

## Editorial

## Can Environmental Pollution Cause Asthma?☆



## ¿Puede la contaminación ambiental causar asma?

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Asthma is a worldwide health problem that is of particular significance in industrialized countries, where prevalence, which can range between 8% and 10% of the population, is increasing.<sup>1</sup> This generates a high socioeconomic burden in terms of absenteeism from work and school, use of resources (consultations, hospitalizations), and deaths. The World Health Organization (WHO) estimates that globally around 235 million people suffer from asthma.<sup>2</sup> In Spain, it is estimated that 3 million individuals are asthmatic.<sup>3</sup>

Although the increase in asthma figures may be due to improvements in diagnosis criteria and techniques, the importance of factors such as environmental pollution in industrialized countries must be taken into consideration.<sup>4</sup> Environmental pollutants can aggravate existing asthma,<sup>5–9</sup> or may be the cause of the disease. It is well known that high levels of particulate matter (diesel particles), ozone, sulfur dioxide and nitrous oxide (O<sub>3</sub>, SO<sub>2</sub> and NO<sub>2</sub>) can precipitate the onset of symptoms in asthma patients, increasing the number of visits to the emergency services and hospitalizations due to worsening disease.<sup>5</sup> However, a more controversial claim is that environmental pollution may be the cause of asthma. Chanel et al.<sup>6</sup> showed that living near roads with heavy traffic could account for 15%–30% of all new cases of asthma in children. Similarly, Gehring et al.<sup>7</sup> found that exposure to environmental pollution in early life could contribute to the development of asthma during childhood and adolescence. The SCAPE study also showed that an increase of 10 µg/m<sup>3</sup> in the environmental concentration of NO<sub>2</sub> was associated with the appearance of new cases of asthma in adults, although no association was found for increased particulate matter (PM).<sup>8</sup>

To establish causality, both significant epidemiological associations and biological plausibility need to be demonstrated. In this respect, the exact mechanisms by which environmental pollution can aggravate or cause asthma are still unclear. In individuals

with asthma, exposure to high concentrations of environmental pollutants can induce changes in lung function, basically via irritative mechanisms mediated by transient receptor potential (TRP) cation channel receptors. However, exposure to lower concentrations, as observed in European cities, may produce more specific inflammatory changes.<sup>9</sup> For example, exposure to ozone can produce neutrophilic inflammation in the lung, along with macrophage and epithelial cell changes that would generate proinflammatory mediators such as IL6, IL8 or TNFα.<sup>10</sup> Diesel particles can increase neutrophilic inflammation and the production of TH17 lymphocytes, which, combined with allergens, may cause increased bronchial hyperresponsiveness.<sup>11</sup>

In individuals without previous asthma, the combination of certain genetic factors and exposure to environmental contaminants may be the cause of the disease. Recent studies have shown a relationship between environmental pollutants and certain allelic variations in genes, some of which are involved in oxidative stress and inflammation.<sup>12,13</sup> Thus, some gene polymorphisms encoding antioxidant enzymes, such as glutathione S-transferase, may increase the risk of asthmatic responses to exposure to pollutants. Furthermore, the interaction of these genes with TNF can cause changes in the inflammatory response that predispose to the development of asthma.<sup>9</sup>

Environmentally-induced epigenetic changes could also cause asthma: environmental contaminants can directly cause epigenetic modifications. For example, exposure to diesel particulates has been shown to affect the methylation of genes involved in the innate immune system<sup>14</sup> and asthma.<sup>15</sup> Pollution can also indirectly cause epigenetic changes by modifying the composition of the microbiome. The mechanisms by which a specific microbiome can affect the epigenome have not yet been exactly clarified, but metabolic activity may play a relevant role.<sup>16</sup>

In addition to these genetic and epigenetic factors, changes in certain immunological mechanisms may also play an important role in the development of asthma. Animal and in vitro models suggest that exposure to pollutants such as diesel particles can cause the immune system to differentiate towards a TH2 and TH17 type mechanism. Interactions may also occur between allergens and diesel particles that could increase their antigenic properties, facilitating the development of asthma.<sup>11</sup> In any case, more in-depth

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studies on individual exposure to pollution and the phenotypic characterization of asthma are needed to broaden our understanding of the effect of atmospheric pollutants on the incidence of asthma.

In short, it seems likely that environmental pollution must be taken into consideration as a causative factor, not only of exacerbations but also of the disease itself, when treating a patient with asthma. On a wider level, although reducing the effects of pollution on health is to a large extent beyond the reach of the healthcare community, as medical professionals we must continue to make the authorities aware of the serious impact of environmental pollution on health. There is little doubt that much progress will be made in asthma research in the coming years, which will be of great interest to both the medical community and to society in general.

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