

Air pollution and allergens

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■ Summary

It is well known that the prevalence of allergic diseases has increased in recent decades in the industrialized world. Exposure to environmental pollutants may partially account for this increased prevalence. In effect, air pollution is a growing public health problem. In Europe, the main source of air pollution due to particles in suspension is represented by motor vehicles - particularly those that use diesel fuel. Diesel exhaust particles (DEPs) are composed of a carbon core upon which high-molecular weight organic chemical components and heavy metals deposit. Over 80% of all DEPs are in the ultrafine particle range (< 0.1 µm in diameter).

Air pollutants not only have a direct or indirect effect upon the individual, but also exert important actions upon aeroallergens. Pollen in heavily polluted zones can express a larger amount of proteins described as being allergenic. Through physical contact with the pollen particles, DEPs can disrupt the former, leading to the release of paucimicronic particles and transporting them by air - thus facilitating their penetration of the human airways. Climate change in part gives rise to variations in the temperature pattern characterizing the different seasons of the year. Thus, plants may vary their pollination calendar, advancing and prolonging their pollination period. In addition, in the presence of high CO₂ concentrations and temperatures, plants increase their pollen output. Climate change may also lead to the extinction of species, and to the consolidation of non-native species - with the subsequent risk of allergic sensitization among the exposed human population.

In conclusion, there is sufficient scientific evidence on the effect of air pollution upon allergens, increasing exposure to the latter, their concentration and/or biological allergenic activity.

Key words: Allergen. Climate change. Air pollution. Diesel exhaust particles.

■ Resumen

Es bien sabido que la prevalencia de las enfermedades alérgicas en los países industrializados se ha incrementado en las últimas décadas. La exposición a los contaminantes ambientales puede justificar en parte este aumento de prevalencia. Actualmente la contaminación atmosférica es un problema de salud pública que va en aumento. En Europa, el principal causante de la contaminación atmosférica por partículas en suspensión son los vehículos a motor, sobre todo a expensas del diésel. Las partículas de emisión de diésel (PED) están conformadas por un núcleo de carbono, sobre el que se depositan componentes químicos orgánicos de alto peso molecular y metales. Más del 80% de las PED están en el rango de partículas ultrafinas (tamaño < 0,1 µm de diámetro).

Los contaminantes atmosféricos no solamente tienen un efecto directo o indirecto sobre el individuo sino que tienen una importante acción sobre los aeroalérgenos. Los pólenes de zonas con gran contaminación pueden expresar mayor cantidad de proteínas descritas como alergénicas. Las PED pueden ocasionar, por contacto físico con los granos de polen, su disrupción liberándose partículas paucimicrónicas y aerotransportarlas, facilitando su llegada a la vía respiratoria. El efecto del cambio climático se traduce en parte en una variación en el patrón de temperatura que caracteriza las estaciones. De este modo las plantas pueden variar su calendario polínico avanzando y alargando su período de polinización. Además, en presencia de elevadas concentraciones de CO₂ y temperatura, las plantas aumentan su producción de polen. El cambio climático también puede comportar la desaparición de especies así como el arraigamiento de especies no autóctonas con el consiguiente riesgo de sensibilización alérgica para la población expuesta.

En conclusión, existen suficientes pruebas científicas sobre el efecto que la contaminación atmosférica tiene en el alérgeno incrementando su exposición, su concentración y/o su actividad biológica alergénica.

Palabras clave: Alérgeno. Cambio climático. Contaminación atmosférica. Partículas de emisión diésel.

Introduction

It is well known that the prevalence of allergic diseases has increased in recent decades in the industrialized world [1-4], probably as a result of interaction between the environment and the individual. Since this increase in prevalence has taken place in a relatively short period of time, genetic changes are unable to explain the phenomenon. Other factors external to the individual (i.e., of an environmental nature) therefore appear important. Thus, life style, exposure to certain allergens and to environmental contaminants or pollutants both indoors (e.g., tobacco smoke) and outdoors (air pollution), or exposure to microorganisms, may globally account for the observed increase in prevalence (Table 1).

Since 1980, a number of clinical, epidemiological and experimental studies have been made to elucidate the complex interactions between environmental pollution and allergic disease. However, this interaction is presently of a speculative nature, since there are other factors that intervene and confound such an association (Figure 1). In other words, while it is plausible for environmental pollution to play an important role in the increased prevalence of atopic disease, it is very difficult to demonstrate such an association on the basis of epidemiological studies.

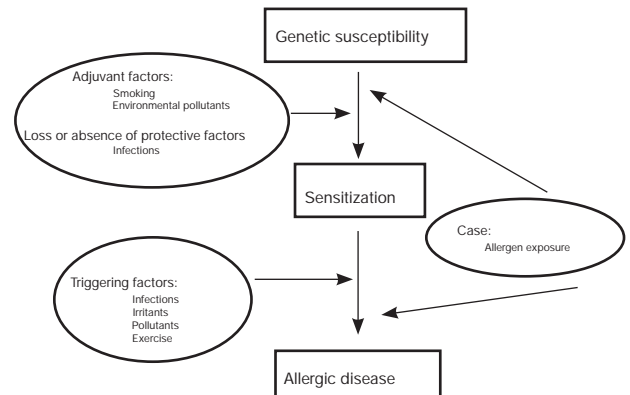


Figure 1. Genetic and environmental factors in allergic disease.

Table 1. Hypothesis regarding the factors explaining the increase in the prevalence of atopic disease

Genetic predisposition
Allergen exposure
Increased allergological diagnoses
Hygiene hypothesis
Environmental pollution
Exterior (air pollution)
Interior (e.g., smoking)
Others
Socioeconomic level
Older age of women at first child birth

Environmental pollution

Although environmental pollution is viewed as a recent problem, its risks have been known since ancient times. One of the first documented descriptions of death resulting from environmental pollution corresponds to Plinius the Young (I Century AD). In effect, Plinius described the death of his uncle, Plinius the Old (in the year 79 AD), as a result of inhalation of the volcanic fumes from Mount Vesuvius.

However, it was not until the XIII Century, during the reign of Edward I of England, when the first data on respiratory disease and air pollution secondary to human intervention were reported. Pollution resulting from the burning of coal was the cause of respiratory problems in the cities of England. In effect, we now know that the burning of mineral coal releases considerable amounts of sulfur into the air - resulting in acid rain. Edward I prohibited the burning of coal in the ovens of craftsmen, because of the illnesses they produced. Centuries later, Elizabeth I of England prohibited the burning of coal in London while the Parliament was in session - this time for esthetic reasons. Over the years, pollution worsened, though it was still not perceived to be a public health threat. In the late XIX and early XX Century, many norms came into effect to control smog (air pollution resulting from the burning of coal) in both England and the United States. Such legislation was the first of its kind designed to control air pollution.

The starting point for awareness of the serious problem posed by air pollution can be found in London in 1952, where intense smog exceeding 2000 $\mu\text{g}/\text{day}$ of SO_2 was recorded during five consecutive days. During this interval, several thousand inhabitants died. This episode proved to be a triggering point for world public opinion, and led to the adoption of a series of measures to reduce such pollution.

In effect, important efforts were made to replace coal as a source of energy - introducing petroleum derivatives instead. While this led to an important decrease in smog, it also gave rise to an increase in other environmental contaminants, including particularly diesel fuel particles. Thus, the situation has changed from so-called type I pollution, characterized by a predominance of SO_2 and heavy dust particles, to type II pollution, derived from the combustion of petroleum products - with the emission of volatile organic components, ozone and particles in suspension, including the so-called diesel exhaust particles (DEPs) (Table 2). Type I pollution has been correlated to the appearance of inflammatory and irritative problems of the airways [5], while type II pollution has been associated with the appearance of allergic processes [6] - though inflammatory and irritative respiratory disorders are

Table 2. Types of air pollution and their principal composition

Coal derivatives (Type I)	Petroleum derivatives (Type I)
SO ₂	NO _x
Total suspended material: "Dust fall"	Volatile organic compounds
	O ₃
	Particles in suspension
	Diesel exhaust particles

also possible. This observation agrees with the fact that the prevalence of atopic problems is greater in urban areas than in the rural setting [7-10].

Air pollution is a growing public health problem, and this growth is largely attributable to increases in: a) the world population, b) economical activities, c) energy consumption, d) industrial activities, and e) motor vehicles. In Europe, the main source of air pollution due to particles in suspension is represented by motor vehicles - particularly those that use diesel fuel [11].

Although optimum diesel fuel combustion should produce only water and CO₂, in practice combustion is incomplete, and a series of gases are produced as a result (CO, nitrogen oxides, aldehydes), as well as solid particles including particularly DEPs. It is estimated that diesel engines generate ten times more DEPs than gasoline engines or engines that use other petroleum products, and 100 times more than gasoline engines with catalytic converters [11]. DEPs are composed of a carbon core upon which high-molecular weight organic chemical components (CO, NO, NO₂, SO₂, hydrocarbons) and heavy metals deposit [12,13]. Over 80% of all DEPs are in the ultrafine particle range (i.e., measuring < 0.1 μm in diameter).

There is scientific proof of the direct relationship between air pollution, respiratory and cardiovascular disease exacerbation and the resulting mortality rates [14-17].

Regarding IgE-mediated allergic disease, and following the study published by Muranaka et al. [18], in which DEPs were shown to be able to induce IgE responses in a murine model, other studies have concluded that DEPs can enhance allergic responses. In murine models of asthma, DEPs have been shown to be able to induce: a) increased total and specific IgE production, b) the production of cytokines inherent to Th2 cell response, c) eosinophilic inflammatory response, d) goblet cell hyperplasia, and e) bronchial hyper-responsiveness [19-23]. In guinea pigs sensitized to pollen, DEPs have also been shown to induce rhinitis and nasal hyper-responsiveness, as well as eosinophilic inflammation [24]. In studies involving healthy subjects, DEPs have demonstrated: a) inflammatory effects upon the airways, b) increases in the number of peripheral blood neutrophils and platelets, c) increases in histamine levels, and d) increases in the expression of ICAM-1 (intracellular adhesion molecule-1) and VCAM-1 (vascular cell adhesion molecule-1). In patients with mild asthma, DEPs increase bronchial hyper-responsiveness as assessed by methacholine, with an increase in the production of both IL-6 and IL-10 [25-27].

Air pollutants not only have a direct or indirect effect upon the individual, but also exert important actions upon aeroallergens. In effect, the allergenicity of such aeroallergens may be increased, their transport may be favored, and their atmospheric concentration may even be increased secondary to a rise in their production or exposure time.

DEPs as "transporters"

Pollen particles contain pollinic allergens. High environmental humidity conditions can subject the pollen particles to osmotic shock, resulting in the release of microparticles or paucimicronic particles that may contain allergenic proteins [28]. The presence of these paucimicronic particles would explain the discordance occasionally observed between the appearance of respiratory allergic symptoms in a pollinic patient and the absence of actual pollen particles in the atmosphere [29,30]. In the same way, through physical contact with the pollen particles, DEPs can disrupt the former, leading to the release of paucimicronic particles and transporting them by air - thus facilitating their penetration of the human airways. It should be remembered that DEPs may measure less than 10 μm in diameter, and many are even less than 0.1 μm in size; as a result, they can easily penetrate the airways and even reach the lower respiratory tract [31,32]. In vitro studies have shown that Lol p 1 and Bet v 1, which are the prevalent or majority allergens of *Lolium* (a gramineous species) and birch, respectively, bind to DEPs thanks to the absorptive capacity resulting from their physicochemical characteristics [33,34]. Such "affinity" has also been demonstrated for other allergens such as Der p 1, Fel d 1 and Can f 1 [35].

Other plant-derived allergenic particles are the so-called Ubish bodies. These are spheroid structures that develop with pollen exine and are found in the anthers of many plants [36]. These structures, measuring only a few μm in diameter, may also contain allergenic proteins [37]. Non-biological particles in suspension, such as DEPs, act as transporters for these structures, in the same way as for other pollen-derived paucimicronic particles [38].

Influence of environmental pollution upon pollen allergenicity

Environmental pollution influences pollen allergenicity. Scientific evidence shows that pollen in heavily polluted

zones expresses a larger amount of proteins described as being allergenic, compared with areas characterized by lesser pollution.

The study of Cortegano et al. concluded that *Cupressus arizonica* in areas of heavy air pollution express a larger amount of Cup a 3 compared with pollen from areas with significantly lower pollution levels [39] - thus favoring sensitization of the exposed population or the appearance of respiratory allergic disease in sensitized individuals.

Armentia et al. have confirmed that the protein content and biological allergenic activity of gramineous pollen - specifically Lol p 5 - is greater in areas of heavy air pollution [40].

The pollen of *Parietaria* has also been considered in the investigation of the interaction between environmental pollution and allergenic expression. The emissions of gasoline engines without catalytic converters and of diesel engines increase the allergenic potential of *Parietaria* pollen compared with emissions from vehicles with catalytic converters [41,42].

Climate change, environmental pollution and allergens

Climate change refers to the global variation in the climate of the planet [43]. Such changes take place on very distinct time scales, particularly as regards climatic parameters such as temperature, rainfall or cloud cover. Such changes are due to natural causes and, in the last few centuries, to human action.

The term "climate change" is typically used in reference only to climatic changes taking place at the present time, as a synonym for "global warming". The United Nations Convention on Climate Change used the term only in reference to changes of human origin [43]. In effect, "climate change" is understood as climatic variation directly or indirectly attributable to human activity, and which modifies the atmospheric composition of the planet in combination with the natural climate variations observed over comparable periods of time. In some cases, the term "anthropogenic climate change" is used in reference to changes of human origin.

Humans presently constitute one of the most important climatic agents, though our species has become part of the list of such factors only recently. Human influence began with deforestation to produce pastures and land for the growing of crops, though at present our influence has increased greatly as a result of the emission of abundant gases that generate a greenhouse effect (Table 3 and figure 2): carbon dioxide from factories and transportation, and methane from intensive livestock production and crops.

Climate change in part gives rise to variations in the temperature pattern characterizing the different seasons of the year. Thus, plants may vary their pollination calendar, advancing and prolonging their pollination period [44-46]. The advance in the pollinic season is estimated to be 0.84-0.9 days/year [47-50]. In addition, in the presence of high CO₂ concentrations, plants increase their photosynthetic activity, water requirements, reproductive effort and biomass [49-52]. This could be regarded as a positive situation for agriculture, though not so in relation to pollinosis.

Table 3. Principal greenhouse effect gases

	Contribution
CO ₂	76%
CH ₄	13%
N ₂ O	6%
CFC _s *	5%

*Chlorofluorocarbon aerosols.

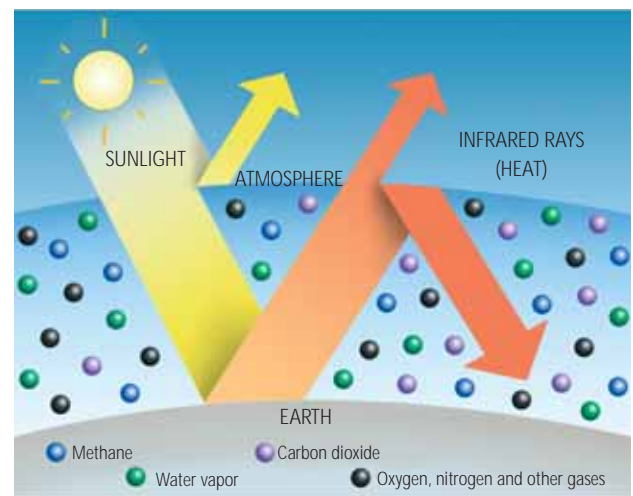


Figure 2. Graphic representation of the "greenhouse effect": planet temperature rise caused by a certain group of gases, some of which are produced on a massive scale by human activity (e.g., carbon dioxide), and which retain the heat of the atmosphere.

Experimental studies under controlled atmospheric conditions and involving high CO₂ concentrations show *Ambrosia* to increase both its biomass and pollen output (between 60-90%) [53,54]. Other experimental studies have reported synergism between CO₂ and temperature. High CO₂ concentrations and temperatures induce increased pollen production on the part of *Ambrosia* [55]. Climate change may also lead to the extinction of species, and to the consolidation of non-native species - with the subsequent risk of allergic sensitization among the exposed human population [56,57]. In the great majority of studies, pollen is the model used to reflect the effect of air pollution upon allergen production. Considering that fungal spores may have air concentrations far higher than those of pollen, and are much more conditioned by atmospheric variables, it comes as no surprise that air pollution may also exert a direct influence upon fungal spore concentration and allergenic production.

In conclusion, there is sufficient scientific evidence on the effect of air pollution upon the appearance of allergic respiratory disease, acting as a coadjuvant to IgE and/or inflammatory response, in exposed individuals, and also upon allergens - directly increasing exposure to the latter, their concentration and/or biological allergenic activity. However, at present and at the general population level, we are unable to affirm that air pollution is the main and direct cause of the increased prevalence in atopic disease, since other factors inherent to the individual and to the surrounding environment may play an equally if not more important role.

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