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REVIEW

The Effects and Pathogenesis of PM2.5 and Its Components on Chronic Obstructive Pulmonary Disease

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Abstract: Chronic obstructive pulmonary disease (COPD), a heterogeneous disease, is the leading cause of death worldwide. In recent years, air pollution, especially particulate matter (PM), has been widely studied as a contributing factor to COPD. As an essential component of PM, PM2.5 is associated with COPD prevalence, morbidity, and acute exacerbations. However, the specific pathogenic mechanisms were still unclear and deserve further research. The diversity and complexity of PM2.5 components make it challenging to get its accurate effects and mechanisms for COPD. It has been determined that the most toxic PM2.5 components are metals, polycyclic aromatic hydrocarbons (PAHs), carbonaceous particles (CPs), and other organic compounds. PM2.5-induced cytokine release and oxidative stress are the main mechanisms reported leading to COPD. Nonnegligibly, the microorganism in PM 2.5 may directly cause mononuclear inflammation or break the microorganism balance contributing to the development and exacerbation of COPD. This review focuses on the pathophysiology and consequences of PM2.5 and its components on COPD.

Keywords: particulate matter 2.5, chronic obstructive lung disease, oxidative stress, inflammation, DNA methylation, microorganisms

Introduction

The detrimental consequences of air pollution on human health have long been a worry for industrial development's impact on worldwide public health. According to The World Health Organization, approximately 7 million people die yearly from air pollution.[1] Around 9 million premature deaths in 2015 were attributed to diseases associated with pollution.[2] Significant pollutants include particulate matter (PM), carbon compounds, ozone, nitrogen compounds, and sulfur compounds.[3] The main environmental factor influencing the worldwide disease burden is exposure to ambient PM2.5 (particulate matter with an aerodynamic diameter of fewer than 2.5μm).[4,5] The impacts of ambient PM on mortality and Disability-adjusted life years (DALYs) in China were among the leading four risk factors.[6]

In vitro studies have indicated that exposure to confident PM may increase the susceptibility of pulmonary cells,[7] which could cause lung, trachea, or bronchus damage.[8] The exposure route and alveolar deposition capacity of PM vary according to its size, with the coarse fraction (PM10μm −2.5μm) having the ability to enter the upper bronchi. In contrast, the fine fraction (PM≤2.5μm) can directly access the respiratory system's gas exchange area and deposit in the airway and lung tissue, leading to an aberrant immunological inflammatory response and impaired epithelial cell function.[9,10] In addition, exposure to PM2.5 early in lung growth and development will result in permanent irreversible damage.[11] Through the blood-air barrier and circulatory system, ultrafine particles (PM≤1μm) can accumulate in various body organs, causing a range of health problems.[12,13] Therefore, it is essential to recognize the effects of air pollution on the respiratory system.

In 2017, chronic respiratory conditions ranked third among causes of death. COPD accounted for most chronic respiratory disease-attributable deaths and DALYs.[14] The burden of COPD in China estimates for 2019 disclosed that

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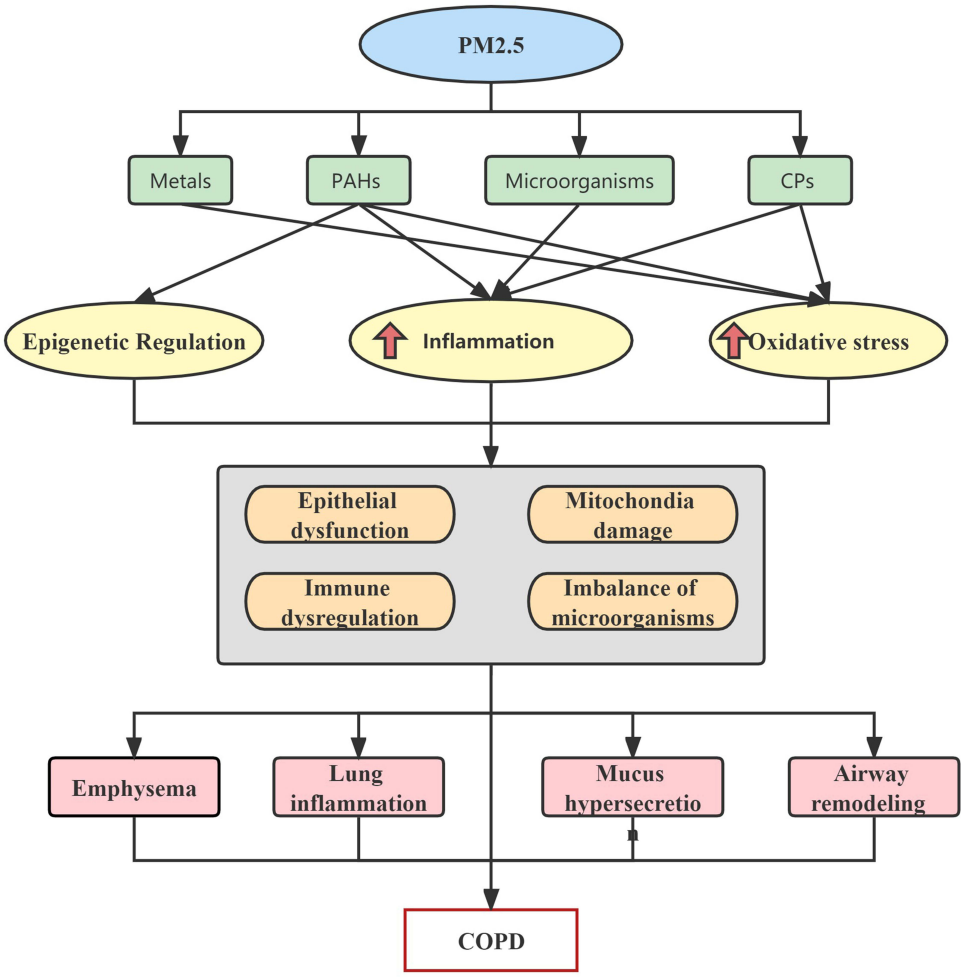
Graphical Abstract



COPD remains a significant public health problem in China.[15] COPD is a diverse illness that causes persistent inflammation, alveolar damage, and irreversible airway obstruction. It has long been believed that cigarette smoke (CS) is the main factor contributing to the onset of COPD.[16] However, there is growing evidence that non-smokers are developing COPD at a higher rate. According to estimates, 25–45% of patients with COPD are nonsmokers.[17,18] Studies have pointed out that PM2.5 can trigger COPD and reduce lung function.[19] Researchers are interested in discovering if these COPD patients who do not smoke are affected by PM2.5 pollution. Determining the precise mechanism via which COPD manifestation caused by PM2.5 occurs is therefore necessary.

As this review aims to provide the foundation for preventing and managing COPD, it will explore the relationship between PM2.5 constituents and COPD as well as PM2.5 on the development, exacerbations, and pathogenesis of COPD.

Effects of PM2.5 on COPD: Epidemiological Evidence

PM2.5 is a high risk of COPD.[20] Recent epidemiological studies have revealed that PM2.5 increased the incidence and prevalence of COPD during long-term exposure.[21,22] Ambient concentrations of PM2.5 was strongly correlated with lower pulmonary function and increasing emphysema, even at relatively low concentrations.[23,24] Research found that a rise in PM2.5 (2.4μg/m^3) was associated with a drop in FEV1 of 101.7 mL,[25] which aided in the progression of COPD.

Epidemiological research revealed a link between atmospheric pollution and COPD exacerbation.[26] Air pollution was significantly correlated to the hospitalization rate of COPD.[27] What is noteworthy is that among COVID-19 patients with COPD, hospitalization rates were more significant when exposed to PM2.5.[28] Numerous studies have discovered a connection between PM2.5 concentrations and AECOPD episodes.[29,30] According to a meta-analysis, with every 10μg/m^3 elevation in PM2.5, the probability of COPD-related emergency room visits and hospital admissions rose by 1.4–2.5%.[31] More PM exposure causes individuals with chronic obstructive pulmonary disease to have worse lung function,[32,33] lower FEV1 and oxygen saturation, more severe emphysema,[34] higher Blood Pressure, and cardiovascular mortality.[35,36] Furthermore, Patients with COPD are more vulnerable to pulmonary inflammation after exposure to PM2.5, especially those with poorer lung function.[19,37,38] These might be to blame for the disease's deterioration.

The adverse effects of particulate matter can affect the elderly more severely.[39] Despite recent improvements in general air quality, the disease burden from air pollution is still relatively high as the ageing process speeds up. The second most frequent reason contributing to the DALYs rates for COPD still was particulate matter.[40] Air pollution is thought to be a contributing factor in roughly 1.6 million deaths from COPD.[41] Especially in a region with a low Socio-demographic index, particulate matter was the main cause of COPD fatalities.[42] Especially particles <0.5μm in diameter might be responsible for the adverse effects of particulate air pollution on COPD mortality.[43]

Moreover, A study indicates that the risk of acquiring COPD was reduced by 12% for each 5 μg/m^3 decrease in PM2.5.[44] A different study also supports this claim. It shows that in comparison to the estimated figures based on the natural trends in exposure to PM2.5, 0.27 million deaths could be avoided if the global particulate matter concentration achieves its control targets by 2030. Early mortality would be reduced to 0.52%,[45] suggesting that interventions to lessen patients' exposure to PM2.5 may benefit for those with COPD.

The aforementioned epidemiological evidence taken together strongly suggests that exposure to PM2.5 is significantly linked with the occurrence, death, and progression of COPD. Air pollution reduction may be an effective strategy for lowering the chances of developing COPD.

PM2.5 Components and COPD

Physicochemical characteristics (size, water solubility, and chemical composition) of PM affect its mechanism. Research shows that airborne oil mist particulate matter (OMPM) of 1.0–10μm induced oxidative stress and increased the production of pro-inflammatory cytokines. However, only OMPM<1.0 induced disruption of the pulmonary epithelial barrier.[46] Thus, the magnitude of PM should be considered when analyzing its adverse effects. We will not go into great detail about this in this article. We concentrate on the mechanisms of the various PM2.5 components.

PM2.5 can be classified as aqueous and organic extracts, depending on how soluble it is. Interestingly, the variations in respiratory and immunological effects can also be attributed to the differences in PM2.5's constituents. A study from Japan found that organic extracts of PM2.5 generated IL-6 rather than aqueous extracts, promoting inflammation. Additionally, compared to extracts from the urban region, those from the industrial sector appeared to have more potent effects.[47] A Brazilian study found that PM2.5 aqueous extracts reduced the release of IL-6 and IL-8.[48] This phenomenon might be because the study's water-soluble extracts of PM2.5 samples had metal components and polar organic constituents. It is still unknown how specific PM2.5 components contribute to the decline in cytokines. According to a similar study, metal-rich water-soluble extracts impact metabolism and the respiratory system.[49] In general, water-soluble extracts significantly contribute to DNA oxidative damage and plasma-membrane peroxidation, while organic extracts are primarily linked to genotoxicity and mutagenicity.[50,51] Furthermore, the cell toxicity of PM2.5 water-soluble and organic extracts was not consistently demonstrated.[52,53] Therefore, more investigation is required to completely comprehend the mechanisms and immediate effects of the diverse PM2.5 components.

Significant components of PM2.5, such as organic compounds (organic carbon, polycyclic aromatic hydrocarbons, and benzene), inorganic compounds (sulfate, nitrate, ammonia, quartz, silica, mineral oxides), and biological components (bacteria, fungi, and virus), are typically similar. However, The ratios of the various components vary greatly depending on the local sources and emissions.[54] PM's composition, concentration, and specific surface area influence its pathophysiological effects.[55–57] It has been determined that the most toxic PM components are metals, polycyclic aromatic

hydrocarbons (PAHs), carbonaceous particles(CPs), and other organic compounds, they have different toxicity to human health.[58]

Metals

Interestingly, the different metal composition of PM2.5 affects different organs. For instance, As or Cr harms the lungs typically. However, Pb^{2+} predominantly affects the kidneys.[59] Research reported that several metal components in PM2.5 were directly related to lower LVEF, FEV1, FVC, and PEF.[60] Some redox-active metals (As, Zn, and Fe) in them play a role that can promote the production of reactive oxygen species (ROS) and thereby decrease antioxidant enzyme activity, causing cells to experience oxidative stress.[61,62] According to the biological solubility of metals, they can be divided into water-insoluble and water-soluble metals. Zhao et al found that water-insoluble metals of PM2.5 inhibits Nrf2, thus reducing the body's antioxidant capacity, resulting in excessive lung oxidation.[63] Another investigation on soluble metals present in PM2.5 revealed that they could activate both the pro-oxidative and anti-oxidative systems in these pulmonary cells.[64] In conclusion, the metals in PM2.5 can cause an imbalance between oxidative and antioxidant effects in the body, leading to lung damage.

Polycyclic Aromatic Hydrocarbons (PAHs)

Particles' carbon surfaces can absorb harmful organic compounds. Polycyclic Aromatic Hydrocarbons (PAHs) are the leading organic compounds of PM2.5. For elderly patients with COPD, exposure to PAHs-rich PM2.5 could impair their small airway functions.[65] FEV1/FVC is also decreased by exposure to PAH-enriched PM2.5.[66] Nevertheless, the exact mechanism is still unknown. The well-known PAH can result in lung cancer by elevating the expression of the CYP1A1 gene and promoting DNA damage.[67] Recent research has revealed that OGG1 expression and methylation are responsible for PAH's ability to produce oxidative DNA damage.[68] Furthermore, it was also discovered that PAHs could induce the expression of oxidative stress genes (HMOX-1) and inflammatory cytokine genes (IL-6 and IL-8).[69] Many studies have shown that PAHs can induce ROS formation and inflammatory response.[70,71] Additionally, PAHs may cause the mitochondrial ROS to produce to activate the NLRP3 inflammasome, further inducing lung damage.[72] The inflammatory signaling pathways nuclear factor kappa B (NF-κB), Akt phosphorylation, and MAPK pathway can all be activated by acute 1-NP, a type of nitrated polycyclic aromatic hydrocarbons (NPAHs).[73] Through the AhR/ROS axis, PAHs cause pro-inflammatory mediators to enter the bloodstream, which ultimately causes damage to the lung epithelium or tissue.[70]

Microorganisms

It is reported that household dust's microbial makeup may impact adults' allergy reactions.[74] Bacteria, eukaryotes, and viruses are among the microorganisms found in PM2.5.[75] A component of gram-negative bacteria's cell walls called LPS is an endotoxin linked to a chronic inflammatory pulmonary illness.[76] It has been proved that indoor and outdoor PM2.5 contain endotoxins.[77] Recent research has discovered that most outdoor airborne LPS stems from Artemisia pollen.[78] According to earlier research, the concentration of LPS determines how it affects the lungs. High LPS exposure triggers a Th17 cell response that increases the synthesis of IL-17 and leads to neutrophilic inflammation, which aids in the emergence of severe pulmonary illnesses.[79] On the other hand, exposure to low concentrations of LPS in the airways is associated with a Th2 immune response, promoting asthma onset.[80] Extracellular vesicles (EVs) produced by bacteria are another critical element of biological UPF. Th1 cell induction and Th17 cell induction are two ways whereby bacteria-derived EVs cause inflammation in the body's immune system.[81] Because LPS is a vital ligand for TLR4, Chen et al revealed that the dust fall-activated TLR4/NF-κB signaling pathway might be mediated by LPS present in PM2.5.[82] Pretreating PM2.5 with an antibiotic that selectively suppresses endotoxin could effectively inhibit the inflammatory reaction.[83] Antibiotics may be a selection for reducing the inflammatory response brought on by PM2.5.

Carbonaceous Particles

A significant fraction of PM is CPs. Elemental carbon (EC) and organic carbon (OC) are makeup CPs.[84] EC consists of black carbon (BC) and carbon black (CB).[85] By causing oxidative stress and inflammation, CPs seriously impair lung function and result in COPD.[86] Some works demonstrated that CB drove pulmonary fibrosis

through an activated NLRP3 inflammasome pathway[87] and mediated autophagy.[88,89] One study found that when exposed to both CB and metals, CB can increase the permeability of cells membrane and ultimately result in increased cytotoxicity caused by Cadmium (Cd).[90] Pan et al made a PM2.5 Models Base that contains all possible combinations of four types of harmful contaminants, where Cr/Pb pairings result in cell cycle arrest.[91] So, evaluating the health impacts of PM2.5, we should also take into account how its various complex components work together.

PM2.5 Induced Pathogenesis in COPD

Epithelial Alterations

The first line of defense against inhaled PM2.5 is the lining of the airways. Studies have shown that exposure to PM2.5 can alter cilia movement and increase mucus formation, which reduces their capacity to perform airway clearing and delays the prompt removal of PM2.5 from the lungs and airways.[92] PM2.5 can impair the expression of 8-oxoguanine DNA glycosylase 1 (OGG1) in alveolar epithelial cells,[93] which prevents Type 2 alveolar epithelial cells damaged by PM2.5 from proliferating and renewing themselves.[94] After being exposed to PM2.5, it is observed that there are fewer multilamellar bodies in the Alveolar epithelial type II; cell (AT2) increases mitochondrial swelling, collagen deposition, and pulmonary inflammation.[95] In addition, it can be observed that the dysregulated AT2 cells into AT1 cells in the PM2.5-induced COPD mouse model[96] damage cellular repair mechanisms. Even worse, it has been shown that inflamed bronchial epithelial cells caused by air pollution particles trigger apoptosis,[97] particularly when PM2.5 is injected into those inflamed by cigarettes.[98] Another study has found that PM2.5-induced apoptosis of alveolar epithelial cells through the PI3K/AKT/mTOR pathway regulates autophagy.[99] By turning on the AMPK-Beclin1 pathway, PM2.5 can also cause ferroptosis.[100] PM2.5-induced cell death encourages the evacuation of cell contents, aberrant pro-inflammatory mediator hyperplasia, and inadequate macrophage clearance of dead cells, all of which contribute to small-airway illness and emphysema in COPD.[101] Therefore, it is crucial to understand the effects of cells induced by PM2.5 exposure to find the appropriate reversal methods.

Imbalance of Microorganisms

Humans' airway micro-environment includes the microbiome as a constitutive component. The severity of COPD has been reported to correlate with microorganisms' components and functions.[102] Exposure to PM2.5 significantly impacts the airway microbiota.[103] A study on animals found that exposed mice to diesel exhaust particles had an expansion in Proteobacteria in their BALF.[104] The altered microbiota composition can promote and affect pulmonary inflammation and oxidative stress during PM2.5 exposure.[105] In a recent study, Jia et al found that PM2.5-induced differential expression of miRNAs was enriched in microbial signaling pathways, including HIF-1 signaling, IL-17 signaling, and Th17 cell differentiation pathways. MiR-149-5p might connect to how PM2.5 leads to dysbiosis in the lung's microbiome.[106] This might be an effective way to prevent the PM2.5-induced imbalance of the lungs' microbiota. Moreover, a rat model of chronic obstructive pulmonary disease is induced by chronic exposure to ambient particulate matter, which leads to gut microbial dysbiosis.[107] The intestinal microbiome encourages PM-induced neutrophilia in the lung, which may be related to Tγδ17 cells.[108] However, there are still a lot of unanswered concerns about how the microbiome and PM2.5-related COPD interact.

Potential Mechanisms

The development of COPD is assumed to involve a number of mechanisms, including proteolytic–anti-proteolytic imbalance, oxidative stress, inflammatory response, epigenetic alterations, and more. The lung tissue proteomics analysis showed that the proteins involved in oxidative stress, cellular metabolism, inflammatory responses, and actin dynamics are dysregulated under exposure to traffic-related air pollution.[109] Chronic exposure to PM2.5 causes significant impairment in lung function, emphysematous lesions, inflammation in the lungs, and remodeling of the airway walls.[110] PM2.5 could harm COPD development and progression. In order to better understand how

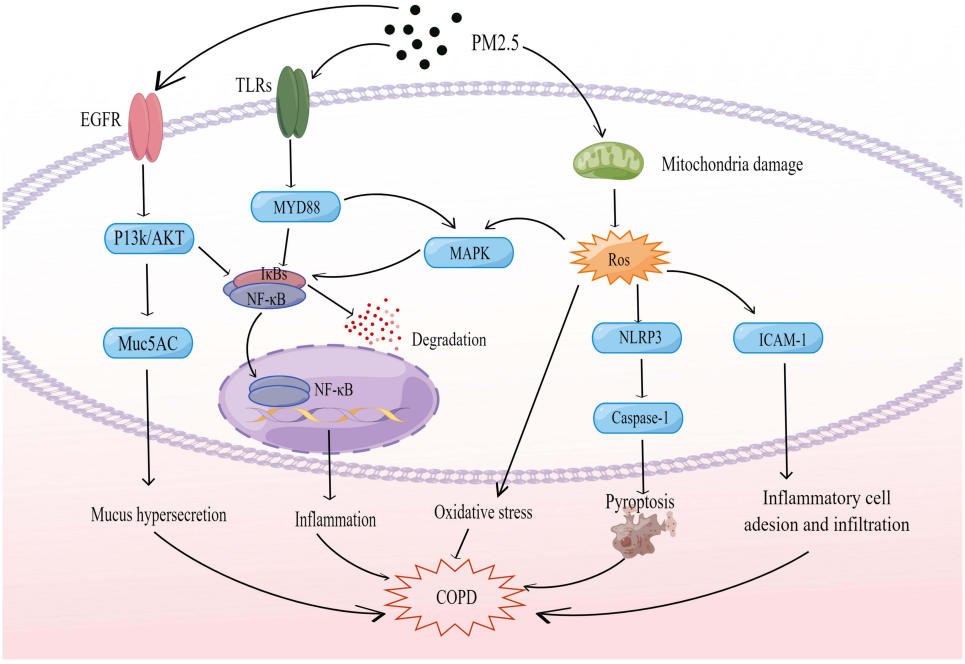


Figure 1 Pathways of COPD induced by PM2.5.
Notes: Exposure to PM2.5 upregulates the expression of TLRs. The recruitment of MyD88 by an activated TLR leads to inflammation via activating the MAPK and NF-κB signaling cascades. Endogenous ROS is mostly produced by mitochondria. PM2.5 induces mitochondrial damage, which results in significant amounts of ROS being created. The MAPK pathway is directly activated by ROS, which then triggers the downstream NF-κB pathway to increase the production of many inflammatory factors. EGFR signaling pathway is activated by PM2.5. Its activation consequently causes the overexpression of its downstream effectors, PI3K and AKT, which increases the expression of the MUC5AC gene, causing mucus to secrete excessive amounts of mucus and mediating inflammation through NF-κB. ROS trigger the NLRP3 inflammasome and the production of ICAM-1. NLRP3/Caspase-1 activation results in pyroptosis. ICAM-1 overexpression promotes inflammatory cell infiltration and adhesion. COPD will eventually develop as a result of all these pathways being activated. Created by Figdraw.

PM2.5 causes COPD, it is necessary to better understand its pathophysiology and probable mechanisms. Inflammatory reactions and oxidative stress were once thought to be the two main factors in COPD (Figure 1).[111]

Oxidative Stress

Cellular damage results from an imbalance between the endogenous antioxidant defense system and the generation of ROS production, known as oxidative stress.[112] Studies have shown that PM2.5 contributes to an imbalance between oxidants and antioxidants. For example, there was a trend toward reduced antioxidant production (SOD1 and SOD2) in bronchial epithelial cells after exposure to diesel emissions.[113] In COPD rats, PM2.5 increased malondialdehyde (MDA) levels while decreasing total superoxide dismutase (T-SOD).[114] Besides, in the lungs of COPD rats exposed to PM2.5, there was a decreasing trend in the expression of the Nrf2 protein and its downstream component heme oxygenase-1 (HO-1).[115] The transcription factor Nrf2, which is inversely correlated with the severity of COPD, controls the majority of antioxidants.[116] The primary source of endogenous ROS in mitochondria.[117] Damage to redox equilibrium and structural abnormalities in the mitochondria will result from exposure to PM2.5, which leads to a persistent rise in ROS.[10,118] Meanwhile, ROS function as intermediary signaling molecules and can activate the NF-κB, TLR, and MAPKs.[119] These signaling pathways affect cell-signaling proteins, which contribute to the beginning of inflammatory responses.[120] BEAS-2B cells, normal HBECs, and in particular sensible COPD HBECs exposed to PM2.5 caused ROS overproduction and activated oxygen-sensitive NRF2 and NF-kB signaling pathways.[10] By activating the IL-6/AKT/STAT3/NF-κB signaling pathways in the epithelial cells of the lungs, PM2.5-induced ROS also can contribute to intercellular adhesion molecule-1 (ICAM-1) expression.[53] ICAM-1 facilitates the adhesion and infiltration of inflammatory cells, such as monocytes and macrophages, into inflammatory sites that result in lung lesions.[121,122]

Inflammation

Inflammation and oxidative stress are two biological processes that are connected and appear to occur together to increase harm.[123] Previous research has revealed that biomarkers of inflammation were increased by brief PM2.5 exposure.[124,125] In COPD patients, short-term exposure to PM2.5 elevates Th1 and Th17 cytokines while decreasing Th2 cytokines. This improves circulation levels of IL-2, IL-12, IL-17A, IFN-γ, MCP-1 and sCD40L, which exacerbated systemic inflammation.[126] Urban particulate matter may worsen inflammation by inducing epithelial remodeling and malfunctioning dendritic cells (DCs) in COPD patients.[127] An in vivo experiment found that the activation of lung DCs by biomass smoke caused Th17 responses and emphysema in rats.[128] Another study found that early-life exposure to PM2.5 caused young adult mice to develop COPD-like phenotypes, which caused inflammation and had long-term negative effects on lung development.[11]

The activation of toll-like receptors (TLRs) is one of the suggested pathways for the inflammatory response in PM2.5-induced COPD. The most important receptors in the COPD's clinical manifestation development are TLR-2 and TLR-4.[129] Myeloid differentiation marker 88 (MyD88), one of the downstream adaptor proteins that TLRs recruit, is recruited by activated TLRs, starting the TLR-2/MyD88 and TLR-4/MyD88 signaling cascades. PM2.5 Causes TRAF6 accumulation, thereby promoting the synthesis of inflammatory chemokines and the activation of the NF-κB pathway.[130] Following exposure to PM2.5, TLRs and MAPKs can also trigger NF-κB signaling.[111,131]

Moreover, epidermal growth factor receptor (EGFR) signaling is a paramount regulator of inflammation associated with COPD. A pro-inflammatory response to PM2.5 exposure has been reported in BEAS-2B cells by triggering EGFR signaling,[132] which also caused MUC5AC overexpression.[133] Similar findings were made by Val et al, who discovered that PM2.5 exposure activates the EGFR pathway and results in MUC5AC over-production in rat airways and primary epithelial cells.[134] Amphiregulin (AREG) is an essential ligand for EGFR. AREG promotes the production of IL-1α, IL-1β, and Muc5AC to increase PM2.5-induced inflammation and mucus hypersecretion via activating the EGFR-PI3K-AKT/ERK pathway.[135] Subsequently, chronic effects such as reduced expiratory flow and permanent remodeling may occur.[136]

The NLRP3 inflammasome, a crucial part of the inflammatory response, is linked to COPD exacerbations.[137] ROS could activation of Transient Receptor Potential Melastatin2 (TRPM2), inducing the influx of Ca^{2+} intracellular, with subsequent activation of NLRP3.[138] Particulate matter in the environment reduces Sirtuin1 and increases the SREBP1-PIR/NLRP3 axis to cause inflammation in human lung fibroblasts.[139] As a result of PP2A dephosphorylating IRE1α,[140] PM2.5 activates the NLRP3/Caspase-1 mediated macrophages pyroptosis, causing inflammation and oxidative stress to damage the lungs.[141] Accordingly, NLRP3-mediated macrophage pyroptosis may present an attractive therapeutic target for PM-induced COPD. By preventing the production of NLRP3 inflammasomes and apoptosis through the Nrf2-dependent pathway, the gaseous signaling molecule hydrogen sulfide (H_2S) protected mice from developing emphysema and airway inflammation brought on by PM2.5.[142]

In COPD patients, exposure to ambient ultrafine particles was also linked to higher levels of IL-8, MCP-1, MIP-1α, MIP-1β, TNF-α, and IL-1β.[143] There is also evidence that PM2.5 can release pro-inflammatory compounds into the blood circulation, resulting in systemic inflammation, which is indicated by white blood cells (WBC), C-reactive protein (CRP) and serum cytokine levels.[144] This further contributes to the progression of COPD and its incidence.[145] Hence, it is crucial to prevent and treat the inflammatory reaction caused by PM2.5 effectively.

Epigenetic Regulation

DNA methylation is impacted by long-term exposure to ambient air pollution,[146] which is considered a vital regulator when PM2.5 induces lung injury. When PM2.5 dust levels were high enough, the PI3K/Akt/DNMT3b pathway was stimulated, increasing the hypermethylation of the interferon-gamma IFN-γ gene promoter.[147] Rats exposed to traffic-related PM2.5 experienced an aggravation of inflammation because the exposure altered the methylation state of the IFN-γ and interleukin 4 (IL-4) genes and the levels of their associated cytokines.[148] A study revealed that DNA hypomethylation, a P16 gene promoter hypermethylation, and a decreasing DNA methyltransferase activity in HBE after repeated exposure to PM2.5.[149] PM2.5 exposure may influence TNF-α

through a reduction in methylation.[150] Exposure to PM2.5, CO, and O_3 also alters the methylation patterns of numerous CpG sites of the immunoregulatory genes, including Foxp3, IL-4, IL-10, and IFN-γ, are also altered by exposure to, which alters the immune response.[151] The DNA methylation patterns of several genes, including p53, p15, p16, APC, RASSF1A, HIC1, iNOS, hTERT, and IL-6, are altered by PM exposures, and these alterations have an impact on the development of respiratory illnesses.[152] Ji et al found that lung injury and recovery are impacted by changes in H3K27ac brought on by PM2.5 exposure.[153] To better understand how histone alterations affect PM2.5-related disease, the connection between PM2.5 and histone modification requires further study.

MiRNAs are non-coding, 20–25 nucleotide length, short RNA molecules. MiRNAs have drawn interest because they are important pathogenic pathway regulators.[154] After exposure to PM2.5, miR-194-3p is downregulated and positively correlates with FVC and FEV1.[155] A low expression of miR-140-5P induced by PM2.5 can trigger a strong inflammatory response by over-activating TLR4.[82] The ability of the lungs of rats to eliminate 8-OHdG, which is linked to DNA damage, is further impacted by high miR485/miR-145 levels and suppressed mRNA expression of MTH1 in rat lung tissues.[156] Interestingly, lncRNAs are a viable diagnostic and therapeutic tool since they have amazing tissue selectivity that mRNA lacks.[157] TRAPM2.5 can up-regulated lncRNA RP11-86H7.1, which acts as a competing endogenous RNA of miR-9-5p to promote airway inflammation.[158] Air pollution PM regulates the immune activities of DCs via the GATA3/lncRNA MHC-R nexus, which leads to the immune dysregulation of COPD patients.[159] lncRNA NONMMUT065867, lncRNA NONMMUT064312, lncRNA NONMMUT018123 up-regulated following exposure to PM2.5. These lncRNAs might be linked to lung inflammation.[160] It is poorly understood how air pollution affects lncRNAs and eventually leads to illness.

Conclusion

In this article, we have reviewed how PM2.5 and its components affect COPD and its possible mechanisms. However, only few reports demonstrated the potential effects of PM2.5 compositions on COPD and the specific mechanisms. Another problem is that the toxicity of specific PM2.5 components needs to be accurately determined, as well as the exact proportion of these components in the PM mix. Therefore, it is of great importance to comprehensively characterize the composition of environmental PM2.5 and identify the significant pathogenic components, and make it possible to investigate the underlying mechanisms by which PM2.5 components contribute to COPD. This is essential to treat health problems caused by PM2.5.

Abbreviations

AT1, Alveolar epithelial type I cell; AT2, Alveolar epithelial type II cell; BC, black carbon; CB, carbon black; CPs, carbonaceous particles; COPD, Chronic obstructive pulmonary disease; CRP, C-reactive protein; CS, cigarette smoke; DALYs, Disability-adjusted life years; DCs, dendritic cells; EC, Elemental carbon; EGFR, epidermal growth factor receptor; EVs, Extracellular vesicles; IFN-γ, interferon-gamma; MAD, malondialdehyde; NF-κB, nuclear factor kappa B; OC, Organic carbon; OGG1, 8-oxoguanine DNA glycosylase 1; PAHs, polycyclic aromatic hydrocarbons; PM, particulate matter; ROS, reactive oxygen species; TLRS, toll-like receptors; TRPM2, Transient Receptor Potential Melastatin2 WBC, white blood cells.

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Disclosure

The authors declare no conflicts of interest in this work.

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