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Challenges in studying the toxicity of particulate air pollution on the respiratory system

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Air pollution, particularly particulate matter (PM) from vehicular emissions, poses significant risks to human health, with evidence linking it to respiratory and other systemic effects. This review provides a brief historical overview of air pollution to understand the evolution of pollution sources and their health effects. Key challenges in PM exposure assessment are explored, particularly the difficulty of accurately estimating exposure and inhaled dose. The review also addresses PM deposition in the lungs, its elimination, and its impact on both local and systemic health. The role of the lung microenvironment, specifically the extracellular matrix, is critical to understanding PM-induced tissue damage and its broader implications. Despite research advancements, uncertainties persist regarding PM toxicity mechanisms, its role in chronic diseases, and the development of reliable biomarkers. This review emphasizes the need for a multidisciplinary approach to address these health challenges, utilizing technological innovations to improve exposure assessment and better understand PM's toxicological effects. Global collaboration is essential to mitigate health risks and protect public health.

KEYWORDS

air pollution, exposure, deposited particles, lung microenvironment, health effects

1 Introduction

Air pollution, particularly from particulate matter (PM), is a demanding environmental and public health issue in modern urban centers. Over the past century, industrialization, urbanization, and increased vehicular traffic have dramatically transformed the atmospheric environment.

Knowledge about the negative health effects of environmental air pollution, especially the particles generated by the burning of fossil fuels, has grown enormously in the last three decades. We now understand that the effects are not limited to the respiratory and cardiovascular systems. Changes in fertility, impaired fetal development, metabolic changes, kidney diseases, neurodegenerative diseases, and neurobehavioral effects are associated with exposure to air pollution (Simkova et al., 2020; Johnson et al., 2021; Rasking et al., 2022; Manisalidis et al., 2020; Thiankhaw et al., 2022; Weitekamp and Hofmann, 2021). Most of the effects pointed by epidemiological studies have been confirmed through controlled animal studies (Duan et al., 2019; Di Domenico et al., 2020; Yariwake et al., 2021; Qiu et al., 2021; Lee et al., 2021). Furthermore, the size and composition of these airborne particles and the concentration of exposure are decisive for the severity of the outcomes (Zeka et al., 2006; Kelly and Fussell, 2012; Mack et al., 2019).

Despite significant advancements in research, challenges remain in studying the impact of air pollution on human health, particularly the respiratory system. Key obstacles include accurately characterizing both exposure and dose, effectively visualizing PM in tissues, estimating the dynamics of lung deposition and elimination, and understanding how the pulmonary microenvironment responds to these particles. This narrative review aims to address these critical issues, emphasizing the need for improved methodologies and research strategies.

2 Brief historical context of urban air pollution

Air pollution is not a recent environmental issue. Before scratching the already written historical overview and data on air pollution, it is essential to recognize that this narrative is not merely about airborne particles and gases but also about the history of industry, politics, and the socio-economic relationships that shape them.

As Loeanhart aptly suggests, there is a growing demand to rewrite modern version of human history and earth-bound natural history as an atmostory – a correlating planetary atmospheric narrative (Loeanhart, 2022). This perspective means that the retrospective concern about air pollution has been dictated by alterity (nature-society), maintaining a distance between one and the other. However, the current environmental crisis makes it clear that this separation is no longer tenable; our history is inextricably linked with nature, including the atmosphere and its constituents. Our "pyromaniac" history has brought us to a pivotal point, where, ironically, "the birth of modern meteorology and climate science coincides with the massive transformation of the air through pollution and rising CO_2 emissions during the Industrial Revolution" (Loeanhart, 2022). Additionally, the critical disruption of breathable air, particularly from modern urban particulate pollution, coincides with a troubling realization: humanity can no longer exempt itself from the natural limits it once seemed to transcend. Despite this recognition, nuances remain. One of the key moments in 20th-century air pollution history was the invention of Eugene Houdry's platinum catalytic converter in the mid-1950s—a figure who had already revolutionized the oil industry in the late 1940s with a new petroleum processing method. The pollution from urban motor vehicles, like the earlier socio-metabolic shift from steam to combustion, was driven by economic concerns. As Beth Gardiner notes, it took two decades for the passage of the Clean Air Act in 1970 to transform Houdry's invention from a pipe dream into a practical necessity, forcing companies to reduce emissions by 90% in response to lead additives in gasoline (Gardiner, 2019).

Following World War II, there was a shift in the sources of urban air pollution, with motor vehicles replacing coal burning as the primary emission source. Although air pollution levels in this period were lower than those during the peak of coal combustion, its negative health effects continued to be observed globally. This era marked the beginning of heightened attention from toxicologists, with numerous studies investigating the health impacts of air pollution, a focus that continues to this day as new health effects are discovered.

Source apportionment studies, which identify the contributing sources to ambient PM, generally classify them into categories such as traffic, industry, domestic fuel burning, natural sources (e.g., soil dust, sea salt), and other human-made pollution. A systematic review by Karagulian et al. (2015) revealed that traffic was the primary contributor to urban $PM_{2.5}$ in several regions, including India (37%), Southeast Asia (36%), Southwestern Europe (35%), Southern Asia (34%), Brazil (33%), and the rest of the Americas (30%) (Karagulian et al., 2015). These classifications rely on analyzing the elemental composition of particles. For instance, the presence of carbon, Fe, Ba, Zn, Cu, and Pb indicates traffic sources (Viana et al., 2008), while elements such as Cu, Zn, Mn, Sb, Sn, Mo, Ba, and Fe serve as markers of brake wear and traffic resuspension (Amato et al., 2010; Schauer et al., 2006). Despite nearly 30 years of research (with over 47,000 studies published on PubMed), gaps remain in understanding the full health impacts of air pollution, particularly on the respiratory system. A more detailed exploration of molecular pathways, population-specific vulnerabilities, and the long-term effects of chronic low-dose exposures would provide greater depth and clarity to this critical issue.

3 Exposure assessment of particulate air pollution

Numerous epidemiological studies have shown associations between environmental PM concentration and adverse health effects, potentially indicating cumulative effects (Jiang et al., 2018; Chen et al., 2018). The data generated by these studies supports public health protection policies. However, one of the greatest challenges remains accurately estimating both exposure and dose (Han et al., 2017).

Estimating exposure is complex, as it involves assessing the physical and chemical properties of particles and considering individual factors such as age, occupation, transportation methods, residence, and socio-economic status (Gray et al., 2013; Tan et al., 2017; Song et al., 2021). Many studies use environmental concentrations of PM as a surrogate for dose, due to the difficulty of estimating the actual dose. While concentration measurements provide a proxy for exposure, they may not accurately reflect the true dose due to various modulating factors (Oberdorster, 1996; Winkler-Heil et al., 2014; Cox, 2017). The dose represents the amount of PM that interacts with the body, and in the case of inhalation, it is influenced by respiratory parameters, particle properties, and daily activity patterns (Foster et al., 1999).

Fixed monitoring stations, while valuable for air quality assessment in epidemiological studies over large populations, have notable limitations that may introduce biases in exposure estimates and health outcome analyses. The distance between individuals and these monitoring points, as well as spatial differences in pollution levels across a city, can introduce inaccuracies in exposure estimates (Zeger et al., 2000; Weis et al., 2005; Avery et al., 2010). These stations often lack adequate spatial and temporal coverage, failing to capture localized pollution variations, particularly in rural areas where monitoring infrastructure is sparse. Additionally, exposure misclassification can occur as fixed monitors do not account for individual

mobility throughout the day, leading to underestimation or overestimation of actual exposure. In fact, a static method for estimating exposure tends to result in underestimation (Tayarani and Rowangould, 2020) and the reliance on these measurements may obscure the real health impacts of PM exposure, particularly for populations spending time in microenvironments with higher pollution levels.

To address these limitations, integrating supplementary data sources such as mobile monitoring and satellite observations can enhance exposure assessments and improve the accuracy of epidemiological findings, particularly in specific subpopulations (Vilcassim and Thurston, 2023). Models such as Land Use Regression (LUR) and meteorological dispersion models have been developed, though both require monitoring data and emission source inventories (Han et al., 2017). LUR models predict exposure based on limited monitoring sites, which may introduce errors due to spatial misalignment (Vlaanderen et al., 2019).

Different tools were developed to measure human exposure to particulate air pollution, from computational models to lung lifetime accumulation of black carbon, however dose is still a matter of debate. The inhaled dose can be calculated by multiplying the environmental concentration of particles by the exposure time and the rate of pulmonary ventilation, and also incorporating adjustments for body weight, and exposure frequency (US-EPA, 2009; Nyhan et al., 2014; Wang et al., 2014; Li et al., 2019). Although several studies have estimated inhalation doses using U.S. Environmental Protection Agency (EPA)-based models, many rely on standardized assumptions that may not accurately reflect the specific characteristics of the population under study and may not be suitable for all demographic or geographic contexts (US-EPA, 2011).

An alternative method for improving exposure estimation is personal monitoring, where individuals wear portable devices that measure real-time PM concentrations, offering a more accurate reflection of individual exposure. Costs are a limitation for this approach, and different alternatives and low-cost portable samplers that allow measurement of individual exposure have been created (Borghi et al., 2017; Agrawaal et al., 2020). For instance, a study conducted by Manojkumar et al. (2020) in India, where participants used a portable SidePak aerosol monitoring instrument, had shown that there is great variability in exposure of motorized and active commuters, pointing out that indirect estimates of exposure can be biased, unless spatial and time exposure variation are considered (Manojkumar et al., 2021).

Using personal monitors, it became possible to perceive that the hours of the day, location in the city and way of commuting caused changes in the amount of air pollutants in contact with individuals, increasing the number of parameters that could bias exposure assessment. They solved a crucial point in exposure detection and included the displacement/relationship variable with the medium that neither computer models nor mathematical models had. However, portable devices still face logistical constraints, and the data are typically limited to short time periods.

Uncertainties in estimating exposure should always be considered to avoid biased results. Wu et al. (2019) reviewed major errors type in exposure assessment and principal statistical approaches to adjust them (Wu et al., 2019). A review on this topic conducted by Borghi and cols. (2021) examines all these issues in detail (Borghi et al., 2021). In addition, not only addressing the previous points, it is also possible to assess exposure to pollution within the individual (lung, for example,) (Waked et al., 2024; Takano et al., 2019). Similarly, this one from the inside of the individual is also not possible to be accurately estimated.

The evaluation of exposure, associated with knowledge related to health effects and the limits considered safe, allows the establishing of priorities and forms of effective intervention to protect health. There are several biological parameters that may be altered as a result of the interaction between $PM_{2.5}$ and the organism. However, the quantitative determination of these parameters used as exposure biomarkers is only possible if there is a correlation with the intensity of exposure. Currently, no specific biomarker exists for $PM_{2.5}$ exposure. Some proxies, such as urinary polycyclic aromatic hydrocarbon (PAH) metabolites and PAH DNA adducts, have been explored, but studies correlating PAH content in $PM_{2.5}$ with biomarker levels in exposed individuals remain limited (Topinka et al., 2007; de Oliveira et al., 2014; Desai et al., 2017). Emerging biomarkers indicating $PM_{2.5}$-respiratory system interactions are primarily related to oxidative stress, inflammation, DNA damage, and epigenetic modulation (Yang et al., 2017; Guo et al., 2022) and continue to be investigated.

No single exposure assessment tool is flawless, and Table 1 provides a summary of their respective strengths and limitations. A more comprehensive and precise evaluation of exposure can be achieved by integrating multiple assessment methods, including fixed monitoring data, personal monitoring, computational modeling, and biomarker evaluations. However, implementing this approach on a large scale in epidemiological studies remains a significant challenge due to logistical, financial, and methodological constraints, making it difficult to achieve widespread application.

4 Deposition and elimination of airborne particles in the lungs

More recently, researchers have focused on the pathways traveled by these tiny particles in our bodies and their accumulation in vital organs. Since publications in 2002, which showed that these particles can exit the airways and enter the bloodstream (Ober et al., 2002; Nemmar et al., 2002), the challenge has been to determine where they accumulate outside the lungs. There is evidence of particle deposition in the placenta and other organs of the central nervous system (CNS) (Bové et al., 2019), indicating that PM may have far-reaching health impacts beyond the respiratory system, particularly for vulnerable populations such as pregnant women, developing fetuses, and individuals with pre-existing health conditions. Ultrafine particles and nanoparticles can bypass the placenta leading to fetal exposure, which has been associated with adverse birth outcomes such as low birth weight and preterm birth, as well as increased risk of cardiovascular diseases and neurodevelopmental disorders later in life (Bongaerts et al., 2020). For the CNS, PM translocation has been associated with neuroinflammation, oxidative stress, and cognitive impairments, which may exacerbate conditions such as Alzheimer's disease and Parkinson's disease (Shi et al., 2020; You et al., 2022). This raises

TABLE 1 Overview of exposure assessment tools with their strengths and limitations.

Exposure assessment tools	Strenghts	Limitations
Fixed monitoring stations	Reliable, validated, long-term data	Poor spatial resolution, exposure misclassification, costly
Land Use Regression (LUR) Models	Integrate multiple data sources, high spatial resolution, scalable	Weak temporal resolution, region-specific limitations
Personal monitoring devices	Real-time, individual-level data, reflects personal activity patterns	Costly, burdensome, variable data quality
Biomarkers	Reflect biologically relevant exposure, integrate all exposure routes	Temporal uncertainty, confounding, costly, complex interpretation

concerns about the potential for these particles to affect vital systems with both local and systemic consequences.

Once these particles are inhaled and gain access to our respiratory system, several aspects must be evaluated to understand their fate. Coarse particles (or PM_{10}, particles ≤10 μm in diameter) tend to become trapped in the upper airways and are eliminated or swallowed. The respiratory system has defense mechanisms that allow the elimination of these larger particles; however, this same defense system can be negatively affected by pollutants, gases, and particles, reducing its effectiveness (Smyth and Georas, 2021). Fine particles (particles ≤2.5 μm in diameter or also called $PM_{2.5}$) usually make their way to bronchiole. Smaller, ultrafine particles ($PM_{0.1}$, or particles ≤0.1 μm in diameter, by contrast, are capable of reaching the alveoli in the deepest regions of the lungs, where they may translocate across the blood-air barrier.

It is estimated that approximately 40% of inhaled particles deposit along different regions of the respiratory tract (ICRP, 1994). Deposition of these particles is determined by different factors, such as physicochemistry of particles, anatomy and physiology of the respiratory tract (Heyder et al., 1986; Morawska and Buonanno, 2021). Depending on the characteristics of the particle, even when it cannot translocate across the blood-air barrier, the compounds adsorbed on its surface can be released affecting both local lung tissue and distant organs via systemic circulation (Cheng et al., 1996; Brown et al., 2002; Hopke and Wang, 2012).

The elimination of these particles from the lungs relies on several protective mechanisms, such as mucociliary clearance and alveolar macrophage activity. Mucus traps particles, while cilia work to move them out of the lungs. Phagocytic cells like alveolar macrophages further engulf and digest particles, helping to clear them from the respiratory system. However, the efficiency of these mechanisms can be compromised by prolonged exposure to high levels of PM, leading to persistent inflammation and tissue damage (Geiser and Kreyling, 2010). Additionally, studies have shown that chronic exposure to PM can impair the function of alveolar macrophages, reducing their ability to clear particles and increasing the risk of respiratory infections (Ling and van Eeden, 2009; Hussain et al., 2011).

Two decades ago, another short pathway to the CNS through the olfactory bulb was proposed. However, more studies are needed to confirm if this is an entrance or an exit route, since the lymphatic drainage of the CNS is associated with nasal lymphatic vessels (Oberdörster et al., 2004; Johnston et al., 2004). This suggests the need to investigate the impact of airborne particles beyond the lungs and highlights the importance of understanding the full body burden of PM and its implications for human health.

To conclude, the distinction between larger, fine, and ultrafine particles is essential for understanding their differential fate within the respiratory tract and the broader implications for human health. Current regulatory frameworks, such as those established by the U.S. EPA and the World Health Organization (WHO), primarily rely on mass-based concentration limits for $PM_{2.5}$ and PM_{10}. However, these standards may not fully account for the toxicological effects of ultrafine particles, which have the potential to translocate beyond the lungs and impact other vital organs. Despite growing evidence highlighting the health risks associated with ultrafine particles, specific regulatory standards for this particle size class have yet to be established. Addressing this gap is critical to refining air quality metrics and ensuring more comprehensive protection against the far-reaching effects of airborne PM.

5 Detection and quantification of particles in lung tissue

Our research group has been evaluating deposited particles in the lung pleura as a measure of exposure (Waked et al., 2024). We employed epidemiological, spatial analysis, and autopsy-based approaches to determine if urban air pollution is associated with pleural anthracosis, also known as black carbon (Takano et al., 2019; da Motta Singer et al., 2023). After controlling for residential location, socio-demographic factors, occupation, smoking status, time of residence in the city, and time spent commuting, we found that the area fraction of the pleural surface occupied by anthracosis is a potential index of lifetime exposure. This exposure estimation method can be used to investigate the association between long-term exposure to air pollution and health outcomes (Taka et al., 2024).

Another method for evaluating deposited particles involves microscopical approaches. This includes the simple quantification of particles observed in histological sections of lungs (Balchum et al., 1963) or elemental analysis of particles retained in the lung and associated lymph nodes (Saieg et al., 2011). Other studies using lung samples obtained by autopsy have recovered these particles by digesting the tissue or using other complementary methods to assess the mass and characteristics of deposited particles (Mastin et al., 1988; Brauer et al., 2001; Dos Santos et al., 2022). The particles deposited in tissues still need to be better studied to understand their local and systemic toxicity. While additional methods have been used in experimental models exposed to air pollution

(Hameed et al., 2022), applying these techniques to humans presents significant challenges.

Overall, the mentioned forms of evaluating particles deposition represent a significant part of the lungs and airways, as there are limitations to investigating the entire respiratory system in this context. Additionally, it is not known whether these particles aggregate when they deposit, whether their properties are modified, or whether there are removal mechanisms depending on the tissue. Detecting the amount of PM particles in different tissues is difficult because of their variable size and complex chemical compositions. As a result, there are limited studies that focus on measuring air pollution derived particles across various tissues to establish deposition rates.

A recent study described an artificial intelligence algorithm, 'Machine-Learning algorithm for Engulfed cArbon Particles (MacLEAP)', for quantifying airway macrophage black carbon (Jiang et al., 2024). Despite some challenges, advancements in technology and artificial intelligence offer new avenues for detecting and quantifying particles in lung tissue, improving our ability to study the distribution and effects of PM in human tissues.

6 Particulate matter and the lung microenvironment

The lung microenvironment, which consists of a combination of cells and extracellular matrix (ECM) components, plays a crucial role in determining cellular behavior. The ECM not only provides structural support for cells but also influences tissue development, repair, and cellular communication. It has long been known that this dynamic network continuously undergoes remodeling to maintain homeostasis (Dunsmore and Rannels, 1996).

The lung ECM comprises a diverse mix of proteins, proteoglycans, and biological factors, which can be grouped into core molecules (e.g., collagens, proteoglycans, and glycoproteins), matrix-affiliated molecules (e.g., mucins, lectins, syndecans), matrix regulators like matrix metalloproteinases (MMPs) and their inhibitors (TIMP), and soluble factors such as cytokines and growth factors (Iozzo and Gubbiotti, 2018; Lamandé and Bateman, 2020). These elements coordinate responses to environmental stimuli, such as PM, which can disrupt normal ECM functions.

Pathological changes in the ECM can arise from genetic alterations, aging, or exposure to harmful environmental agents, including PM. Understanding how the lung microenvironment responds to these agents is critical in assessing their toxic effects. For instance, in cancer research, it is well established that the tumor microenvironment plays a significant role in malignancy and tumor progression (Lamandé and Bateman, 2020). Similarly, in the lung, the ECM's interaction with inhaled pollutants may either mitigate or exacerbate adverse effects.

Briefly, fibroblasts, myofibroblasts, and to a lesser extent, airway epithelial cells and airway smooth muscle play essential roles in ECM production. The composition and functionality of the lung ECM vary across different regions of the lung, depending on the developmental stage and exposure to pollutants. While this review does not delve deeply into the ECM of the lung, a detailed review of the role of the extracellular matrix in lung development, homeostasis, and disease was conducted by Zhou et al. (2018).

Investigating the effects of PM on lung tissue typically involves animal models and *in vitro* systems (Sun and Shang, 2018; Zavala et al., 2020). Although these methodologies were able to greatly advance our knowledge of health effects, both have aspects that must be considered when interpreting the results. These models have limitations, as animal responses do not fully predict human outcomes, and traditional cell cultures lack the complexity of the lung microenvironment.

Advancements in technologies, such as 3D organ-on-a-chip models, have begun to bridge these gaps, providing more physiologically relevant insights (Tavares-Negrete et al., 2023). These models are available for different organs, and lung-on-a-chip systems are developed by co-culturing epithelial and endothelial cells on both sides of a porous polymeric membrane to approximate the alveolar–capillary barrier (Huh et al., 2010). A study conducted by Xu et al. (2020) to evaluate $PM_{2.5}$ pulmonary risk recapitulates effects observed in human and animal studies, including adherent junction disruption, increased oxidative stress, apoptosis, inflammation, elevated permeability, and monocyte attachment (Xu et al., 2020). Although lung-on-a-chip technology offers a promising alternative to traditional *in vitro* models by replicating key aspects of lung physiology, it still faces technical and biological challenges (Shrestha et al., 2020). While these models have great potential to reduce reliance on animal studies, we agree that hybrid approaches by integrating advanced *in vitro* systems with carefully selected animal models, remain essential for producing robust and translational research outcomes. Notably, lung-on-a-chip models provide an opportunity to investigate ECM remodeling under PM exposure in controlled environments, potentially offering insights into unresolved questions regarding this context.

It is known that pulmonary effects of inhaling particulate pollution include ECM remodeling, which plays a crucial role in the progression of chronic diseases associated with PM exposure. Chronic PM-induced inflammation leads to ECM degradation and excessive deposition of fibrotic components, contributing to airway remodeling and systemic effects. Studies have shown that PM exposure can induce oxidative stress and inflammation activate fibroblasts, promoting excessive collagen deposition and fibrosis (Saputra et al., 2014; Xu et al., 2019; Chang et al., 2023; Chen et al., 2025), which can impair lung function over time. While some therapeutic targets for ECM remodeling have been explored (Liu et al., 2021), research specifically addressing PM-induced ECM dysregulation remains limited. Further investigations into targeted interventions could help mitigate the long-term health consequences of PM exposure. Several other critical questions remain regarding the interaction between PM and the lung ECM: Does PM directly affect ECM components, or are the observed changes a secondary response to inflammation and oxidative stress? How do these changes impact tissue homeostasis, and are they reversible? How deposited PM interacts locally with the ECM and cell? Are the ECM 3D structure and organization affected? Moreover, could prenatal exposure to air pollution impair lung development through disruptions in the ECM? Does PM-induced ECM remodeling increase lung cancer risk?

Cutting-edge technologies, including tissue microdissection, *in situ* hybridization, precision-cut lung slices, and advanced microscopy techniques, will likely be pivotal in answering these questions (Campagnola, 2011; Perry et al., 2012; Koziol-White et al., 2024). While these techniques provide exceptional insights into PM-induced cellular and ECM changes, their high operational costs and specialized training requirements may limit their routine application in large-scale studies. Emerging technologies, such as automated imaging systems and AI-assisted analysis, may help reduce costs and improve efficiency.

7 Final considerations and conclusions

Despite decades of studying the negative effects of air pollution on human health, the search for answers is still an endless road. We have yet to fully uncover the underlying pathophysiological mechanisms, identify precise biomarkers of exposure, or determine whether the effects of air pollution are passed down across generations. Additionally, we do not know whether our lungs can adapt to prolonged exposure to poor air quality. While clean energy technologies are emerging, the overwhelming evidence of the health risks and mortality attributed to particulate air pollution has not yet spurred a unified global effort to reduce pollution levels. Current air quality regulations, such as WHO Global Air Quality Guidelines, provide scientifically backed standards, yet their enforceability varies across regions since they serve as recommendations rather than legally binding mandates. National governments face challenges in implementing these guidelines due to economic constraints, industrial interests, and political priorities, while socio-economic disparities further hinder compliance, particularly in lower-income communities with higher pollution exposure and weaker enforcement mechanisms.

Investigating the toxicity and health effects of PM exposure, as well as exploring novel approaches to mitigating the health and toxic impacts of air pollution, are areas that present considerable challenges. One major limitation is the difficulty in obtaining precise individual exposure assessments, as personal monitoring remains costly and inaccessible for large-scale applications. Standardized exposure estimates often fail to account for individual variability in pollutant inhalation and retention. Additionally, the lack of reliable specific biomarkers for PM exposure hinders efforts to establish direct causal links between air pollution and long-term health effects. Identifying robust biomarkers remains a priority to improve risk assessments and early detection of air pollution-related diseases.

Another challenge lies in extrapolating findings from animal models to human populations. While experimental studies have provided valuable insights into PM-induced physiological responses, differences in species-specific pulmonary structures and metabolic processes complicate direct comparisons. Advancements in three-dimensional tissue models and organ-on-a-chip systems offer promising alternatives that more closely mimic human lung microenvironments, providing complementary findings that enhance the translational relevance of the research.

The complexity of air pollution's impact on human health requires a multidisciplinary approach to research. By integrating data from epidemiology, toxicology, and clinical studies, researchers can gain a more complete picture of how PM affects various biological systems. Recent technological advances, such as high-resolution imaging and machine learning algorithms, have opened new possibilities for detecting and quantifying particles in lung tissue, thereby improving our understanding of their distribution and impact. These technologies can also help unravel the intricate relationships between PM exposure, tissue damage, and long-term health outcomes.

Collaborative efforts among scientists, policymakers, and public health officials are essential for developing effective strategies to mitigate the adverse health effects of air pollution and protect vulnerable populations. By leveraging interdisciplinary research and technological innovation, we can move closer to identifying solutions that reduce air pollution exposure and improve public health on a global scale.

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