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Perspective

Air pollutants and early origins of respiratory diseases

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Abstract

Air pollution is a global health threat and causes millions of human deaths annually. The late onset of respiratory diseases in children and adults due to prenatal or perinatal exposure to air pollutants is emerging as a critical concern in human health. Pregnancy and fetal development stages are highly susceptible to environmental exposure and tend to develop a long-term impact in later life. In this review, we briefly glance at the direct impact of outdoor and indoor air pollutants on lung diseases and pregnancy disorders. We further focus on lung complications in later life with early exposure to air pollutants. Epidemiological evidence is provided to show the association of prenatal or perinatal exposure to air pollutants with various adverse birth outcomes, such as preterm birth, lower birth weight, and lung developmental defects, which further associate with respiratory diseases and reduced lung function in children and adults. Mechanistic evidence is also discussed to support that air pollutants impact various cellular and molecular targets at early life, which link to the pathogenesis and altered immune responses related to abnormal respiratory functions and lung diseases in later life.

Keywords: Air pollutants; Polycyclic aromatic hydrocarbon; Particulate matter; Early disease origin; Respiratory diseases

Air pollution has become a major global threat to human health. Historically, multiple major episodes of air pollution occurred world wide in the early twentieth century have produced severe health outcomes. Most tragically, the "killer fog" in London in 1952 has caused 12,000 unexplained deaths and severe long-term effects in human health.[1] Even in 2012, indoor and outdoor air pollution still caused an estimated 6.5 million deaths, which covers 11.6% of total global deaths.[2] Exposure to air pollutants mostly occurs in industrial and rural areas due to various manufacturing, traveling, and living activities. Multiple review articles and meta-analyses have described a direct impact of air pollutants on respiratory responses and diseases.[3–7] We will focus on the liaison of the later onset of respiratory diseases in childhood and adulthood with early life exposure to air pollutants at prenatal and perinatal stages.

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Air pollutants

Air pollutants have complex chemical and physical features dependent on the sources of pollutants. Outdoor air pollutants are either derived from human activities, such as industrial emissions, road traffic, residential heating, shipping, air traffic, construction, agricultural activities, war and fire accidents, or from natural hazards, such as earthquake, tsunami, volcanic eruption, spontaneous forest fires, and extreme temperature.[8,9] Although natural hazards occur independent of human activities, they affect the living environment, health, and lives of humans as hazardous events.[4,10] Indoor air pollutants are generally released from smoking, building materials, air conditioning, house cleaning or air refreshing proucts, heating, lighting, and wood, fuel, or coal usage in cooking.[6] Chemically, these pollutants can be presented as the vapor forms of inorganic pollutants, such as ozone (O_3), carbon monoxide (CO), nitrogen dioxide (NO_2), and sulfur dioxide (SO_2), or as the vapor forms of organic pollutants, such as polycyclic aromatic hydrocarbons (PAHs), monocyclic hydrocarbons benzene, toluene, xylene, and aliphatic chemicals.[4,5] The particulate forms of air pollutants, however, usually consist of an inner carbon core with various organic pollutants and/or heavy metals on the surface (Fig. 1). The most harmful forms of particulate matter (PM) include PM_{10} (<10 μm in aerodynamic diameter), fine particles $PM_{2.5}$ (<2.5 μm), and ultrafine particles (less than 0.1 μm or 100 nm), which can be released from diesel engines, volcanoes, asbestos, unpaved roads, plowing, burning fields, lint, pollens, and spores.[11,12] Detailed chemical components of these air pollutants have been summarized in multiple reviews[4−6,13−15] and we will focus on the health impact of these air pollutants with different chemical and physical natures.

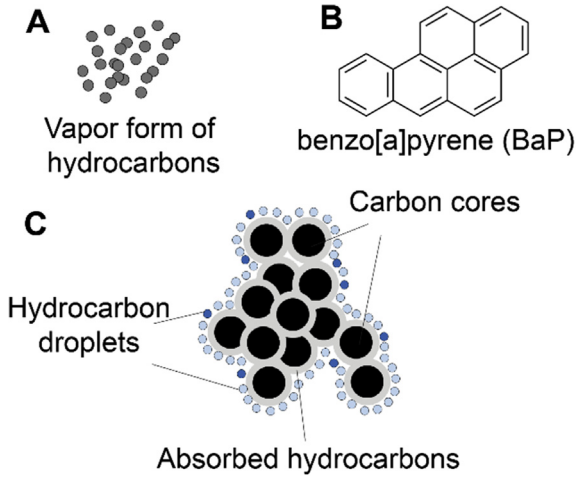

Fig. 1. **Schematic demonstration of air pollutants:** the vapor form (A) of organic air pollutants exemplified with the structure of benzo [a]pyrene (B) and the particulate form (diesel exhaust particles or particulate matters) of air pollutants (C).

Air pollution in respiratory diseases

Although the bronchopulmonary tract has multiple protective mechanisms, such as mucosal cilia and air-blood barrier, air pollutants are able to accumulate in or pass through lung tissues dependent on the size and chemical nature of pollutants.[13] The vapor of air pollutants is prone to be absorbed by human tissues or dissolved in body fluids, mainly relying on their hydrophilicity and hydrophobicity. PM_{10} particles with larger size (~10 μm) are able to reach the proximal airways and be mostly eliminated by mucociliary clearance. $PM_{2.5}$, as a notable risk factor for health, can invade more deeply into the lungs.[10,16,17] The ultrafine particles are capable of translocation through blood circulation to distal organs and tissues, such as liver tissue for detoxification and placental tissues during pregnancy.[10] Negative health effects of air pollutants have been shown on multiple respiratory diseases, including respiratory infections,[18−20] asthma,[21,22] chronic obstructive pulmonary disease (COPD),[23] lung cancer, even in combination with stroke and heart diseases as reviewed.[3,24−26] We briefly outline these direct negative effects of air pollutants on major respiratory diseases as below.

Respiratory infections

Air pollution enhances the severity of respiratory infections, particularly in children.[18−20] Especially, outdoor pollution in large cities is associated with a high burden of various acute respiratory infections, which together are responsible for nearly a third of all deaths in children under 5 years old.[18] Exposure to NO_2 and PMs in five German cities was associated with increasing cases of laryngo-tracheo-bronchitis mostly due to influenza viral infections.[27] Another study conducted in three cities in Finland supported similar conclusions.[28] However, indoor pollution contributes to high rates of chronic bronchitis of non-smoker cooking mothers in hilly regions of Nepal,[29] suggesting that indoor pollution is likely more associated with respiratory infections in developing countries and rural areas. The adverse impact of air pollutants can be highlighted especially in individuals with pre-existing lung infections or other lung diseases, because they are likely at greater risk, and also in children, possibly

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