

EDITORIAL

Outdoor air pollution, climate and allergic respiratory diseases: evidence of a link

There is compelling evidence that the prevalence of allergic respiratory diseases such as rhinosinusitis and bronchial asthma has increased in recent decades and a great deal of research is being done to identify the causes [1–3].

Allergic respiratory diseases are the result of an interaction between genetic background and the environment. However, the increased prevalence has occurred in too short time to attribute it to genetic changes and identification of environmental factors is useful to develop strategies for prevention. Although the exact cause of the rise in asthma prevalence and mortality is not known, among the various factors implicated, indoor and outdoor air pollution is felt to play an increasingly important role [4–9].

Health effects of air pollution have received attention because it appears that the increase in allergic respiratory diseases, which is observed more in urban than in rural areas, is paralleled by increasing atmospheric concentration of traffic-related air pollutants as gases and respirable particulate matter, and rhinitis and bronchial asthma are diseases which can be aggravated by inhaled compounds. A correlation has also been found between increased atmospheric levels of air pollution and increased frequency of mortality for respiratory and cardiovascular diseases [10–14].

There is evidence that living near roads with high levels of car traffic is associated with impaired respiratory health and that road traffic, with its gaseous and particulate emissions, is currently, and is likely to remain, the main contributor to air pollution in most urban settings [15–17].

The air pollution level of urban cities is also continuously increasing in areas of the world such as eastern Europe and China, where until now there were low levels of air pollution.

Attention has been focused on the role of motor vehicle-derived air pollutants not only in the exacerbation of symptoms in already allergic subjects but also in the facilitation of allergic sensitization of the airway in predisposed, atopic subjects [8, 18, 19].

The effects of air pollutants on lung function depend largely on the type of pollutant and its environmental concentration, the duration of pollutant exposure, the total ventilation of exposed subjects and their predisposition to develop airway hyper-responsiveness.

The most frequent components of traffic-related urban air pollution are inhalable particulate matter (PM₁₀ and PM_{2.5}), nitrogen dioxide (NO₂) and ozone (O₃). Various studies have demonstrated that inhalation of air pollutants such as O₃, NO₂ and sulphur dioxide (SO₂), either individually or in combination, can enhance the airway response to inhaled allergens in atopic subjects inducing asthma exacerbations [8, 19, 20]. In particular, they have been found to enhance airway inflammation and to enhance both the immediate- and late-phase response to inhaled allergens.

However, despite evidence of a correlation between the increasing frequency of respiratory allergy and the increasing trend in air pollution, the interpretation of some studies is confounded by the effect of exposure to indoor pollutants such as cigarette smoke and to aeroallergens. As for the inter-relationship between air pollution and aeroallergens, it has been observed that air pollution and climatic variations can have an indirect effect on allergic responses by influencing the pollen production of allergenic plants both qualitatively and quantitatively [20, 21]. Moreover, allergenic pollen grains or paucimicronic particles carrying allergens can interact in atmosphere with components of air pollution with increasing allergenic effects or inhaled air pollution can prime the respiratory mucous membranes of predisposed subjects facilitating the inflammatory response of airways to the aeroallergens [19–21]. In other words airway mucosal damage and impaired mucociliary clearance induced by air pollution facilitate the access of inhaled allergens to the cells of the immune system.

It has also been demonstrated that air pollutants such as diesel exhaust particulate (DEP) [18, 22] and O₃ [23] can not only trigger allergic exacerbations in previous sensitized subjects but also favour the appearance of allergic respiratory symptoms in subjects who previously did not show any clinical symptoms. In particular, it has been observed that combined diesel exhaust particulate and ragweed allergen challenge enhances human *in vivo* nasal ragweed-specific IgE and skews cytokine production to a T-helper cell 2-type pattern [18]. Recently it has been observed that the incidence of new diagnoses of asthma are associated with heavy exercise in communities with high concentrations of O₃, thus, air pollution and outdoor exercise could contribute to the development of asthma in children [23].

Among gaseous air pollutants motor vehicles produced NO₂ appears to be a marker of vehicle-generated air pollution. Periodically in urban areas high concentrations of NO₂ can be found, even though the most significant exposure to NO₂ occurs indoors in conjunction with the use of gas cooking stoves and kerosene space heaters [24]. NO₂ is a precursor of photochemical smog, is generated by the burning of fossil-derived fuels in outdoor air in urban and industrial regions and, in conjunction with sunlight and hydrocarbons, results in the production of ozone (Fig. 1). Automobile exhaust is the most significant source of outdoor nitrogen dioxide, although power plants and other sources that burn fossil fuels also release nitrogen dioxide into the environment. Like ozone, nitrogen dioxide is an oxidant pollutant, although it is less chemically reactive and thus probably less potent. Outdoor levels of nitrogen dioxide are not usually associated with notable changes in bronchial function in asthmatic patients and controlled exposure studies of subjects with asthma have produced contradictory results regarding the ability of nitrogen dioxide to enhance non-specific

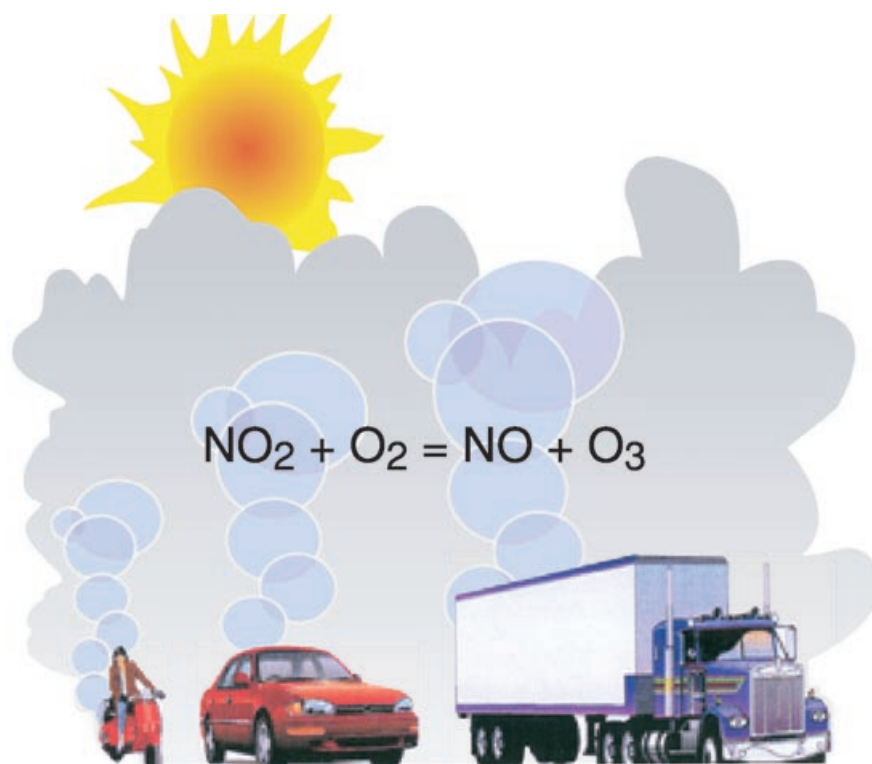


Fig. 1. Ultraviolet radiation in urban polluted air acting on nitrogen dioxide favour the formation of ozone and photochemical smog which is exacerbated by elevated daytime temperature, low wind speeds and clear skies.

airway responsiveness with some evidence of a subgroup with increased sensitivity [25–27]. Controlled exposure studies indicate a low increase of bronchial hyper-responsiveness in asthmatic subjects as a consequence of NO_2 inhalation. Limited data from epidemiologic studies suggest that exposure to high levels of nitrogen dioxide may be associated with acute decrements in lung function in subjects with asthma.

There are two European studies on the acute effects of NO_2 and one of which has found adverse effects of NO_2 [28, 29].

The PEACE (Pollution Effects on Asthmatic Children in Europe) evaluated 2010 children with chronic respiratory symptoms and time-series analyses revealed no clear associations of air pollution with symptoms and lung function [28]. However, bias factors should be low level of air pollution in the 14 involved European centres.

The Air Pollution and Health: the European Approach (APHEA) project utilized data on daily pollutant levels from 15 European cities with a population of more than 25 million. It has been found that an increase of $50 \mu\text{g}/\text{m}^3$ in 1-h maximum of NO_2 and O_3 was associated with a 1.3% and 2.9% increase in daily all-cause mortality, and a $50\text{-mcg}/\text{m}^3$ increase in 24-h average NO_2 alone was associated with an increase of 2.6% in asthma admissions [29].

Among other controlled human exposure studies Bayram et al. [30] demonstrated that ozone and nitrogen dioxide modulate the airway inflammation of diseases such as bronchial asthma by increasing the release of inflammatory mediators from bronchial epithelial cells and that the cells of asthmatic subjects may be more susceptible to the adverse effects of these pollutants.

Devalia et al. [19] 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.

The impact of climate and long-term exposure to NO_2 on allergic rhinitis and asthma was assessed by de Marco et al. [31] in a cross-sectional study conducted on young adults living in 13 areas from two different Italian climatic regions (subcontinental and Mediterranean). Mediterranean areas had a significantly higher prevalence of asthma-like symptoms, higher annual mean temperature, lower temperature range and lower NO_2 levels than subcontinental ones. Moreover, Mediterranean climate was associated with an increased risk of wheeze, tightness in the chest, shortness of breath and asthma attacks. After adjusting for climate, an increase of $18.3 \mu\text{g}/\text{m}^3$ in NO_2 levels moderately increased the risk of asthma attacks, tightness in the chest and wheeze. When the levels of outdoor NO_2 exposure rose, the prevalence of allergic rhinitis increased significantly in the Mediterranean region, but not in the subcontinental one, while the prevalence of asthma became greater when the annual mean temperature increased and temperature range decreased. Moreover, climate interacting with outdoor NO_2 increased the risk for allergic rhinitis in subjects exposed to high stable temperatures. The positive relationship between NO_2 and most asthma-like symptoms suggests that long-term exposure to

traffic-related air pollution increases the risk of having asthma, while the positive association between the prevalence of allergic rhinitis and NO₂ detected only in the Mediterranean region may show that climate interacts with outdoor air pollution. In other words climate was significantly and positively associated with asthma attacks and asthma-like symptoms and this means that in multicentre studies on air pollution climate should be a confounder factor if not controlled when centres belong to different climatic regions [31].

However, considering that in Mediterranean area the long-term presence of ultraviolet radiation induces frequently high levels of O₃, which derives from NO₂, O₃ too is likely to exert an inflammatory action stronger than NO₂ on the airways. Unfortunately, the data on O₃ concentration were not available for all centres participating in the study of de Marco [31]. However, so many are the reports of inflammatory effects of gaseous and particulate compounds on airways that we can no longer afford to put off taking preventive measures to reduce current levels of traffic-related air pollution.

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G. D'AMATO

Division of Pneumology and Allergology

Department of Chest Diseases

Hospital A. Cardarelli

Naples,

Italy

E-mail: gdamato@qubisoft.it