

REVIEW

Urban air pollution and plant-derived respiratory allergy

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Summary

Respiratory allergic diseases are increasing in both prevalence and severity in most industrialized countries, and subjects living in urban areas are more likely to experience allergic respiratory symptoms, particularly those induced by pollen allergens, than subjects living in rural areas. This increase has been linked, among other factors, to urban photochemical smog, which is characterized by high levels of nitrogen dioxide, ozone and particulate matter. In atopic subjects exposure to air pollution probably increases airway responsiveness to aeroallergens.

Evidence suggests that pollen allergens can interact with components of air pollution, by adhering to the surface of allergenic pollen grains or paucimicronic allergen-carrying particles, air pollutants could modify the antigenic potency of these particles. In addition, diesel exhaust emissions are thought to stimulate IgE synthesis, thereby facilitating allergic sensitization in predisposed subjects and the subsequent development of atopic respiratory diseases. Since concentrations of airborne allergens and air pollutants are frequently increased contemporaneously, an enhanced IgE-mediated response to aeroallergens and enhanced airway inflammation could account for the increasing frequency of allergic respiratory diseases, particularly those induced by pollen allergens, in urban areas. Lastly, allergens carried in the dust of such cereals as soy are able to induce outbreaks and even epidemics of asthma, which are not easily differentiated from asthma caused by urban air pollution.

Introduction

It is to Plinius the Younger [1] that we owe the first description of a fatal respiratory disorder induced by natural air pollution.

'Leaning on two servants, he brought himself upright and immediately collapsed again, I suppose because his breathing was affected by the dense fog that obstructed his

airways that were of a weak nature, narrow and subject to inflammation' [1].

The patient was Plinius the Elder, writer, scientist and head of the Roman fleet, who had moved to Pompeii in the Bay of Naples (Italy), to observe better the eruption of Mount Vesuvius in the year AD 73.

Plinius the Younger vividly describes the clouds of airborne matter (mainly sulphur dioxide and particulate matter) issuing from the volcano. In his letter he used for the first time the term 'inflammation of the airways' and in defining the airways of Plinius the Elder as being 'of a weak nature', he evokes the patient's constitutional predisposition. More than 2000 years later, millions of people in the nearby city of Naples are inhaling high levels of photochemical smog and many of these are affected by respiratory allergic disorders mainly induced by *Parietaria*, which grows abundantly in the city [2,3].

To my knowledge, the earliest report of a link between air pollution and a respiratory disorder is found in Henry Hyde Salter's book 'On asthma: its pathology and treatment' [4] where he lists 'impure air, animal emanations, hay fever and foods' among the causes of asthma. About 50 years later, William Lloyd observed that hay fever was a result of urbanization and agricultural changes [5].

Allergic respiratory diseases such as bronchial asthma and rhinitis have become more common in the last two decades [6–10]. In particular, pollen-related allergy affecting the nose and the tracheal-bronchial tract have become more frequent in the industrialized world [2,3,9,10].

Allergy to grass pollen is now very common. In fact, between 8% and 35% of young adults in countries of the European community show IgE serum antibodies to grass pollen allergens [11]. Subjects living in urban areas tend to be more affected by plant-derived respiratory disorders than those who live in rural areas. A classical study in this sense is work by Ishizaki and co-workers who showed that the prevalence of respiratory allergy was higher in subjects living near roads bearing heavy traffic than in subjects living in areas with higher atmospheric concentrations of pollen allergens but with less traffic [12]. However, these results should be interpreted with caution because various factors, which were not examined, can affect the findings.

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In 1992, shortly after the fall of the Berlin Wall, von Mutius and colleagues [13] investigated whether the diverse types of pollution and different lifestyle found in East versus West Germany influenced the incidence of allergic respiratory diseases. They found that allergic conditions such as hay fever were more common in Munich (former West Germany) than in Leipzig (former East Germany), whereas the prevalence of chronic bronchitis was higher in East Germany. This difference was related, among various factors, to the type of air pollution; i.e. prevalently vehicle emissions (nitrogen dioxide and respirable particulate matter) in West Germany whereas in East Germany the air pollution was mainly characterized by high concentrations of suspended particulate matter and even higher concentrations of sulphur dioxide arising from the burning of coal with a high content of sulphur for heating and energy production. The same group subsequently demonstrated [14] that the prevalence of hay fever in schoolchildren living in Leipzig increased from 2%–3% in 1991–1992 and to 5.1% in 1995–1996 (i.e. 6–7 years after the unification of Germany), while the prevalence of all IgE-mediated sensitizations increased from 19.3% in 1991–1992 to 26.7% in 1995–1996. Thus, the difference in type of allergic disorder formerly observed between sensitized subjects from East and West Germany is progressively decreasing as the former East Germany becomes more westernized and more exposed to vehicle traffic [15]. In a study carried out in the UK, the majority of preschool children admitted to hospital for asthma attacks lived in areas with intense traffic [16]. Similarly, Pershagen and colleagues in Sweden observed a significant correlation between exposure to outdoor nitrogen dioxide derived from vehicle emissions and hospital admissions from wheezing in Swedish preschool girls [17].

The high concentrations of gases and particles produced by motor vehicles now found in urban areas have resulted in a severe deterioration of air quality. Every 100 km, a car emits a mean value of about 1 kg of pollutants into the atmosphere. However, correlations between clinical responses and levels of air pollution should be viewed with caution even though air pollutants are known to increase bronchial hyper-reactivity and, hence, induce a temporary vulnerability of asthmatic subjects to other environmental agents that are not normally of clinical significance. Similarly, despite evidence of a correlation between respiratory pollen allergy and air pollution, the nature of this link is still a matter of speculation [3,18–23]. In studies on air pollution and respiratory allergy, the effects of single pollutants cannot be separated, so that correlations between individual components and effect on the airways do not necessarily imply a unique and direct relationship of cause and effect. Moreover, it is important to take account the confounding effects of cigarette smoke, indoor pollutants, exposure to perennial

or seasonal allergens in atopic subjects, meteoroclimatic conditions, etc. The issue is further confounded by the fact that measurements made in the laboratory do not consistently reflect what happens under natural conditions. There are various differences between natural and simulated exposure: in the laboratory we cannot reproduce the variable exposure to air pollution and allergen-carrying pollen that occurs in urban areas. As a consequence, even though it is plausible that urban air pollution plays a role in the onset and in the increasing prevalence of allergic respiratory diseases, including pollen allergy, it is not easy to show that this happens at urban level.

Nonetheless, the WHO National Institutes of Health report on asthma [24] lists components of air pollution among the asthma risk factors that act not only as inducers (involved in the onset or development of asthma in previous nonasthmatic individuals) but also as trigger risk factors involved in the development of exacerbations in asthma sufferers (already sensitized individuals).

Urban outdoor air pollutants and plant-derived airborne allergens implicated in allergic respiratory diseases

Although the nature and concentration of outdoor pollutants vary from one area to another, the most abundant pollutants in the atmosphere of urban areas are nitrogen dioxide, ozone and respirable particulate matter. Outdoor levels of nitrogen dioxide, which exert an oxidizing effect, are not usually associated with notable changes in bronchial function in asthmatic patients. Differently, particulate matter and ozone cause inflammation of the airways of susceptible subjects. This leads to increased permeability, thereby favouring penetration of pollen allergens in the mucous membranes and, in turn, easier access and interaction with cells of the immune system [25]. There is also evidence that predisposed subjects experience enhanced airway reactivity after exposure to air pollution and consequent increased airway responsiveness to inhaled allergens [26].

Ozone

Ozone is the main component of photochemical oxidants and probably accounts for up to 90% of total oxidant levels in cities that enjoy a mild sunny climate. It is generated at ground level by photochemical reactions involving nitrogen dioxide, hydrocarbons and ultraviolet radiations. Ozone trends depend not only on substrate supply (emissions of nitrogen dioxide by cars) but also on sunny weather that facilitates the transformation of nitrogen dioxide into ozone, thereby producing photochemical smog. Current safety standards for ozone levels are frequently exceeded in most Mediterranean countries.

Environmental ozone could affect pollen viability by influencing its production and its allergenic content [27]. This effect seems to be enhanced by ultraviolet radiation [28].

Ozone can affect both the upper and lower respiratory tract. Dose–response studies in healthy exposed subjects show that about 20% of persons are more sensitive to ozone than average, and that forced expiratory volume in 1 s (FEV₁) values decrease continuously with length of exposure, up to 6 h [25]. However, ozone induces more adverse effects in asthmatic individuals than in healthy subjects [26].

Exposure to ozone may increase the risk of allergic sensitization in predisposed subjects. Indeed, by lowering the threshold concentration of allergen able to induce the appearance of clinical symptoms, it can enhance the airway responsiveness of sensitized subjects. In this context Molino *et al.* [29] found that the mean provocation dose of ragweed necessary to reduce FEV₁ by 15% was significantly reduced to about half the dose of allergen when the patients were pre-exposed to ozone versus pre-exposure to air. Differently, Ball *et al.* [30] observed that pre-exposure to ozone versus pre-exposure to air did not decrease significantly the dose of allergen required to reduce FEV₁ by 15%. The discrepancy between the two studies is probably due to methodological differences in sample selection and to repeated exposure to the allergen used for the challenge.

Jorres *et al.* [31] demonstrated that previous exposure to a concentration of ozone higher than normal for a prolonged period of time increased airway responsiveness to allergen administered by inhalation in allergic exercising asthmatics. Peden *et al.* [32] showed that 0.4 p.p.m. of ozone for 2 h enhanced the concentration of eosinophils in the nasal mucosa after nasal allergen challenge and also reduced the dose of allergen necessary to induce a preset symptom score.

Devalia *et al.* [33] investigated the effect of previous exposure to ozone and nitrogen dioxide on subsequent allergen-induced changes in the nasal mucosa of patients with seasonal allergic rhinitis or perennial allergic asthma. They found that exposure to these pollutants significantly increased the allergen-induced release of eosinophil cationic protein in nasal lavage. These results suggest that exposure to ozone and nitrogen dioxide may 'prime' the eosinophils to subsequent activation by inhaled allergen in atopic patients. Taken together, these studies indicate that the concentration of ozone and length of exposure is critical, with a possible threshold in the region of 0.1–0.2 p.p.m. However, it is noteworthy that over 40 years ago Stokinger *et al.* [34] showed that exposure to nonlethal doses of ozone in rats enhanced their capacity to withstand subsequent exposure to higher levels – a peculiarity that was defined 'tolerance'. Subsequent studies [35,36] showed that of 4–5

days of ozone exposure, the highest effect on spirometric evaluations (FVC and FEV₁) are observed on the second day, after which there is a progressive decrease of subjective and spirometric measurements [36–38]. The reduction of responsiveness to ozone has been defined 'adaptation' and persists for 4–7 days after cessation of exposure, declining progressively thereafter [36–38]. Bronchial alveolar lavage studies show that tissue damage and inflammation usually progress, despite adaptation observed at spirometry [38].

Particulate matter

Airborne particulate matter, which is a major component of urban air pollution, is a mixture of solid and liquid particles of different origin, size and composition. The inhalable particulate matter is constituted by particles less than 10 µm in diameter (PM₁₀) and there is a fine fraction <2.5 µm (PM_{2.5}), which can reach the lower airways. According to the United Nations data, particulate matter is the most severe air pollution problem in many cities and towns [10]. Studies carried out in various geographical areas showed that particulate air pollution is significantly associated with enhanced mortality from respiratory and cardiovascular diseases, exacerbations of allergies, asthma, chronic bronchitis, respiratory tract infection and hospital admission [39–43]. However, although the statistical approach has provided evidence for a correlation and has shown it is biologically plausible, conclusive proof of a causal relationship is still outstanding. Adverse health events have been observed also in a range of air concentrations considered safe according to WHO guidelines [44].

Diesel exhaust particulate (DEP) accounts for most of the airborne particulate matter (up to 90%) in the atmosphere of the world's largest cities [45]. Thanks to its ultrafine size, DEPs present a large particle number (about 100 times more particles per mile than petrol engines of equivalent power) and surface area to the airways per unit of deposited mass of particles [46].

Experimental studies have shown that DEP causes respiratory symptoms and is able also to modify the immune response in predisposed animals and humans [47–57]. In fact DEP seems to exert an adjuvant immunological effect on IgE synthesis in atopic subjects thereby influencing sensitization to airborne allergens [47,49–51]. Nearly a decade ago Rudell *et al.* [48] showed that healthy volunteers exposed to DEP had a greater number of alveolar macrophages, neutrophils and T lymphocytes in bronchial alveolar lavage than did controls. In the wake of these and other observations [49,50], recent studies confirmed the effects favouring airway inflammation and demonstrated an atopy-enhancing effect of diesel exhaust.

Diaz-Sanchez *et al.* [53] studied the effect of DEP on antigen in ragweed-sensitive subjects challenged (nasal

provocation test) with DEP, Amb a1 (the major ragweed allergen) and a combination of DEP and Amb a1. Nasal washes, performed 18 h, 4 days and 8 days after challenge were examined to evaluate total and ragweed-specific IgE. Provocation with ragweed led to an increase in both total and ragweed-specific IgE in nasal lavage fluid. The DEP challenge increased the concentration of ragweed-specific IgE 16-fold versus concentrations observed after challenge with ragweed alone. The same group observed that combined exhaust particulate and ragweed allergen challenge markedly enhances human *in vivo* nasal ragweed-specific IgE and skews cytokine production to a T-helper cell 2-type pattern [50]. All these results are in agreement with a role for DEP in the enhanced allergic inflammatory response.

As to the underlying DEP-related allergic respiratory disease, we know that DEP can adsorb aeroallergens released by pollen grains and can prolong the retention of the allergen so as to provide for an enhanced IgE-mediated response. Diesel exhaust particulates exert their effect by way of components such as the hydrophobic polyaromatic hydrocarbons [51–53]. The DEPs are deposited on the airway mucous membranes (epithelial cells and macrophages are the first cells to come into contact with inhaled particulate matter) and the aromatic hydrocarbons allow them to diffuse easily through cell membranes and bind to a cytosolic receptor complex. Through the subsequent nuclear action, aromatic hydrocarbons can modify the growth and the differentiation programmes of cells [51,53].

Human epithelial cells and macrophages are able to phagocyte the particles leading to the production of the inflammatory cytokines IL-6, IL-8 and GM-CSF [54,55]. IL-8, which is increased in lung and nasal washes of asthmatic and/or rhinitic subjects, plays a role in the atopic inflammatory response of airways activating chemotaxis of lymphocytes, neutrophils and eosinophils, and inducing release of histamine, plasma leakage, smooth muscle contraction of airways

and a consequent increase of airways hyper-responsiveness [54,55].

The data on DEP are of particular interest in view of the increasing percentage of new cars with diesel engines in industrialized countries. In Europe, for example, more than 25% of cars purchased in 1998 were diesel-powered (Table 1), and it is forecast that 50% of all new cars will be diesel-powered in 10 years thanks to their lower maintenance costs. Diesel-powered cars are usually promoted as being environmentally friendly because they produce up to 25% less CO₂, which is a major contributor to global warming. However, since diesel engines are a major source of PM₁₀, perhaps the policy of encouraging their use should be reconsidered.

Plant-derived allergens

Pollens of urban areas

Two factors are required for the onset of allergic respiratory symptoms: sensitizing agents and genetically-committed individuals. Among the sensitizing agents, pollen allergens, besides being potentiated by air pollutants, can in themselves trigger acute, and sometimes also severe exacerbations of allergic respiratory diseases [3,24,25]. Of course, pollen grains, which are the primary carriers of pollen allergens, reach their highest levels in the atmosphere in coincidence with pollination seasons.

The most allergenic pollen grains are those from grasses, ragweed and *Parietaria*. The peculiarity of the latter is to grow inside the city (see section on Naples) [58]. The Japanese cedar has proved useful in illustrating the higher frequency of plant-related allergic respiratory disease in urban versus rural areas [12,59].

Because of the increase in pollen-related allergy and the increase in travel for professional and recreational purposes, it has become increasingly important to 'map' airborne pollen concentrations [60,61]. Pollen calendars, which are compiled from the number of pollen grains 'trapped' in a collecting device, although useful do not consistently reflect the exact amount of allergen in the air because they do not take account of the allergen carried by paucimicronic particles, which can be measured only with immunological methods. In addition, pollen calendars should be regularly updated because airborne concentrations of pollen are affected by various factors, i.e. climatic changes that affect some plants, fluctuations in gardening trends with new trees (e.g. birches) planted, colonization of central Europe by ragweed, etc. [60,61].

As for prevention of pollen allergy, an ideal but hardly feasible approach, is to minimize the risk of contact with these agents, by moving to a nonrisk area. A much easier alternative, is to reduce inhalation of pollen allergens by remaining at home with the windows closed [62].

Table 1. Percentage of diesel-powered cars in Europe in the year 1998. European mean value: 25.3.

Austria	54.0
Belgium	52.2
Spain	47.3
France	40.2
Italy	22.5
The Netherlands	20.3
Portugal	18.8
Germany	17.6
UK	15.3
Sweden	11.0

Paucimicronic particles carrying pollen allergens

According to aerodynamic calculations, airborne allergen-carrying particles greater than $10\text{ }\mu\text{m}$ in diameter such as all allergenic pollen grains, are too large to penetrate medium-sized and small airways. However, bronchial asthma and its equivalents such as irritative cough, which derive from the tracheal-bronchial tract, are not infrequent in pollen-allergic patients. Moreover, patients monosensitized to pollen antigens and with classical symptoms during the flowering period can experience symptoms also out of the pollen season. In other words, even though it is plausible that, despite aerodynamic principles, a small number of pollen grains may penetrate into the lower respiratory tract, particularly by mouth breathing, there is now evidence of the presence in the atmosphere of allergen-carrying particles much smaller than intact pollen grains, which can interact with pollutants in much the same way as with pollen grains [61,63–70]. Thanks to their size, these microdroplets may penetrate deep into the airways, inducing asthma in sensitized-atopic subjects. It is also conceivable that antigens associated with these minute particles are present during the pollen season, and that these antigens are responsible for allergic respiratory symptoms, particularly before the start and after the end of the pollen season, so prolonging the 'disease window' of sensitized patients. An offshoot of these studies is that the traditional 'pollen count' may be misleading as an index of outdoor allergen exposure in particular situations. In fact, the pollen count technique consists of examination under the microscope of pollen grains collected in volumetric pollen traps and the measurement of their concentration per m^3 of air, whereas aero-allergens carried by plant-derived airborne paucimicronic particles can only be identified by immunological methods [63–66].

The exact origin of these allergen-carrying paucimicronic particles has yet to be established. They probably derive from plant debris, e.g. fragments of vegetal parts. Indeed, they have been detected on leaves and stems of allergenic plants such as pellitory of the wall (*Parietaria*) and grasses (*Dactylis glomerata*) [67]. Allergens from pollen grains could also be transferred by physical contact or by elution in the atmosphere to other small particles, e.g. DEP. Another possibility is that under wet conditions or during thunderstorms, pollen grains may release, after rupture determined by osmotic shock, tiny starch granules ($0.5\text{--}2.5\text{ }\mu\text{m}$), which can reach the lower airways triggering asthma attacks in previously sensitized subjects [68–70].

'Air pollution' by plant-derived allergens

Among the various plants that are thought to be responsible for respiratory diseases including asthma are soybean and

ricinus. Soybean dust has been responsible for outbreaks of asthma frequently characterized for their clinical severity and that were first attributed to urban air pollution. Examples are the asthma epidemics that have occurred in cities with large industrial port facilities. From 1981 to 1987, 26 outbreaks of asthma with 11 deaths occurred in the city of Barcelona. Nitrogen dioxide was first thought to be the cause, but the components of air pollution were not correlated with the asthma attacks [71]. The aetiological agent was subsequently found to be soybean dust released into the air during unloading of cargo into a harbour silo that was not equipped with a dust-control device. Antò and colleagues showed that about 74% of epidemic cases had specific IgE-antibodies versus a commercial soybean antigen in comparison with 4.6% of controls [72]. In addition, using the assays of urban aerosols collected with high-volume samplers and the RAST-inhibition technique they [73] demonstrated highly significant differences in the atmospheric content of soybean antigens between days marked by the asthma epidemic and days free of an excess of asthma cases. The strong association between airborne soybean dust and asthma outbreaks was reinforced by the allergen results of studies in atmosphere showing high values in epidemic days that contrasted the low values of nonepidemic samples [72,73]. In other words all these observations showed that asthma outbreaks were a 'point-source' epidemic. The protective measures, i.e. cargo unloading was allowed only after filters were fitted to the grain elevators, dramatically reduced airborne allergen levels of soybean dust and visits for asthma to the emergency room [74]. The specific IgE-serum levels in exposed subjects also progressively decreased.

Other outbreaks of asthma caused by soybean dust pollution have been reported in the Spanish cities of Tarragona and Cartagena [75,76]. In Naples, more than 100 patients were admitted to hospital for asthma in a single day in December 1993 [20]. This asthma outbreak coincided with the unloading of a cargo of soybean. Interestingly, neither in the Barcelona nor in the Naples outbreaks were there cases of severe asthma attacks in children.

Recently the asthma epidemic that occurred in New Orleans [77,78] has been re-examined [79]. In fact, the number of asthma attacks was higher on days when ships carrying soybean were anchored in the harbour. Attacks were also higher in concomitance with air stagnation and with winds carrying particles from two grain elevators. No association was observed between asthma attacks and the presence of ships carrying cargoes of wheat or corn [79].

Climate

Climatic changes, which are a consequence of the 'greenhouse' effect (warming of the atmosphere resulting from the

accumulation of carbon dioxide and ozone), influence the growth of allergenic plants. Over the last 20–30 years, some plants have become more abundant, and others less abundant. In addition, meteorologic conditions such as sunshine not only favour the formation of ozone, which derives from nitrogen dioxide, but also the flowering of allergenic plants.

The epidemics of asthma attacks that occur in association with humid weather or with thunderstorms (see section on paucimicronic particles) are probably induced, at least in part, by the interaction between climatic conditions and allergenic pollen. In concomitance with thunderstorms, pollen grains, in particular grasses, may rupture and release into the atmosphere part of their cytoplasmatic content, mainly starch granules, which can carry allergens. These granules measure between 0.5 and 2.5 μm and can be inhaled deeply into the airways [68,69].

Wallis *et al.* [80] observed that 283 of the 640 patients attending the emergency departments of various London hospitals for asthma attacks or other airway diseases after a thunderstorm were not known asthmatics. The authors suggested that this asthma outbreak was probably induced by rupture of grass pollens and release of their allergenic content carried by starch granules.

Interaction in the atmosphere of air pollutants with pollen grains or with paucimicronic particles

Some atopic subjects develop respiratory allergic diseases in response to the stimulation induced by components of air pollution. The effect is more pronounced when these components are inhaled in combination with aeroallergens. It has been suggested that air pollutants may favour sensitization and development of allergic respiratory diseases by increasing or reducing the allergenic potency of airborne antigens carried by pollen grains or other debris of vegetal origin. The rationale for an inter-relationship (in atmosphere and/or on airways of exposed subjects) between agents of air pollution and pollen allergens or airborne paucimicronic particles carrying allergens is described:

- Interaction between components of the air pollution (in particular diesel exhaust particles) and pollen grains, i.e. increased release of antigens characterized by modified allergenicity;
- Interaction in atmosphere between air pollution and paucimicronic particles derived from plants and carrying allergens. (The source of these particles is unclear, but they may be breakdown products of pollen grains, such as starch granules or derived from part of the plant such as leaves and stems);
- Inflammatory effects of components of the pollution on airways of exposed subjects, i.e. increased permeability, easier penetration of pollen allergens in the mucous

membranes and easier interaction with cells of the immune system;

- Increased airway reactivity in predisposed subjects induced by air pollution and increased bronchial responsiveness of these patients to inhaled allergens or to a specific irritative agents.

Thomas *et al.* [81] studied the effect of a 4-h exposure to 50–200 p.p.b. nitrogen dioxide on the viability, germination and protein release from freshly collected birch, rye, alder and hazel pollen grains. They showed that exposure to 100 p.p.b. nitrogen dioxide modulated the protein content of pollen grains.

Behrendt *et al.* [82] observed that pollen collected from areas with high levels of air pollution (roadsides with heavy traffic, etc.) were covered with airborne microparticulates (5 μm or less in size) and postulated that interaction between pollen allergens and these particules is able to alter the allergenicity of pollen antigens. It has been also suggested that the quantity of inorganic air pollution attached to the surface of pollen grains could be a marker of air pollution [83].

As mentioned above, airborne paucimicronic particles, pollen-derived or not, can carry plant-derived allergens and plant-derived allergens can be carried by airborne particulate matter such as DEP. In this context, Knox *et al.* [70] studying the binding of two grass pollen allergens (Lol p 1 and Lol p 5) to DEP, observed that Lol p1 bound to DEP *in vitro*, whereas Lol p5 did not. This difference was attributed to the glycosylation of the allergen (Lol p1 is an acidic glycosylated allergen, whereas Lol p5 is a basic one, nonglycosylated) and/or to isoelectric point. At the pH used in their study Lol p1 was negatively charged and Lol p5 positively charged. However, the process of transfer of pollen allergen from pollen grains to nonspecific environmental particulate matter might explain the wide range of size (from submicronic to paucimicronic) of these allergen carriers [61,63,67–70].

Naples as a model of interaction between air pollution and pollen allergens

The city of Naples serves as a good model with which to study the interaction between pollen-derived allergen and air pollution. It has about 2 million inhabitants and very dense traffic. It is located in a coastal area enclosed on three sides by hills and mountains. The year-long sunny days favour high levels of ozone. This situation, on days without wind and rain, favours critical episodes of air pollution. The climate also favours the pollination of *Parietaria*, which grows in abundance throughout the city [2,3,58]. About 30% of inhabitants are allergic to this plant and more than 50% of these *Parietaria* pollen-allergic subjects experience bronchial asthma and its equivalent, with high level of bronchial hyper-responsiveness [2,3,58,84].

The prevalence of *Parietaria*-induced allergic respiratory disorders tends to increase and there is a peak in the number of emergency room visits for allergic asthma attacks when there is an increase in airborne concentrations of *Parietaria* pollen grains and a parallel increase of ozone levels. This parallel increase usually starts in February and peaks between May and June when *Parietaria* pollen grains reach levels of about 1000 grains/m³ of air. After July the production and release of *Parietaria* pollen usually decreases, while ozone levels remain high also in autumn during which the concentration of *Parietaria* pollens is low. There is also a diurnal correlation of both peaks, since *Parietaria* pollen and ozone reach their highest levels in morning. *Parietaria* peaks earlier than ozone because of the time required for the photochemical reaction to develop.

In studies ongoing in our Department on the interrelationship between components of air pollution and *Parietaria* pollen allergens and using the RAST-inhibition, we found that exhaust emissions from noncatalytic cars increased the allergenic potency of *Parietaria* pollen as compared with exhaust emissions from catalytic cars.

Concluding remarks

The prevalence of allergic respiratory diseases is increasing in industrialized countries, so much so that it is being called the 'epidemic of the 21st century'. The prevalence of plant-derived respiratory diseases is higher in urban than in rural areas, and there is a large body of evidence of an interaction between urban air pollution, mainly due to vehicle traffic, and plant-derived respiratory disorders. Studies are now ongoing in various laboratories aimed at clarifying the mechanism underlying the interaction, if any, between urban air pollution and pollen-related, or more extensively plant-related respiratory disorders.

Other studies are required to establish the aetiological role of air pollutants, the modality of penetration into the body after inhalation (e.g. the role of dendritic cells in capturing them), etc.

According to United Nation's figures [10], in the year 2000 about 50% of the world's population will live in urban areas and about 400 million of city inhabitants will be exposed to levels of air pollutants derived from motor vehicles that are a risk to health – a sobering thought.

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