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Perspective

Fine particulate matter ($PM_{2.5}$): The culprit for chronic lung diseases in China

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Abstract

Air pollution is a world public health problem. Particulate matter (PM), a mix of solid and liquid particles in the air, becomes an increasing concern in the social and economic development of China. For decades, epidemiological studies have confirmed the association between fine particle pollutants and respiratory diseases. It has been reported in different populations that increased Fine particulate matter ($PM_{2.5}$) concentrations cause elevated susceptibility to respiratory diseases, including acute respiratory distress, asthma, chronic obstructive pulmonary disease, and lung cancer. This review will discuss the pathophysiology of $PM_{2.5}$ in respiratory diseases, which are helpful for the prevention of air pollution and treatment of respiratory tract inflammatory diseases.

Keywords: Air pollution; Particulate matter; Lung diseases; Chronic obstructive pulmonary disease

Introduction

Air pollution is a major environmental and public health problem worldwide. Exposure to air pollution has a number of adverse effects on human health. The most abundant air pollutants in the urban environment today are ozone (O_3), nitrogen dioxide (NO_2), and particulate matter (PM). A further concern is the harmful ambient toxins in the air to human health.[1] China has experienced a drastic epidemiological and demographic transition during the past few decades,[2] resulting from rapid economic development. This has coincided with rising levels of air pollution caused by increased energy exhaust and industrial waste. Air pollution can affect respiratory, cardiovascular,

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cardiopulmonary, and reproductive systems, and may even lead to cancer.[3–5] Epidemiological data demonstrate a consistent correlation between levels of PM in the ambient air and increases in respiratory and cardiovascular morbidities. Particulate air pollution has a significant impact to the populational health in Chinese cities. Fine particulate matter ($PM_{2.5}$), as a major health burden, plays an increasingly negative role in Chinese social and economic development. This review will focus on how $PM_{2.5}$ affects the human respiratory system and its role in chronic respiratory diseases in China.

Burden of air pollution

The impact of air pollution on human health has been proved as an immense health burden in China. The most prevalent diseases are cardiovascular, gastrointestinal, and chronic respiratory diseases. Evidence is limited concerning the acute health effects of $PM_{2.5}$ air pollution in developing countries. In China, approximately 1.3 billion people are exposed to ambient fine PM. Of note, the levels of PM have exceeded the World Health Organization (WHO) Air Quality Guidelines (AQG).[6]

Recently, a growing amount of evidence has demonstrated that respirable particles are related to the morbidity and mortality of human diseases. Ambient air pollution in large cities resulted in an increase in the risk of pulmonary and systemic oxidative stress, immunological modifications, hypoxemia, atherosclerosis, and a faster progression of chronic obstructive pulmonary disease (COPD), and cardiovascular diseases.[7] Recent epidemiological investigations have illustrated that $PM_{2.5}$ exposure contributes to the incidence of diabetes mellitus (DM) and unfavorable outcomes.[8] Even, long-term exposure to ambient air pollution is associated with increased all-cause and cause-specific mortality.[9] In China, house hold air pollution, derived from residential energy use such as heating and cooking, has the largest impact on premature mortality.[1] Lanzhou is one of the most seriously air-polluted cities in China and demonstrates a significant association between air pollutants and respiratory hospital admissions. This relationship is stronger in females and persons aged $\geq$65 years.[10]

The fine particles are those 2.5 μm or less in diameter, and $PM_{2.5}$ is used as a main indicator of risk to health from particulate pollution in many countries. Ambient $PM_{2.5}$ was the fifth leading cause of death, resulting in 4.2 million deaths and 103.1 million disability-adjusted life-years (DALYs) in 2015. Deaths attributable to ambient $PM_{2.5}$ have increased over the past 25 years.[11] The Pearl River Delta (PRD) region is a highly urbanized and developed region in China. This region saw its greatest economic loss (14,768 to 25,305 million USD) in 2013, which is equivalent to 1.4%–2.3% of the local gross domestic product (GDP).[12] Analyses of PM pollution concentrations were conducted in 190 Chinese cities during 2014–2015. The total premature mortality attributable to $PM_{2.5}$ and PM_{10} were 722,370 and 1,491,774, respectively, and the total DALYs were 7.2 and 20.66 million, respectively. This may be related to the loss in economic productivity observed in 2013. The total economic cost attributed to PM_{10} pollution accounts for approximately 2.94% of China's GDP.[13]

To evaluate the short–term association between $PM_{2.5}$ and daily cause-specific mortality in China, a nationwide time-series analysis was performed in 272 representative Chinese cities from 2013 to 2015. As a result, the average annual-mean $PM_{2.5}$ concentrations per city was 56 $\mu g/m^3$ (18–127 $\mu g/m^3$). Each 10 $\mu g/m^3$ increase in daily $PM_{2.5}$ concentrations is associated with an increase of mortality, including 0.22% in total non-accident, 0.27% cardiovascular disease, 0.39% hypertension, 0.30% coronary heart disease, 0.23% stroke, 0.29% respiratory disease and 0.38% from COPD.[14]

Components and sources of air pollutants

PM is defined as "a complex mixture of extremely small particles and liquid droplets, made up of acids, organic chemicals, metals, and soil or dust particles." Particulate pollution is divided into several categories based on its size. PM_{10}, $PM_{2.5}$ and ultrafine particles refer to particles that are less than 10 μm, 2.5 μm and 0.1 μm in diameter, respectively. The size of PM has been directly linked to its potential in causing health problems, wherein smaller particles pose a greater risk than larger ones. Therefore, people experience greater adverse effects from $PM_{2.5}$ than PM_{10} in light of air pollution (Fig. 1).

PM composition is diverse among cities, depending on the predominant emission sources. Particles can include inorganic gaseous pollutants, such as carbon monoxide (CO), sulfur dioxide (SO_2), and NO_2, which primarily originate from biomass fuels (BMFs), coal, and petroleum combustion products. These pollutants contribute to the formation of haze.[15] Another major source of air pollution is agricultural straw burning, in association with many adverse environmental and ecological effects.[16]

PM emitted directly to the atmosphere are called primary PM (including mineral dust, metals, soot, salt

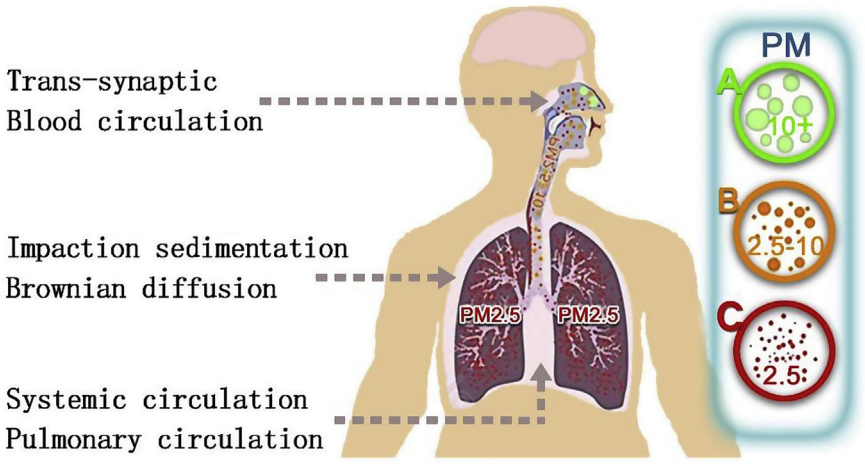

Fig. 1. Different size of particles deposit in the lung and other tissues. Large particles can be deposited in upper airways through sedimentation or impaction while in the lower airways. Brownian diffusion can deposit them in the alveoli. Ultrafine particles can translocate to blood circulation and be deposited in the liver, spleen, or brain, despite of penetrating through trans-synaptic mechanisms. PM: particulate matter.

particles, pollen, and spores). In China, primary PM originates from a variety of anthropogenic activities, including power generation, industrial processes, fossil and BMF combustion, agricultural waste combustion, construction, as well as natural sources such as wind-blown dust.[17] The secondary PM is formed in the atmosphere by gas-to-particle conversion processes, such as sulfates, nitrates, and organic compounds.[18]

The major pollutants in outdoor air are PM, O_3, SO_2, NO_2, CO, and plumbum (Pb). Indoor air pollutants include second-hand tobacco smoke, furniture-derived formaldehyde, nitrogen oxides from natural gas appliances, and volatile organic compounds following new house construction. PM components originating from road traffic include engine emissions comprised of elemental carbon (EC) and organic carbon (OC). Non-exhaust sources of PM contain elevated concentrations of transition metals,[19] and the largest single source is derived from diesel exhaust (DE).

Spatial and temporal variations of $PM_{2.5}$

Air pollution is variable across different times and regions.[20] Pollutants in ambient outdoor differ from pollutants in indoor air, and the components vary across locations, even within the same city.[21] In Shenzhen, the average annual PM_{10} and $PM_{2.5}$ concentrations were 61.3 and 39.6 μg/m^3, respectively. However, hourly $PM_{2.5}$ concentrations in the tourist area were lower than those in downtown all the day. Further, PM_{10} and $PM_{2.5}$ concentrations in the western regions of Shenzhen were higher than those in the eastern regions.[22] It was found that black charcoal (BC) and sulfur (S) concentrations were the dominant fine PM. Elements with crustal and oceanic origins were the dominant coarse PM, such as silicon (Si), calcium (Ca), aluminum (Al) and chlorine (Cl). Most of the elements showed strong diurnal variations.[23] $PM_{2.5}$ displayed seasonal fluctuations with the highest concentrations in the winter, followed by the autumn, spring, and summer.[24]

Air pollution varies considerably among different regions. Strikingly, a research from 188 main cities across China (from 2014 to 2015) has indicated the highest concentration and risk of $PM_{2.5}$ in the Beijing–Tianjin–Hebei economic belts.[25] A study conducted between 2013 and 2014 showed higher levels of $PM_{2.5}$, PM_{10}, CO, and SO_2 in capital cities in northern China compared to those in western and southeastern China. The economic regions represent a more policy-relevant division for China's most critically polluted areas. The Northwestern Region had the highest mean levels of $PM_{2.5}$ at 85.4 μg/m^3, followed by the Northern and Northeastern regions, and the Beijing region was 94.42 μg/m.[326] Another study, conducted between 2014 and 2016, found the annual population-weighted-average (PWA) values for $PM_{2.5}$ in China were 65.8 μg/m^3 in 2014, 55.0 μg/m^3 in 2015, and 50.7 μg/m^3 in 2016, respectively.[27] Finally, the annual PWA concentrations of $PM_{2.5}$, PM_{10}, O_3, NO_2, SO_2, CO in Northern China were 40.4%, 58.9%, 5.9%, 24.6%, 96.7%, and 38.1%, respectively, which were higher than those in Southern China.

Air pollution is correlated with acute exacerbation of COPD (AECOPD) hospitalizations spatially. A 10 μg/m^3 increase of PM_{10} at workplace was associated with a 7% increase of hospitalizations due to AECOPD in Jinan, 2009.[28] Another research showed that national $PM_{2.5}$ related deaths from stroke, ischemic heart disease and lung cancer increased from approximately 800,000 cases in 2004 to over 1.2 million cases in 2012. The health burden exhibited strong spatial variations, with high attributable deaths concentrated in regions including the Beijing–Tianjin Metropolitan Region, Yangtze River Delta, Pearl River Delta, Sichuan Basin, Shandong, Wuhan Metropolitan Region, Changsha–Zhuzhou–Xiangtan, Henan, and Anhui.[29]

Mechanisms of $PM_{2.5}$ on human respiratory system

The effects of ambient $PM_{2.5}$ on mortality in China and other countries have been investigated for decades. Current epidemiological data have revealed a robust correlation between fine particle pollutants and respiratory diseases.[30] $PM_{2.5}$ is known to exacerbate chronic inflammatory lung conditions, including pulmonary hypertension,[31] cardiovascular disease,[32] and autoimmune disease.[33] There are several proposed mechanisms of the impact of $PM_{2.5}$ on human respiratory physiology. These include release of molecular mediators [i.e. extracellular regulated protein kinases (ERK)/protein kinase B (Akt), mitogen-activated protein kinase (MAPK), signal transducers and activators of transcription (STAT)-1] that affect the cells, tissue, and system after PM exposure, and the binding of pathogenic antibodies to pro-inflammatory cell receptors, leading to an exacerbation of chronic inflammation (Fig. 2).

Immune response

$PM_{2.5}$ exposure can stimulate the overexpression of genes for transcription factors and cytokines that trigger the inflammatory response and injury.[34,35] Vascular endothelial cell damage is associated with cardiovascular disease caused by exposure to $PM_{2.5}$, leading to increased morbidity and mortality.[36] Exposure to $PM_{2.5}$ suspension, water-soluble, and insoluble fractions of $PM_{2.5}$ results in increased cell death, reactive oxygen species (ROS), mitochondrial transmembrane potential disruption, and nuclear factor (NF)-κB activation in human endothelial cells.[37] Fractions of $PM_{2.5}$ suspension trigger the activation of NF-κB, resulting in cytotoxicity via an apoptotic process. Human macrophages exposed to smoke *ex vivo* show increased production of cytokines [interleukin (IL)-6 and IL-8] and decreased phagocytosis and oxidative burst in a dose-dependent manner.[38] Ambient polycyclic aromatic hydrocarbons and diesel-exhaust particles affect regulatory T cell (Treg) function.[39] Treg impairment is associated with increased DNA methylation of Forkhead box transcription factor 3 (Foxp3), a key transcription factor in Treg activity.[40]

In a model, short term exposure to air pollution increases the proportion of neutrophils, B and T lymphocytes, and mast cells in bronchoalveolar lavage fluid (BALF).[41] Moreover, novel associations between long-term ambient air pollution exposure and site-specific DNA methylation, but not global DNA methylation, were identified in purified monocytes of a multi-ethnic adult population.[42]

Oxidative stress

Oxidative stress plays an essential role in the pathophysiology of lung disease, and is linked to O_3, NO, and $PM_{2.5}$ pollutant exposure.[43] $PM_{2.5}$-induced oxidative stress is an important mechanism of $PM_{2.5}$-mediated toxicities,[44] and may arise from the direct generation of ROS at the surface of either particles, soluble compounds like transition metals, or organic compounds. Also, it may arise from altered mitochondria or nicotinamide adenine dinucleotide phosphate (NADPH) oxidase, and the activation of inflammatory cells capable of generating ROS and reactive nitrogen species.

Recent studies have demonstrated the role of oxidative stress and inflammatory response in the respiratory epithelium, which contributes to the impairment of epithelial barrier dysfunction following $PM_{2.5}$ exposure.[45] Exposure to $PM_{2.5}$ can induce ROS-mediated oxidative stress and alter cellular permeability in epithelial cells.[46] $PM_{2.5}$ contains environmentally persistent free radicals, especially for combustion-derived particles. Numerous organic chemicals coated on $PM_{2.5}$ can be metabolically activated and augment intracellular ROS.[47] $PM_{2.5}$ exposure enhanced the airway inflammatory response significantly through ROS-mediated activation of MAPK [ERK, c-Jun N-terminal kinase (JNK), p38 MAPK] and downstream NF-κB signaling pathways.[48]

Oxidant/antioxidant imbalance is implicated in the pathogenesis of diseases affecting every organ system, including the lung and pulmonary vasculature. $PM_{2.5}$-induced ROS may function as signaling

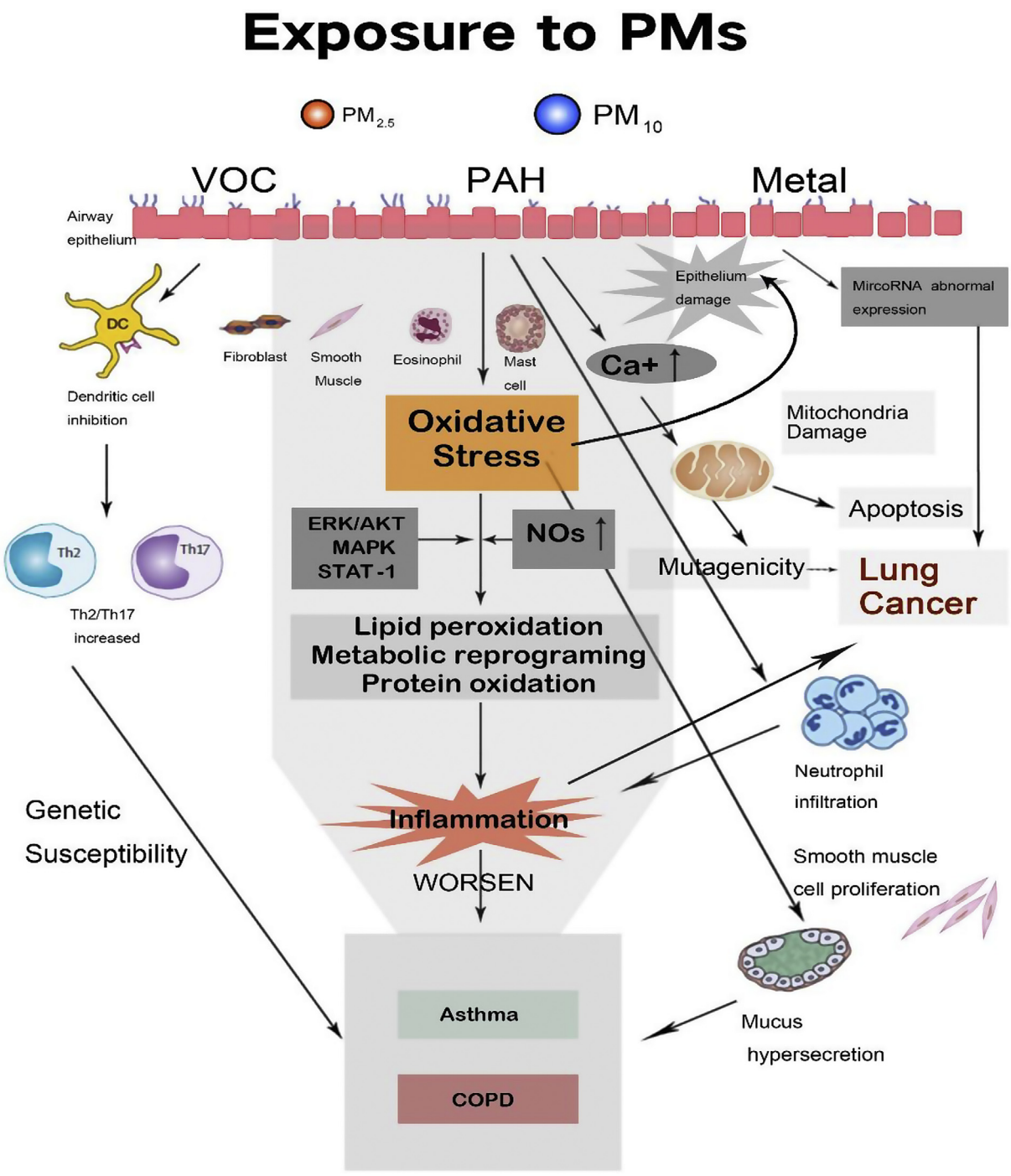

Fig. 2. Principal route of damage on human respiratory system after $PM_{2.5}$ exposure. PM: particulate matter; VOC: volatile organic compounds; PAH: polycyclic aromatic hydrocarbon; ERK: extracellular regulated protein kinases; MAPK: mitogen-activated protein kinase; STAT-1: signal transducers and activators of transcription-1; COPD: chronic obstructive pulmonary disease.

molecules to trigger the translocation of nuclear factor-like 2 (Nrf2) into the nucleus, resulting in altered transcription of antioxidant enzymes.[49]

Furthermore, PM induced the gene expression of enzymes involved in the xenobiotic metabolism pathway. Oxidative stress parameters were highly

correlated with gene expression and protein secretion of inflammatory mediators.[50]

Inflammatory injury

Inflammation is the main cause of respiratory diseases, and short or chronic exposure of $PM_{2.5}$ can stimulate local inflammation of the respiratory system. Experimental studies suggest that the deposition of PM on airway epithelial cells activates inflammatory signaling cascades, which may alter systemic immunologic and inflammatory responses.[45,51,52] Available data showed a relationship between $PM_{2.5}$ induced inflammatory responses and oxidative stress in human bronchial epithelial cells and in rats *in vivo*.[44,53,54] Both pulmonary inflammation and systemic inflammation are strongly associated with the incidence and progression of COPD.

Cytokines play a critical role in chronic inflammation and structural changes in the respiratory tract in COPD by recruiting, activating, and promoting the survival of multiple inflammatory cells. Air pollution PM can trigger inflammatory cytokine expression and induce systemic inflammatory responses. Higher cytokine levels were found in both serum and BALF following exposure to motor vehicle exhaust (MVE) than in those after exposure to BMF.[55]

The $PM_{2.5}$-impaired natural killer (NK) cell response in the lung has been identified as a critical mechanism for $PM_{2.5}$-mediated susceptibility to *Staphylococcus aureus* infection. This provides a potential mechanism to explain the epidemiological findings associated with ambient air pollution and increased bacterial lung infections.[56]

Diesel exhaust particles (DEP) are a major component of traffic-related air pollution conducive to the pathogenesis and exacerbation of asthma. Notably, IL-17A has been linked to severe asthma. Expansion of Th17 cells contributes to DEP-mediated exacerbation of allergic asthma.[57] In addition, DEP co-exposure with house dust mite (HDM) results in persistent Th2/Th17 $CD127^+$ effector/memory cells in the lungs, spleen and lymph nodes of adult and neonatal mice. This suggests a potential secondary allergen recall response by accumulation of allergen-specific Th2/Th17 cells in the lungs following DEP exposure, which promotes the development of allergic asthma.[58]

Mutagenicity

$PM_{2.5}$ is made up of organic components and heavy metals, both of which are strong mutagenic and carcinogenic agents. A number of studies have indicated the mutagenic properties of $PM_{2.5}$-derived organic components.[59,60] Further, both heavy metals and the core of $PM_{2.5}$ may be genotoxic to human cells. $PM_{2.5}$ can increase the frequency of chromosomal aberration and micronucleus formation in human cells, confirming its clastogenic effects.[61,62] The chromosome damage responses triggered by $PM_{2.5}$ may cause a series of alterations in cellular biochemical and physiological processes, especially in gene expression profiles, leading to altered function and cell apoptosis.[63,64]

Impact of $PM_{2.5}$ on chronic respiratory diseases

The mechanism of the impact of $PM_{2.5}$ on the respiratory system is not fully understood. $PM_{2.5}$ is easily inhaled into the respiratory tract and deposited in lung alveoli, where the toxic particles may result in structural damage to the lungs and functional deficits. A small fraction of PM penetrates in the deepest part of the airways. Several epidemiological and laboratory studies have demonstrated that $PM_{2.5}$ increases the risk of respiratory morbidity, hospital admission rates and emergency department visits, aggravates chronic respiratory conditions, and decreases lung function.[14,30,65,66]

A meta-analysis conducted in China to assess the mortality effects of short-term exposure to PM, verified the significant association between air pollution exposure and increased mortality risk in pooled estimates for all pollutants of interest.[67] Specifically, each 10 $\mu g/m^3$ increase in $PM_{2.5}$ was associated with a 0.38% increase in total mortality (95% Confidence Interval, *CI*: 0.31, 0.45).

Asthma

$PM_{2.5}$ contributes to increased prevalence and symptom severity in children and adult patients with asthma.[68] Environmental exposure is a critical factor in the initiation and exacerbation of asthma.[69] The indoor environment may contain pollutants that influence asthma development and morbidity. Inner-city children are exposed to various indoor allergens and pollutants that may lead to development of asthma and even the exacerbation of existing asthma.[70] Potential exposure (from pests, mouse, dust mites, tobacco smoke, endotoxin and NO_2) can influence the development of asthma and morbidity in children with asthma. In a cross-sectional study of 23,326 Chinese children, the prevalence of asthma and asthma-related

symptoms was higher for those residing near areas with serious air pollution, and ventilation device use was associated with decreased odds of asthma in children.[71]

Epidemiologic evidence for an association between black carbon and health outcomes is limited. Black carbon belongs to traffic-related PM. Black carbon is produced as a combustion by-product and is more dangerous than $PM_{2.5}$ in light of the adverse health effects. $PM_{2.5}$ and black carbon were associated with increased asthma admissions. Black carbon has slightly greater effects in both one-pollutant and multi-pollutant models than $PM_{2.5}$.[72]

Four main mechanisms, proposed by the UK's Committee on the Medical Effects of Air Pollutants, have been identified to explain how air pollution might contribute to the development and exacerbation of asthma: oxidative stress and damage, airway remodeling, inflammatory pathways and immunological responses, and enhancement of respiratory sensitization to aeroallergens.[73] The inflammatory response is thought to predispose and exacerbate the asthmatic response to inhaled allergens, thereby precipitating signs of asthma.[36] $PM_{2.5}$ may exacerbate allergic inflammation including increase of IL-5, IL-13, eotaxin and monocyte chemotactic protein-3 (MCP-3) via a Toll-like receptor (TLR)2/TLR4/myeloid differentiation factor 88 (MyD88)-signaling pathway.[52] The idea has long been proposed that air pollution with high levels of $PM_{2.5}$ can precipitate inflammatory and remodeling changes in the lungs, concomitant with increased exacerbation of chronic conditions such as asthma.

COPD

Chronic respiratory diseases bring about a substantial burden on the Chinese health care system. COPD and lung cancer are the third and fourth most common causes of mortality, respectively. Air pollution can aggravate COPD in correlation to immediate hospitalization, and promote respiratory infections that can attribute to either hospitalization or to death at home.[74]

Exacerbations are key events in COPD with progressive decline in lung function and quality of life.[75] It is important to determine the effects of environmental pollution on COPD exacerbations. An increase in 1 mg/m^3 of carbon monoxide resulted in an increase in COPD-related hospital admissions.[76] A number of studies proposed some mechanisms for short-term air pollution exposure and adverse COPD outcomes.[65,66,77] A variety of pathobiological changes have been determined including: lung inflammation, emphysema, small airway remodeling, airway mucus hypersecretion, lung function reduction and systemic inflammatory response.

Approximately, 10%–12% of individuals with COPD have never smoked. Current data show that incomplete combustion of biomass fuel is responsible for the high prevalence of COPD in Chinese never-smokers.[78] In China, household air pollutants primarily originate from cooking with poor ventilation or heating stoves that use biomass, coal, and other solid fuels. Coupled with high levels of second-hand tobacco smoke, frequent occupational exposure to irritant vapors, gases, dusts, and fumes, may contribute to the development of COPD in non-smokers.

The short-term burden of $PM_{2.5}$ on COPD in Ningbo demonstrates the impact of $PM_{2.5}$ on years of life lost (YLL). An increase of 10 $\mu g/m^3$ in $PM_{2.5}$ was associated with an increase of 0.91 (95% *CI*: 0.16–1.66) years in YLL.[79] In a 9-year prospective cohort study, use of improved cooking fuels and kitchen ventilation were correlated with a reduction in forced expiratory volume in 1 second (FEV_1). FEV_1 was reduced by 12 mL/y (95% *CI*, 4–20 mL/y) and 13 mL/y (95% *CI*, 4–23 mL/y) in subjects who used clean fuels and improved ventilation, respectively, compared to those with no intervention after adjustment for confounders.[80]

Indeed, a causative relationship might be established between the chronic ambient air pollution and the prevalence and incidence of COPD in adults.[81] Larger studies are needed for longer follow-up periods and source-specific exposure assessments.

Lung cancer

$PM_{2.5}$ can increase the morbidity and mortality associated with lung cancer.[82,83] It is well known that $PM_{2.5}$ can cause epigenetic and microenvironmental alterations in lung cancer. Possible etiology includes tumor-associated signaling pathway activation mediated by microRNA dysregulation,[64] DNA methylation,[84] and increased levels of cytokines and inflammatory cells.[85] Autophagy and apoptosis of tumor cells may also be detected in lung cancer associated with $PM_{2.5}$ exposure.[86]

The combustion of biomass and coal is a significant contributor to household air pollution and exposure to $PM_{2.5}$ worldwide. Combustion can produce CO, NO_2, PM and other organic matter such as polycyclic aromatic hydrocarbons (PAHs). Some volatile organic compounds, *e.g.,* benzene and formaldehyde, can also

be produced by combustion as well. Epidemiological studies demonstrate an increased lung cancer risk with long-term exposure to airborne PM including $PM_{2.5}$.[87,88] Indoor and outdoor air pollution may play a role in the development of lung cancer. Each 10 μg/m^3 increase in $PM_{2.5}$ concentrations is associated with a 15%–27% increase in mortality of lung cancer.[87] The association between $PM_{2.5}$ and lung cancer mortality was similar in men and women regardless of age or level of education. However, there was a stronger association in those with a normal body mass index and a history of chronic lung disease at enrollment.

Coal furnaces are a very popular form of domestic heating in association with a two times greater risk of lung cancer than clean energy. In addition to pollutants produced by fuel combustion, Chinese style cooking generates carcinogenic air pollutants.[89] Women often cook more than twice a day at home. Thus, women are two times more likely to develop lung cancer. Solid fuel for cooking can increase the levels of PM to three-times than that of noncooking. House layout and ventilation-related characteristics also play a key role in the risk of lung cancer.

Personal and indoor $PM_{2.5}$ exposure from burning solid fuels was observed in vented and unvented stoves in a rural region of China. Evidently, there is a high incidence of lung cancer in this situation. $PM_{2.5}$ levels of vented stoves were 34%–80% lower than unvented stoves and fire pits across fuel types.[4] Mixed effect models indicated that the main factors related to personal $PM_{2.5}$ exposure were fuel type, ventilation, number of windows, season, and burning time per stove. Lower $PM_{2.5}$ among vented stoves reduced the risks of malignant and nonmalignant lung diseases in the region. Existing data support the notion that it is important to evaluate and assess the impact of air quality on health on the local scale, in order to protect the environment and ensure an economic balance.

Summary

In summary, exposure to air pollution results in a substantial number of adverse effects in human lung diseases. The impact of $PM_{2.5}$ depends on the components and sources. In turn, $PM_{2.5}$ produces specific types of damage varying with times and regions. The $PM_{2.5}$-caused burden on the healthcare system plays an increasingly negative role in Chinese social and economic development. Increased exposure to $PM_{2.5}$ is associated with increased morbidity and mortality of chronic respiratory diseases including COPD, asthma and lung cancer, *etc.* This may be explained by $PM_{2.5}$-activated inflammatory cascades and lung injury. These changes harm the epithelium and increase epithelial permeability. Future studies are warranted to identify and quantify the unknown organic and inorganic compounds present in ambient air particles. A better understanding of the impact of $PM_{2.5}$ on pathophysiology is beneficial for addressing chronic lung diseases in China.

Conflicts of interest

No conflicts of interest to declare.

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