidemics in patients with pollinosis [95-100], and that thunderstorms concentrate at ground level pollen grains that release allergenic particles of respirable size into the atmosphere after their rupture by osmotic shock [95-98].

Table 2. Characteristics of Epidemics of Thunderstorm-Associated Asthma

- Asthma epidemics and thunderstorms are linked.
- Thunderstorm-related epidemics are limited to late spring and summer, when pollen counts are high.
- There is a close temporal association between the start of the thunderstorm and the onset of the epidemic.
- There are no high concentrations of air pollution before and during the thunderstorms.
- There are no high concentrations of other aeroallergens such as moulds.
- Individuals with allergic rhinitis only and no previous asthma can experience severe bronchoconstriction during thunderstorms.
- Individuals who experience asthma are not usually taking suitable anti-inflammatory treatment.
- Individuals with pollinosis but who are indoors with the windows closed during thunderstorms are not affected.

Weather conditions such as rain or humidity may induce hydration and fragmentation of pollen grains, which releases allergenic biological aerosols into the atmosphere. Consequently, during the first phase of a thunderstorm, pollen-allergic individuals may inhale a high concentration of dispersed allergenic material, which can induce asthmatic reactions, some of which are severe.

Fortunately, despite the postulated association between thunderstorms and asthma, this climatic phenomenon does not seem to be responsible for a large number of exacerbations. Nevertheless, it is important to determine the mechanisms involved in the release of allergens from pollens during thunderstorms so that patients with pollinosis (including those affected by seasonal rhinitis only) can receive information about the risk of an asthma attack (Table 2).

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