Chapter

Effects of Environmental Emissions on the Respiratory System: Secrets and Consequences

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Abstract

Human health has been affected adversely by air pollution as a serious environmental challenge. Ambient (outdoor) air pollution mainly resulted from human activities (e.g., fuel combustion, heat generation, industrial facilities) causes 4.2 million deaths every year. Moreover, each year, 3.8 million people die from indoor air pollution which means household exposure to smoke from fuels and dirty cook stoves. They are the risks of stroke, heart attack, lung disease, or cancer that resulted from air pollution which assaults our brain, heart, and lungs using its invisible weapons named particulate matter (PM). These inhalable particles are of a nanoscale or microscale size. Upon inhalation, the air with its components enters the human body through the respiratory system. The lungs are the responsible organs for gas exchange with blood. Inhaled particles, such as silica, organic compounds, and metallic dusts, have toxic effects on our pulmonary system. For example, the accumulation of nanoparticles in the kidneys, liver, spleen, and central nervous system through the penetration of the epithelial barriers in the lungs has been observed. The purpose of this chapter is to describe the toxic effects of air particles on the different organs in the human body and to introduce some of the adverse effects of air pollution on human health.

Keywords: pulmonary system, human health, toxicity, nanoparticles, PM2.5

1. Introduction

Environmental emission is the pollutants around us in a gas or vapor phase. They can be gas or even solid particles in the air we breathe. If these materials find a way to get in touch with our human body, they may cause adverse effects on our health. There are various ways that they can reach human organs, from the skin to internal organs such as the lungs and brains. The toxicity of these particles depends on the nature of the particles and their size. In this chapter, the size of the particles that are the most dangerous ones is introduced, and the diseases and some of the mechanism of actions of these pollutants will be discussed.

2. Environmental emissions and human health

Environmental emissions are the pollutants discharged to our surrounding environment in a gas or vapor phase. Therefore, the outspoken result of such extensively spread emissions is air pollution.

According to some similarities among the pollutants, they can be classified in four groups:

1. Gaseous pollutants (e.g., nitrogen oxides, carbon monoxide, volatile organic compounds, ozone, sulfur dioxide)

2. Persistent organic pollutants (e.g., pesticides and dioxins)

3. Heavy metals (e.g., mercury, lead, chromium, vanadium)

4. Particulate matters (PMs) [1]

Air pollution causes 7 million deaths worldwide every year. Ambient air pollution mostly arising from anthropogenic activities [2, 3], e.g., using vehicles, combustion of fossil fuels, and power generation, is the cause of 4.2 million deaths due to acute and chronic effects on human health [4].

The diseases and, consequently, the deaths because of air pollutants are related to the routes of exposure to them. Skin diseases, lung cancer, and strokes are the examples of these illnesses.

The various adverse effects of air pollutants on the human health will be explained in the following sections.

3. Skin diseases

The skin is one of the first barriers against air pollutants. However, if this biological shield is exposed to air particulate matters for a long time, several types of diseases may happen to this largest organ in the human body. Atopic dermatitis, eczema, acne, and psoriasis are some of these diseases [5].

When toxic compounds are absorbed through the skin, they can cause local or systematic toxicity. In fact, the skin is an entrance for PMs to penetrate into the body through transfollicular route.

The particles with a diameter of 2.5 microns or less (PM2.5) and nitrogen dioxide can be effective on eczema and allergic sensitization. Particles with a diameter equal to or less than 10 μm (PM10) along with PM2.5 and ultrafine particles intensify itching as a symptom of atopic dermatitis. Skin aging through the process of extrinsic aging is another skin-related consequence of environmental pollution. In fact, environmental factors that cause the release of harmful free radicals will result in coarse wrinkles and uneven pigmentation of the skin. Skin cancer is the other disease caused by air pollutants such as polycyclic aromatic hydrocarbons as a potential group of carcinogenic materials. There are two potential routes for air particulate matters to diffuse through the skin surface: one of them is hair follicles or sweat ducts and the other one is across the stratum corneum. The skin barrier is degraded by PM2.5 because these particles reduce the levels of filaggrin, cytokeratin, E-cadherin, and tight junction molecules [6].

By interaction between aryl hydrocarbon receptor (AhR), as a receptor, and these air particulate materials, carcinogenic metabolites are generated, and the carcinogenicity in the cells will be induced [7]. It has been shown that there is no carcinogenic effect on the skin of the mice with AhR-deficiency. Moreover, in AhR-positive mice cases, the incidence of squamous cell carcinoma by air particulate matters was detected.

In fact, AhR is a ligand-activated transcription factor, and it has been reported that it is involved in maintaining cellular homeostasis. AhR has been recognized as

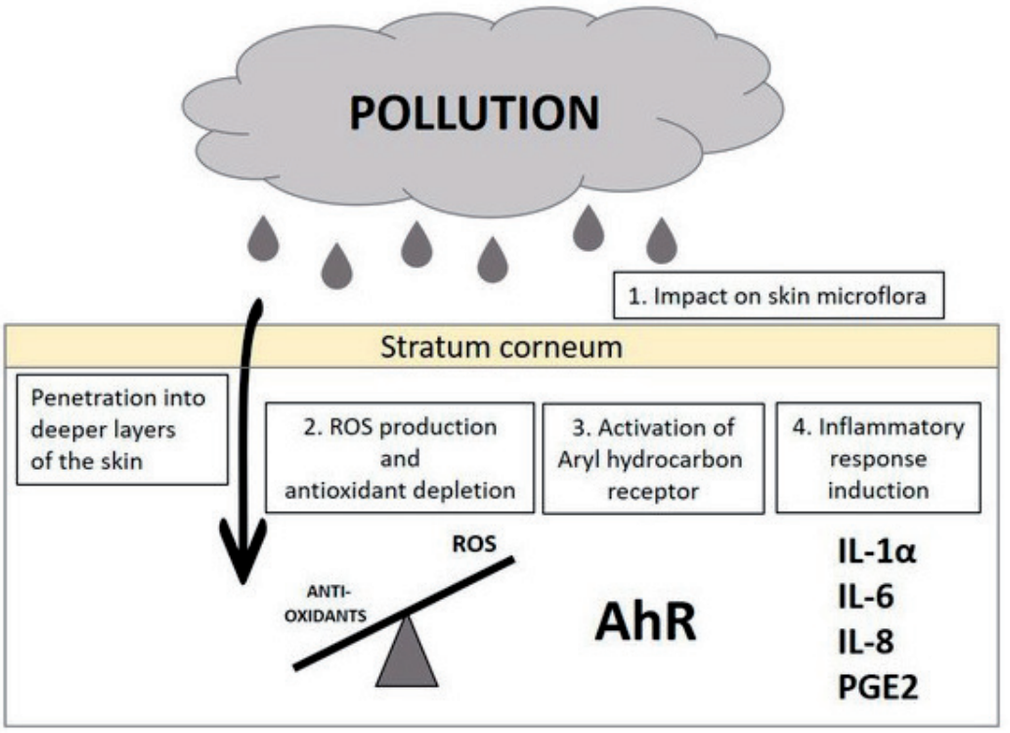

Figure 1.
Mechanism of the actions of pollutants on the skin [12].

a receptor for environmental pollutants, such as polycyclic aromatic hydrocarbons (PAHs). Upon ligand interactions, AhR in the cytoplasm will translocate into the nucleus and will bind to specific regulatory DNA sequences called dioxin response elements (DREs) which have been located in the promoters of target genes. The mentioned target genes are the ones involving detoxification the enzymes such as CYP1A1 and CYP1B1 [8]. Therefore, AhR is a regulator in controlling the CYP1 gene expression [9].

CYP1A1 is one of the cytochrome P450 enzymes that is capable to activate compounds with carcinogenic characteristics [10]. This enzyme can biotransform PAHs to carcinogens [11].

In fact, as **Figure 1** shows, pollution affects the skin microflora, and the pollutants will pass through the stratum corneum layer of the skin. Then, the reactive oxygen species (ROS) will be produced that causes a depletion in the amount of antioxidants in the skin. AhR will be activated, and the overproduction of pro-inflammatory factors will happen. These factors, as the indicators of cell response to the air pollutants, are the inflammation markers, such as prostaglandins (PGE2), interleukins (IL-6, IL-8, IL-1α, and IL-1β), or tumor necrosis factor-α (TNF-α). This mechanism will affect the biological function of the cells in the skin which will result in skin lesions and deterioration of the skin appearance [12, 13].

There are different studies on specific populations, e.g., asphalt-paving workers, chimney sweeps, coke oven workers, and asphalt-roofing workers, which show that skin uptake is a direct route of contamination by pollutants [14].

4. Heart diseases

The main morbidity and mortality caused by air pollutants is because of their adverse effects on cardiovascular system. **Figure 2** also demonstrates the deaths attributable to PM2.5 by the type of disease that it has caused between 1990 and 2015.

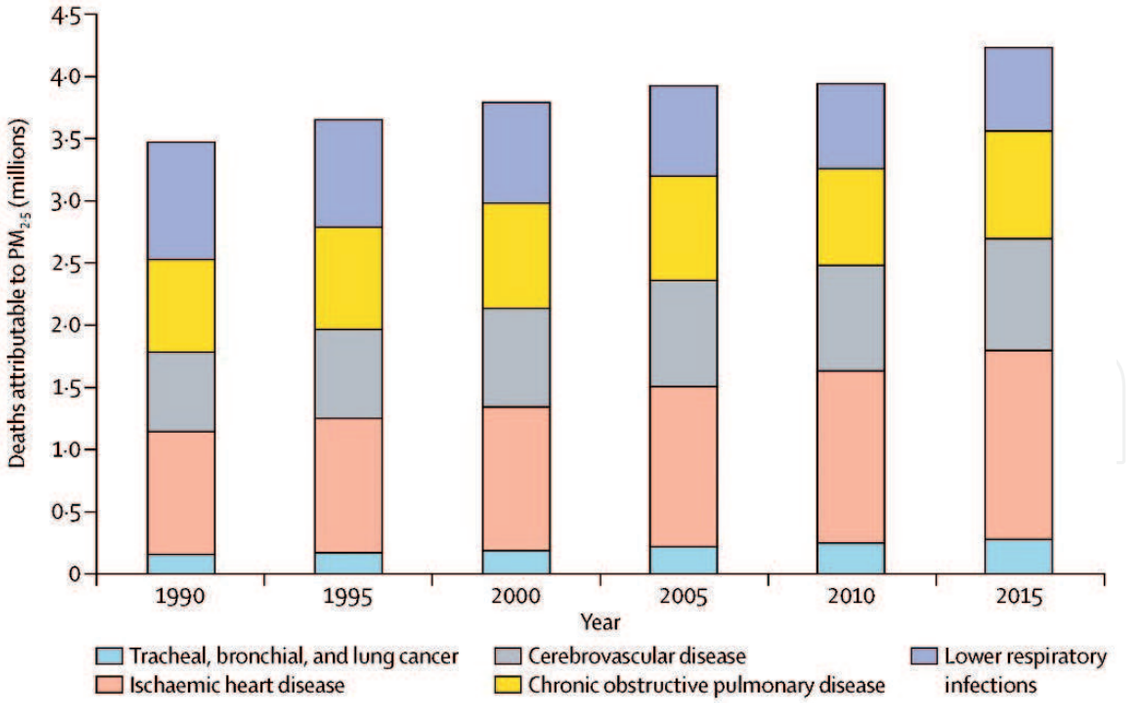

Figure 2.
Deaths attributed to ambient particulate matter pollution according to the type of diseases between 1990 and 2015 [16].

Epidemiological studies have shown that there is a robust association between air pollution and cardiovascular diseases. The Global Burden of Diseases (GBD) study estimated that the air pollution was the cause of 19% of all cardiovascular deaths in 2015 [15, 16].

A study on healthy people who spent 5 days near a steel plant showed that both of the systolic and diastolic blood pressures were higher in those volunteers who did not use mask in this area [17].

Increasing the exposure to the particulate matters will cause a promotion in the relative risk of cardiovascular diseases. A short-term increase in PM2.5 elevates the risk of acute cardiovascular events by 1–3% in a few days. This risk will be increased by almost 10% over several years which means long-term exposures. According to the World Health Organization air quality guidelines, the standard levels of exposure must be <20 μg/m^3 for daily levels and <10 μg/m^3 for annual levels. However, it has been shown that more than 90% of the global population is exposed to the levels exceeding these standard levels.

The secondary pathways through which the air pollution causes the risk of cardiovascular diseases can be classified into six groups:

1. Endothelial barrier disruption/dysfunction

2. Inflammation which involves both of the innate and adaptive immune components

3. Prothrombotic pathways

4. Autonomic imbalance

5. Central nervous system effects on metabolism and hypothalamic-pituitary-adrenal axis activation

6. Epigenomic changes

There are three primary pathways initiating those abovementioned secondary pathways. They are:

1. Oxidative stress and depletion of antioxidants

2. Direct translocation of particles and penetration into the systemic circulation

3. Biological intermediates through increasing oxidized by-products that may be involved in endothelial barrier dysfunction and inflammatory cell recruitment [18]

Exposure to PM2.5 can elevate the blood glucose level and incident cardiovascular disease events such as coronary artery disease [19–21].

The short-term exposure to particulate matters can cause acute cardiovascular diseases such as cardiac arrhythmia and myocardial infarction, while long-term exposure to these particles will result in coronary events [22].

5. Neurological diseases

The other adverse effect of air pollution is on the central nervous system (CNS). Air pollutants exacerbate the neurodegenerative conditions such as Parkinson's and Alzheimer's diseases. An association has also been shown between air pollution and the incidence of dementia, cognitive impairment, and white matter injury [23].

Increased concentration of traffic-related air pollution will increase Attention Deficit Hyperactivity Disorder (ADHD) and autism. It also affects adult cognition (episodic memory) and major depressive disorders [24].

The neuroinflammation and accumulation of B-amyloid peptide (AB42) and alpha-synuclein in the brain is the pathway that provides a potential mechanism for neurodegeneration [23].

There are two mechanisms through which air pollutants reach the brain. The first one is direct mechanism which means the pathways in which the adsorbed and soluble compounds reach the brain. The other mechanism is the peripheral one. Air pollution causes pro-inflammatory signals originating in the peripheral organs and/or tissues such as the lung, cardiovascular system, and liver. It increases the systemic-induced cytokine response which transfers the inflammation to the brain. TNF-α and IL-1β are the circulating cytokines which cause neuroinflammation, cerebral vascular damage, and neurotoxicity. Neuron damage is also caused by systemic inflammation.

Microglia, as the resident innate immune cells in our brain, are activated in neurodegenerative diseases such as Alzheimer's disease and Parkinson's disease. It has been reported that microglia activation happens by air particulate matters, e.g., manganese and titanium nanoparticles with reactive oxygen species.

Brain lipid peroxidation is a result of acute or chronic ozone exposure which can be the inhalation of reactive oxygen species [25–27].

6. Stroke

Stroke can be classified as both a neurological and cardiovascular disorder [28, 29]. As a cardiovascular disease, some mechanisms have been suggested. For example, air particles can be associated with an increase in the plasma lipoprotein-associated phospholipase A2 which has been proved to be an independent risk

factor for stroke. Atrial fibrillation is also a known risk factor for stroke. Some studies on animals have shown that exposure to particles increases the incidence or susceptibility to arrhythmia. Therefore, it can also be considered as a mechanism to explain the observed link between air pollution and cardioembolic strokes [15]. Some molecular and cellular mechanisms of neuronal injury induced by air pollution have been suggested. Using these mechanisms, the association between air pollution and stroke as a neurological disorder can be explained. The blood-brain barrier (BBB), as the major site of controlled blood-CNS exchange, is a physical barrier which protects the CNS from potential pathogenic agents and toxins. So, an intact BBB is essential for the CNS to operate properly. It has been shown that the integrity of BBB is impaired in CNS diseases such as stroke, Alzheimer's disease, and Parkinson's disease. Activation or damage of the different cellular components of BBB results in CNS injury. When air particles are inhaled, systemic inflammation can be induced by them. This effect can disturb the integrity of BBB which increases the risk of stroke [30].

It has been shown that PM2.5 is associated with stroke mortality [31, 32]. The danger of air pollution in this case is as high as it is called a silent killer that needs environmental and public health policies [33, 34].

After exposure to air pollutant, the risk of ischemic stroke will be elevated [35]. Short-term exposure to pollution is considered to be associated with cardioembolic stroke. During peak periods of pollution, special care should be taken for those people susceptible to cerebral embolism [36]. So, cardiovascular diseases as a result of air pollution can also result in stroke. Carbon monoxide, nitrogen dioxide, and sulfur dioxide increase the risk of stroke [37, 38].

7. Pulmonary diseases

Upon inhalation, the air with its components enters the human body through the respiratory system. Based on the function, the respiratory system can be divided into two zones: conducting zone (nose to bronchioles) and respiratory zone (alveolar duct to alveoli). Anatomically, the respiratory tract is classified to the upper respiratory tract (organs outside the thorax—nose, pharynx, and larynx) and the lower respiratory tract (organs within the thorax—trachea, bronchi, bronchioles, alveolar duct, and alveoli) which makes up the lungs [39]. The extra-thoracic region, in the upper respiratory tract, includes the nasal and oral passages, pharynx, and larynx. This is the first line of defense against inhaled particles [40]. The tracheobronchial and alveolar regions are in the lower respiratory tract (**Figure 3**).

The lungs are the responsible organs for gas exchange with blood. This function is performed in alveolar sacs called alveoli located in the deepest region of the lung or alveolated region [43]. In fact, when we breathe, the air reaches the alveolar region (parenchyma) through a conducting airway tree. As the inset in **Figure 3** shows, blood flows in a capillary network in inter-alveolar septa. The last barrier that air and its particles encounter, before entering blood circulation, in the respiratory tract consists of a continuous alveolar epithelium, a continuous capillary endothelium, and a connective tissue layer between them [44].

Type II cells in the alveolar epithelium secrete a material which profoundly decreases the surface tension of the alveolar lining fluid. The important constituent of this surfactant is dipalmitoylphosphatidylcholine (DPPC) [45].

When we inhale the polluted air, a lot of particulate matter enters our respiratory system. However, the deposition of particles in various regions of our pulmonary system is dependent on the size of the particles. **Figure 4** demonstrates the fraction of particle deposition in the pulmonary system based on the particle size.

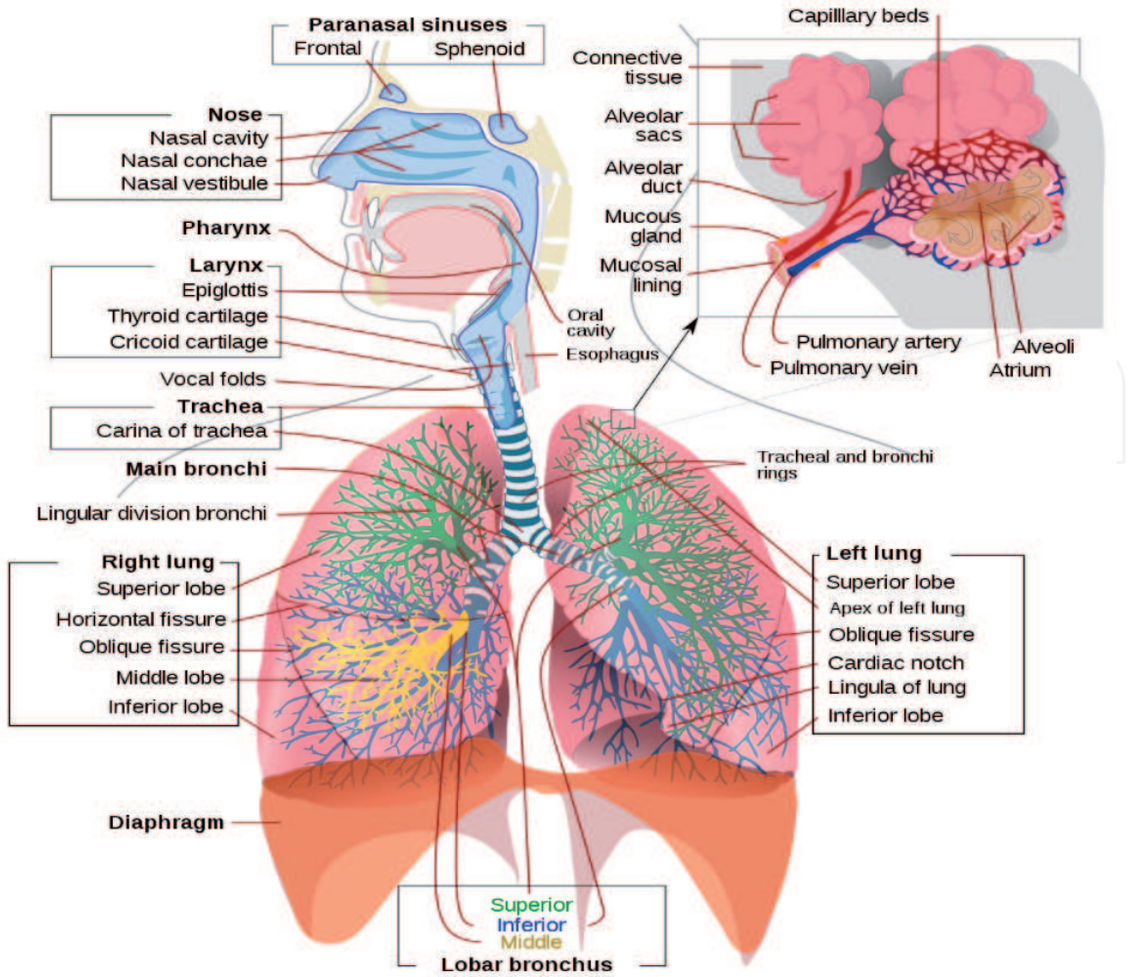

Figure 3.
Human respiratory system [41]. At the end of the branches of the airway tree, alveolar region exists. It contains the alveoli sacs. The gas exchanges between alveolar air and blood of the pulmonary capillaries [42].

In each region of the respiratory tract, various amounts of a certain size of particles (nanoparticles and microparticles) are deposited. For example, the highest deposition in the alveolar region is related to 20-nm and 3-μm particles. The smallest (1-nm) and largest (10-μm) particles are mostly deposited in the extra-thoracic region which includes the nasal and oral passages, pharynx, and larynx. This is the first line of defense against inhaled particles.

Air pollutants, after entering and passing the airways in the pulmonary system, will be changed into a danger for human health. Those particles able to diffuse through the lung barrier and enter the blood circulation will cause perturbation in normal functions in the human body. For example, blocking the vessels causes blood clotting, and consequently, the stroke will happen.

Inhaled particles, such as silica, organic compounds, and metallic dusts, have toxic effects on the pulmonary surfactant [47]. For example, the accumulation of nanoparticles in the kidneys, liver, spleen, and central nervous system through the penetration of the epithelial barrier of the alveolar region has been observed [48, 49].

As it was mentioned above, PM2.5 which also includes nanoparticles can penetrate the lung barrier. In fact, these particles are those which can reach the alveolar region, contact the lung surfactant, and interact with DPPC [50, 51]. Ultrafine particles of diesel exhaust and insoluble silicate particles of micrometer size can adsorb the components of lung surfactant and, therefore, be affected in terms of their in vitro expression of genotoxicity or cytotoxicity [52].

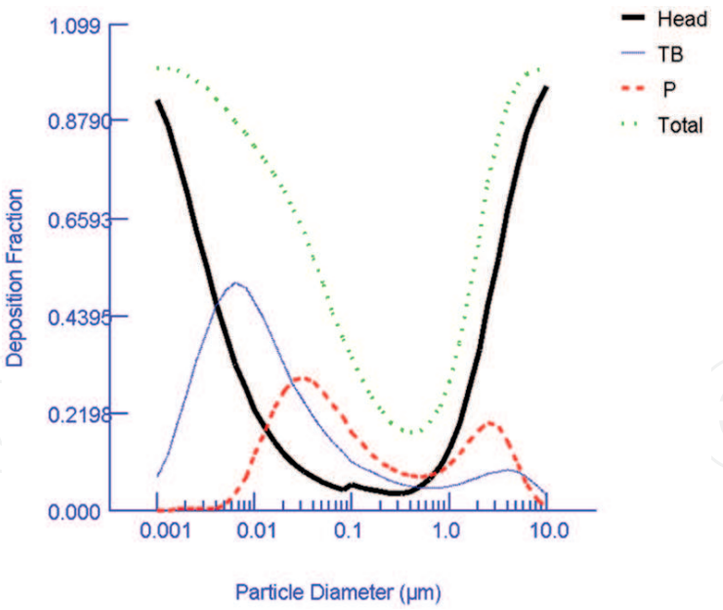

Figure 4.
Deposition fraction of particles in the various regions of the respiratory system according to the particle size. Head, TB, and P are the representatives of extra-thoracic, tracheobronchial, and alveolar regions, respectively. Total means the overall deposition in the three regions (https://www.ara.com/products/multiple-path-particle-dosimetry-model-mppd-v-304) [46].

Nanomaterials are the particles with at least one dimension less than or equal to 100 nm. Although there are a lot of beneficial nanotechnology-based products developed continuously, the number of efforts for the assessment of hazards of the nanoparticles when released in the environment is limited [53, 54].

The National Institute for Occupational Safety and Health (NIOSH) of the USA has identified the toxicity of the nanoparticles as one of the top 10 critical topic areas which should be considered in addressing knowledge gaps. The points below are two concepts classified in this topic:

1. Physicochemical properties (e.g., size, solubility, shape) of nanoparticles because these properties affect the potential toxicity and cytotoxicity of these particles

2. Short-term and long-term impact of nanoparticles on the human body (e.g., lung) [53]

There is an association between lung cancer incidence and PM2.5 air pollution [55, 56]. The International Agency for Research on Cancer (IARC) classified airborne particulate matter and outdoor air pollution as carcinogenic to humans [57]. Asthma and chronic obstructive pulmonary disease (COPD) are the other lung diseases caused by ambient air pollution [58, 59]. There are also some effects of air pollution on pregnancy outcomes, for example, decreased neurological development, chromosomal aberrations casing teratogenic effects, low birth weight, and respiratory syndrome likewise bronchiolitis/bronchitis [60].

8. Conclusions

The human health is threatened by air pollution. When air particulate matters get in contact with our body, they cause adverse effects such as lung diseases,

cardiovascular diseases, stroke, and skin and neurological diseases. There are diverse mechanisms through which these particles cause different diseases. Some of these diseases are caused directly by the adsorption of particles onto the organs and tissues, e.g., lungs, in the human body, and some others are originating from the peripheral circulation which transfers cytokines to the organs such as the brain. Seven million deaths per year resulted from air pollution clearly shows that this is a very significant issue that must be tracked and investigated not only in terms of health and medical effects but also by making a decision on public health policies and environmental regulations. Therefore, it is a requirement for responsible authorities to consider these comprehensive harmful effects of particulate matters and, in general, environmental emissions on human health.

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Conflict of interest

The authors declare no conflict of interest.

Notes

This book chapter is an introduction to the adverse effects of air pollution on human health. So, it can be used as a reference which addresses the reasons why air pollution should be considered as a serious challenge, and the related research must be conducted to investigate these effects and the solutions required.

Abbreviations

PM	particulate matter
PM2.5	particles with a diameter of 2.5 microns or less
PM10	particles with a diameter of 10 microns or less
AhR	Aryl hydrocarbon receptor
PAHs	polycyclic aromatic hydrocarbons
DREs	dioxin response elements
CYP1A1	cytochrome P450 1A
CYP1B1	cytochrome P450 1B1
PGE2	prostaglandins
IL-6	interleukin 6
IL-8	interleukin 8
IL-1α	interleukin 1 alpha
IL-1β	interleukin 1 beta
TNF-α	tumor necrosis factor-α
GBD	Global Burden of Diseases

CNS	central nervous system
ADHD	Attention Deficit Hyperactivity Disorder
AB42	B-amyloid peptide
HRV	heart rate variability
BBB	blood-brain barrier
DPPC	dipalmitoylphosphatidylcholine
NIOSH	National Institute for Occupational Safety and Health
IARC	International Agency for Research on Cancer
COPD	chronic obstructive pulmonary disease

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