**EDITORIAL**

Respiratory effects of air pollution: the importance of a multidisciplinary approach to conduct research

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Investigation of the respiratory effects of air pollution were started in the late fifties after the important "air pollution episodes" in London, UK (1952) and in Donora USA (1948) [1, 2], when daily mortality increased on days with high levels of air pollution. These episodes clearly pointed out that urban air pollution may influence human health. This evidence encouraged research to focus on the identification of the pollutants responsible, and to start experimental studies aimed at identifying the mechanisms by which pollutants may act in the different parts of the respiratory tract. In addition, epidemiological studies were set up with the goal of defining a cause-effect relationship for different epidemiological variables (mortality, morbidity). Studies were initially devoted to the investigation of the possible effects of SO₂ and suspended particles [3].

Subsequently, the initiatives to protect the environment increased and important political actions were undertaken to reduce the burden of pollutants. Simultaneously, technical advancements were achieved to reduce, in the production process, the emission of pollutants (e.g. new devices for car exhausts, unleaded fuel, etc.). Similar examples may be reported for many industrial processes.

Although a significant improvement in the quality of air has been obtained, especially in the developed countries, in the late 1960s and 1970s, urban air pollution is still present; however, with important qualitative modifications. Oxidant pollutants such as NOₓ, O₃ and suspended particles reacting with these substances (nitrates in urban air) are commonly present. In addition, many carcinogens and mutagens have been found in suspended particles (benzopiren, nitropyrene, etc.).

The presence of additional biological pollutants may cause serious respiratory problems, as demonstrated by the case of the asthma epidemics in Barcelona [4]. The current scenario of the developed countries is that of a deep concern about air pollution, with an improvement in the quality of air for certain pollutants (mainly SO₂), but the presence of other air pollutants in urban areas continues to chronically and subtly affect the airways of humans. In fact, recent data clearly demonstrate that even in 'cleaner' cities, mortality is affected by daily peaks in the increase of air pollution.

Recently, all relevant studies were considered in a meta-analysis by Schwartz et al. [5, 6], who confirmed a relative risk of elevated mortality of 1.06 (95% confidence interval (95% CI) 1.05 – 1.07) for 100 mg·m⁻³ of suspended particulate pollutants. Additional analyses pointed out that peaks of air pollution were associated with increased mortality from pneumonia and chronic respiratory disease. Other epidemiological studies reported increased admissions for asthma and chronic obstructive pulmonary disease (COPD), increased prevalence of respiratory symptoms and diminished lung function, with the presence of higher levels of air pollution [3, 7, 8]. At the same time important advancements in knowledge of the pathogenic mechanisms of asthma and COPD were obtained, particularly about the presence of an inflammatory response in the airways and the terminal portions of the lung, and about the functional role of increased bronchial responsiveness [9, 10]. Thereafter, experimental studies in animals were able to document the inflammatory response of the lung after exposure to different pollutants [11–15].

In recent years, direct effects of air pollutants were also investigated by experimental models in humans (normal volunteers and subjects with disease). Initially, studies were devoted to confirming pulmonary function changes after exposure to different concentrations of pollutants (SO₂, particles, NO₂, O₃) in resting conditions and after exercise. Subsequently, more sophisticated techniques, such as bronchoalveolar lavage (BAL), were used [16–19].

In this issue of the Journal, a review series on the respiratory effects of air pollutants is inaugurated. The first paper by Sandstrom [20] deals with experimental studies in humans. It illustrates that the use of BAL confirmed the inflammatory response in the lungs and delineated the different types of cells and mediators involved following exposure to various air pollutants. Both the limitations and the advantages of controlled exposure studies in humans are clearly outlined. Obviously, exposure of humans in closed chambers with standardized atmospheres, containing fixed concentrations of single or mixed air pollutants, over a defined period of time, with or without selected workload, can mimic acute exposure conditions in the environment. Such human exposure models can reveal differences in the reactivity between healthy subjects versus patients with airways disease, or nonsmokers versus smokers [16]. Furthermore, responders and nonresponders, for instance to ozone, may be identified, and the mechanisms accounting for the individual susceptibility may then be investigated at a cellular and molecular level [17]. Limitations of controlled human exposure studies are, however, that only the acute...
Effects but not the long-term effects of chronic exposure over years can be studied, for obvious reasons. Also, large biopsies of the lung parenchyma to obtain sufficient material for detailed tissue analysis are unethical in human volunteers due to the inherent morbidity and mortality. Thus, there is a continuous need for animal studies, including those with large and long-living animals, like monkeys or dogs, over a prolonged period of time, to elucidate the biological effects of long-term exposure in controlled atmospheres for defined air pollutants [18, 19]. In forthcoming issues of the Journal, additional reviews will be published on animal studies and on the current situation of the epidemiological evidence.

It is important to conclude this editorial by confirming the need to continue the research in this field by a multidisciplinary approach. In fact, the epidemiological studies of the first generation (mortality and morbidity data per se), though still important, should now use the new biological tools currently available. In future epidemiological studies, we need to characterize better the exposure to the different air pollutants at an individual level. The determination of "biomarkers" of exposure should be promoted in biological samples (blood, urine, cells) and, possibly, at the level of the target organ (e.g. cells from mucous secretions). Protein or deoxyribonucleic acid (DNA) adducts to carcinogens are examples of the use of markers of exposure [21]. Additional improvement should also be obtained to better define the "outcome" of epidemiological studies (e.g. the characterization of respiratory infections using polymerase chain reaction (PCR) technology, etc.).

Merging molecular biology with the investigation of epidemiology will give rise to an important advancement in this specific research area. Research at basic level (animal and human experimental studies) trying to use air pollution mixtures similar to those currently present in the urban areas on the one side, and epidemiological confirmation using high technology for biological characterization of outcome variables on the other, will allow further advancement of our knowledge on respiratory effects of air pollution.

References