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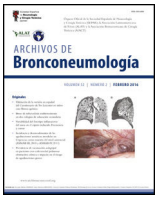

Editorial

Interaction Between Environmental Pollution and Respiratory Infections☆

Interacción entre contaminación ambiental e infecciones respiratorias

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The exposome is defined as the measure of all exposures of an individual during his or her lifetime and how these exposures affect health.[1] Humans are exposed to large quantities of compounds by inhalation, and the change from rural lifestyles to living in overcrowded, industrialized cities, together with the mass use of motor vehicles means that we are exposed to large amounts of contaminants via the respiratory tract. It is estimated that only 1 cubic centimeter of city air contains approximately 100 bacteria and around 10^7 small-diameter particles (less than 300 nm).[2] In fact, we now know that the outcome of an infection depends not only on host- and pathogen-associated factors, but also on key external factors. For example, environmental changes influence the flyways of migratory birds, which are vectors of the virus influenza A, modifying the spread of new variants of the influenza virus.[3]

The major environmental pollutants are basically particles in suspension, known as particulate matter (PM), and include metals or silica, volatile organic compounds, and gaseous pollutants, such as ozone, sulfur dioxide, nitrogen monoxide and dioxide, and carbon monoxide. They are generally produced naturally by sand storms or volcanic eruptions, or by humans, in the form of biomass burning, traffic emissions, mining, and farming. In large cities, however, most pollution is caused by the combustion of diesel engines.[4]

It is estimated that 7 million people die every year as a result of environmental pollution.[5] Poor air quality is a risk factor for the development of numerous respiratory diseases, such as asthma, lung cancer, and respiratory infections, especially in children.[6] Respiratory infections cause the death of more than 4 million people annually. In Europe, almost half a million people die every year due to high concentrations of PM, 78,000 die from exposure to nitrogen dioxide, and more than 14,000 die from exposure to ozone.[7] Exposure to high levels of sulfur dioxide has been associated with an increase in sputum production, chronic cough, and bronchoconstriction, and more frequent bronchiectasis exacerbations.[8]

Environmental pollution particles cause inflammation, airflow changes, and altered defense mechanisms, both in the upper and lower respiratory tract.[9] Larger PMs can be eliminated by mucociliary transport, but the smaller ones can reach the bronchioles. In addition, $PM_{2.5}$ (with a diameter of less than 2.5 μm) that are not phagocytized by macrophages can spread systemically.

Exposure to PM increases susceptibility to bacterial pneumonias and viral respiratory infections.[10] Exposure to environmental pollution in children affects the proper functioning of the respiratory system, especially in the early years of life, when the respiratory and immune systems are not yet fully developed. There is an association between bronchitis and environmental pollution in children under five years of age.[11] In fact, prenatal exposure to $PM_{2.5}$ increases susceptibility to respiratory infections (bronchitis and pneumonia), as many environmental toxins can easily cross the placenta (especially $PM_{0.25}$ and smaller) and accumulate in the fetus in higher concentrations than in the mother.[12] In the elderly, immunosenescence might contribute to an increased propensity to respiratory infections, due, among other factors, to cytokine deregulation.[12]

PM can cause oxidative stress by eliminating antioxidants and producing reactive oxygen species (ROS), which leads to an inflammatory response by producing cytokines IL-6, IL-8 and TNF-α^2. Moreover, exposure to PM can alter the ability of macrophages to inactivate viruses, lyse bacteria, or inhibit the presentation of antigens.[10]

Exposures to different nitrogen oxides can increase the risk of respiratory infections, affecting T cells and NK cells, which play important roles in the defense against viruses.[4] An accumulation of metals may also be a risk factor for infections, since metal availability is generally a factor promoting the growth of microorganisms. In *Mycobacterium tuberculosis* or *Neisseria meningitidis*, an increase in the availability of iron in the host is related to more serious infections.[10]

Tobacco smoke also causes exposure to high concentrations of PM, 15,000–40,000 μg PM per cigarette. In general, tobacco smoke exposure increases the risk of prolonging viral respiratory infections or developing bacterial infection by *Streptococcus*, *Legionella*,

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Mycoplasma, or *Haemophilus*.[10] It is also related to an increased susceptibility to infection by *M. tuberculosis*, and progression to active tuberculosis.[10] In cell cultures, we have observed that smoke negatively affects the phagocytic capacity of macrophages.[13] Exposure to tobacco smoke has also been linked with a delay in the negativization of mycobacterial cultures in treated patients.[14] In fact, exposure to smoke not only alters the immune response of the host, but also has an impact on the microorganism, modifying its phenotype toward other more virulent variants.[15]

Environmental pollution increases the rate of respiratory infections, and is associated with increased costs and premature deaths in chronic patients and children. Some of the causes can be acted upon, such as tobacco exposure and some aspects of environmental pollution. An understanding of how pollution affects the immune response to respiratory infections would help us establish effective epidemiological strategies, and improve clinical treatment and patients' quality of life.

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