Air Pollution, Obesity and Disease

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ABSTRACT

Ninety-nine per cent of the world’s population breathes polluted air and thirty-eight per cent (and growing) of the human population is obese. Both air pollution (AP) and obesity (OBS) are known to cause many of the same diseases in humans via similar oxidative stress (OS) driven mechanisms. Air pollution is a known cause of obesity, which serves to compound disease impact. The commonly produced disease impacts of air pollution and obesity and their mechanisms of action are addressed. Also discussed are early disease onset and the mutagenic and evolutionary impacts of both AP and OBS.

Keywords: Air pollution, comorbidities, disease, obesity.

1. Introduction

1.1. Air Pollution

The World Health Organization (WHO) estimates that virtually all (99 per cent) of the world’s population breathes polluted air, with the combination of ambient and indoor air pollution responsible for about 7 million deaths annually [1].

Chronic inhalation of both ambient and indoor polluted air has been associated with elevated incidence of numerous non-communicable diseases (NCDs) and conditions. Sources across the web address numerous air pollution-caused diseases. These include, but are not limited to; cancer, type 2 diabetes, respiratory diseases, cardiovascular diseases, neurodegenerative diseases, liver disease, kidney disease, immune system disorders and female and male infertility.

All parameters of polluted air, including NO\textsubscript{x}, SO\textsubscript{2}, SO\textsubscript{3}, ozone, volatile organic chemicals (VOCs), polynuclear aromatic hydrocarbons (PAHs), heavy metals, PM\textsubscript{10} (course particles with diameters greater than 10 micrometers), PM\textsubscript{2.5} (fine particles with diameters less than 2.5 micrometers) and mixtures of these, be they from indoor and outdoor sources, contribute to oxidative stress and lead to disease [2].

Particles in the air come from multiple sources, including: energy production, vehicle exhausts, farming, soil erosion, mining, industrial processing, indoor cooking, heating, tobacco smoking, construction materials, furnishings, mining, and natural occurrences (forest fires, storms and volcanoes). All inhaled particulates elevate oxidative stress and lead to disease [3].

It is noted that though numerous chemicals are found in most locations, not all are universally found. Where found, concentrations vary with distances from discharge and prevailing winds. Some are prevalent indoors while others are primarily found in outdoor ambient air. Solid particles, in addition to being toxic themselves, can and do absorb volatile and semi-volatile species and carry these into the body when inhaled. Mixtures of the chemicals listed in Table I produce synergistic, as well as additive, toxic effects when absorbed into the body, particularly when such mixtures contain at least one lipophilic and one hydrophilic species [4].

PM\textsubscript{10} particles are toxic in two ways. They can irritate lung tissue causing chronic inflammation, and soluble pollutants adhered to these can partition into the bloodstream. Those containing transition metal species can interact via the Fenton reaction to raise oxidative stress. Iron contained in asbestos fibers is an example of such an effect as shown by the Fenton reaction (1) [5].

\[
\text{Fe}^{2+} + \text{H}_2\text{O}_2 \rightarrow \text{Fe}^{3+} + \text{HO}^- + \text{OH}^- \tag{1}
\]

The hydroxyl radical (HO\textsuperscript{•}) formed in this reaction is associated with oxidative damage to membrane lipids and the onset of numerous diseases. Copper, like iron, behaves in a Fenton-like manner [3], [6]–[9].

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The trivalent ferric ion produced in the Fenton reaction can be reduced back to the divalent ferrous ion by reaction with hydrogen peroxide to form the hydroxyl and peroxyl free radicals (2) thus producing a continual source of inflammation and associated oxidative stress.

\[
\text{Fe}^{3+} + \text{H}_2\text{O}_2 \rightarrow \text{Fe}^{2+} + \text{HOO}^\cdot + \text{H}^+ \quad (2)
\]

PM$_{2.5}$ are absorbed through the lungs into the bloodstream and circulated throughout the body.

It should be noted that though numerous chemicals are found in most locations, not all the chemicals listed in Table I are universally found. Where found, concentrations vary with distances from discharge, ventilation (indoor) and prevailing winds (outdoor ambient).

The mechanistic pathways by which air pollutants cause disease vary. All, however, elevate oxidative stress which serves to trigger disease onset.

Air pollutants are toxic via two pathways; direct action by a pollutant or indirect action by reacting with other pollutants or with naturally found atmospheric chemicals to form additional toxins. Photochemical smog is an example of the latter as illustrated by the following reaction sequence [10].

1. Nitrogen dioxide (NO$_2$) can be broken down by reaction with solar ultraviolet radiation (UV) to form nitric oxide (NO) and an oxygen-free radical (O$^\cdot$).

\[
\text{NO}_2 + \text{UV} \rightarrow \text{NO} + \text{O}^\cdot
\]

2. Oxygen radicals react with atmospheric oxygen (O$_2$) to form ozone (O$_3$).

\[
\text{O}^\cdot + \text{O}_2 \rightarrow \text{O}_3
\]

3. Ozone reacts with nitric oxide to form nitrogen dioxide (NO$_2$) and oxygen (O$_2$).

\[
\text{O}_3 + \text{NO} \rightarrow \text{NO}_2 + \text{O}_2
\]

4. Nitrogen dioxide reacts with hydrocarbons (R) to form peroxyacetyl nitrate (PAN)

\[
\text{NO}_2 + \text{R} \rightarrow \text{products such as PAN}
\]

5. Reaction of hydrocarbons with the oxygen free radical to form aldehydes and ketones (RCO), some of which can combine with atmospheric oxygen to form very reactive peroxide radicals (RCO$_3^\cdot$).

\[
\text{RCO}^\cdot \rightarrow \text{RCO}
\]

6. Peroxide radicals react with atmospheric oxygen to produce ozone

\[
\text{RCO}_3^\cdot + \text{O}_2 \rightarrow \text{O}_3
\]

7. Peroxide radicals react with nitric oxide to form nitrogen dioxide and other organic products (RCO$_2$)

\[
\text{RCO}_3^\cdot + \text{NO} \rightarrow \text{NO}_2 + \text{RCO}_2
\]

### 1.2. Obesity

Body mass index (BMI) is used to define overweight (BMI 25–30) and obesity (BMI greater than 30) [11]. The World Health Organization and World Obesity Federation estimates predict that by 2030, one billion people globally will be obese, with the number increasing to four billion by 2050 [12], [13].

It has been projected that close to half of the population of the United States will be obese by the year 2030 [14].

Obesity, as air pollution, causes disease in numerous body systems [15]. These include: cardiovascular diseases. Table I lists diseases known to be caused by both air pollution and obesity and representative references.

Air pollution is also a cause of obesity in both children and adults [33], [75]–[78]. Thus, chronic exposure to polluted air further increases obesity and thereby further contributes to promoting the diseases listed in Table I.

### 2. Methods

The impacts of both air pollution and obesity on oxidative stress and disease causation are well-known and fully described in the literature. The combined effects of AP and OBS, which are not fully appreciated however, are hypothesized here via consideration of the common mechanisms by which both promote disease onset.
3. Results and Discussion

3.1. Diseases Caused by Both Air Pollution and Obesity

Numerous diseases are, in part, caused by both exposure to air pollution and a state of obesity.

3.2. Obesity, Adipose Tissue and Chemical Toxicity

In addition to storing fat, adipose tissue (AT) is an endocrine organ and an integral part of several physiological functions, including metabolic regulation and energy storage. AT releases adipocytokines and adipokines as well as serves as a modulator of the actions of toxic lipophilic chemicals [3].

3.2.1. Adipose Tissue and Persistent Organic Pollutants

Highly lipophilic chemicals metabolize very slowly and may persist in the body for decades [79]. These chemicals include persistent organic pollutants (POPs) dubbed the Stockholm Convention “dirty dozen,” originally identified in 2001 [79] (and subsequently expanded to include additional POP [80]) as well as PFAS and other so-called “forever chemicals” [3].

4. Mechanisms of Air Pollution and Obesity Induced Disease

Both air pollution and obesity induce disease via a number of mechanisms, all of which are mediated by increased oxidative stress.

4.1. Oxidative Stress

Reactive oxygen species (ROS) and reactive nitrogen species (RON) are naturally produced endogenously in the body as by-products of cellular metabolic activities. These include highly reactive, free radical intermediates with beneficial effects that include energy production, protection against invading pathogens, wound healing and tissue repair and acting as essential signaling molecules, as well as non-free radical species such as hydrogen peroxide. An overproduction of these, in amounts exceeding the body’s endogenous antioxidants’ ability to neutralize excessive OS production, leads to inflammation and results in an imbalance known as oxidative stress (OS) [81]–[85].

Free radicals in the body are stabilized by three factors: substitution on the radical atom, resonance and geometry [84], [86]. Fig. 1 shows these factors.

1. Substitution on radical carbon: Stability increases with substitution from primary to secondary to tertiary.
2. Resonance: Resonance, with the greater the number of resonance structures imparting the greatest stability.
3. Geometry: Having the radical alpha to a π bond with which it can overlap. The greater stability of the allyl free radical compared with the n-propyl radical is an example.

Fig. 1. Free radical stabilization via radical A) substitution, B) resonance, and C) geometry.

4.2. Air Pollution and Oxidative Stress

OS producing species in air pollution include: Particulate matter (PM), ozone (O₃), carbon monoxide (CO), oxides of nitrogen (NOₓ), sulfur dioxide (SO₂), lead (Pb), other transition metals semi-volatile organic chemicals (SVC) and volatile organic chemicals (VOC) [87]. PM₂.₅ species are associated with diseases in numerous body systems as they are readily absorbed through the lungs into the blood, transported across cell membranes, including the blood brain barrier [75], [87]–[95].

4.3. Obesity and Oxidative Stress

Obesity is an elevation of normal adiposity, due to secretion of excessive oxidative stress caused by elevating inflammatory adipokines [96]. The resulting systemic oxidative stress is associated with the onset of numerous diseases, including cardiovascular disease, osteoarthritis, types 1 and 2 diabetes and various cancers [97]–[105]. Adipose tissue also secretes inflammatory cytokines that cause DNA damage and mitochondrial dysfunction and activate signaling pathways that interfere with normal homeostatic balance, all associated with ROS production and increases in oxidative stress [3].

5. Early Disease Onset

Early-onset disease incidence rates for many diseases are increasing worldwide [106]–[112]. These diseases include:

- Cancer
- Type 1 diabetes
- Type 2 diabetes
- Leukemia
- Obesity
- Respiratory diseases
- Cardiovascular diseases
Neurodegenerative diseases
Arthritis

Of these diseases, cancer has been the one most studied. Institute for Health Metrics and Evaluation at the University of Washington School of Medicine data analyzed by the Financial Times are illustrative of early cancer onset [113]. These data show cancer incidence rate growth for 15-39-year-olds from 1990 to 2019 in the G20 and are listed in Table II.

Much of the reported increase at increasingly earlier age is attributable to air pollution and obesity. Though increases in early onset diseases can be attributed to multiple causes, air pollution and obesity have been mechanistically linked to many of these two factors. Representative examples of such mechanistic links follow.

Early onset of lung cancer, leukemia, asthma, emphysema, COPD, heart disease, stroke, osteo- and rheumatoid arthritis, Alzheimer’s disease and Parkinson’s disease are among those maladies that have linked to air pollution [59], [114]–[120].

Early onset diseases attributable to obesity include: non-alcoholic liver disease, dyslipidemia, sleep apnea, hypertension, and type 2 diabetes [121], [122].

5.1. Combination of Air Pollution and Obesity Early Onset Disease

Air pollution, particularly exposure to PM2.5, NO2, and polynuclear aromatic hydrocarbons (PAHs) in the prenatal period increases obesity in children, leading to early onset of other disease in childhood and early adulthood [123], [124]. Such results are not surprising, given that as air pollution exposure is a known cause of obesity, spiraling disease effects are to be anticipated when obese individuals are chronically exposed to air pollution. Compounding the problem is the fact that disease is both a cause and consequence of oxidative stress. Accordingly, as the number of diseases one is afflicted with increases, the greater one’s total oxidative stress and the greater the likelihood of further disease onset [85].

6. Air Pollution and Evolution

Both air pollution and obesity contribute to evolutionary changes in humans. Adjustment and adaptation to these changes will determine the future of our species.

7. Obesity and Evolution

Body fat serves three valuable body functions in humans: it acts as an insulator, thus reducing energy demands in times of a cold environment; serving as an energy store in times of food shortages; and as a requirement during the reproduction event [130]. Excessive storage of fat, however, leads to obesity. In the past century, obesity levels have dramatically risen to the point of epidemic status [131]. Genetics plays a major role in obesity and three hypotheses have been proposed for the evolution of this phenomenon. These are the thrifty gene hypothesis, the drifty gene hypothesis and the maladaptation viewpoint.

7.1. Thrifty Gene Hypothesis

First proposed in 1962, the thrifty gene hypothesis is based on the premise that pre-industrial society, people often suffered famine due a lack of food and that people with the “thrifty gene” would have a reserve of energy stored to combat famine [131].

7.2. Drifty Gene Hypothesis

Proposed in 2008, the drifty gene hypothesis is based on the premise that once humans mastered weapons and fire, the pressures of predators were eliminated and gene mutation could be passed down through the generations [132].

7.3. Maladaptation Viewpoint

Proposed in 2014, the maladaptation viewpoint that obesity results from natural selection and climate and that only this hypothesis explains different regional obesity rates [133].

Exposure of humans to air pollution began with our early ancestors and has progressed in six phases [125]. These are:

- **Phase I**: Early human ancestors inhaled dust, faecal aerosols, and spores.
- **Phase II**: The use of fire exposed early Homo to smoke and cooking produced toxins.
- **Phases III and IV**: Neolithic to preindustrial Homo sapiens living in densely populated communities suffered from pathogenic exposures from domestic animals and limited sanitation.
- **Phase V**: Industrialization introduced man to toxins from fossil fuels, industrial chemicals and tobacco use.
- **Phase VI**: In the future, global warming with increased air pollution and infections, will further impact humanity.

The human genome has evolved throughout its history, continues to do so and is impacted by both genetic and epigenetic factors, with air pollution inducing heritable DNA mutations [126]–[128]. As it is well established that evolution in a species can come from tampering with its physical and/or biotic environment and coupled with a history of accidental impacts [128], [129] the range of evolutionary effects of air pollution on the human species, though known to be harmful, can only be speculated.

### TABLE II: CHANGE IN CANCER RATES FOR 15–39-YEAR-OLDS IN G20 NATIONS, 1990–2019

<table>
<thead>
<tr>
<th>Cancer</th>
<th>Percent increase</th>
</tr>
</thead>
<tbody>
<tr>
<td>All cancers</td>
<td>24</td>
</tr>
<tr>
<td>Breast</td>
<td>42</td>
</tr>
<tr>
<td>Testicular</td>
<td>51</td>
</tr>
<tr>
<td>Other pharynx</td>
<td>65</td>
</tr>
<tr>
<td>Colorectal</td>
<td>70</td>
</tr>
<tr>
<td>Thyroid</td>
<td>81</td>
</tr>
<tr>
<td>Kidney</td>
<td>88</td>
</tr>
<tr>
<td>Prostate</td>
<td>95</td>
</tr>
<tr>
<td>Nasopharynx</td>
<td>109</td>
</tr>
</tbody>
</table>
Air pollution and obesity are known causative agents for many of the same diseases, acting via identical oxidative stress-mediated mechanisms. Both AP and OBS contribute to the early onset of numerous non-communicative diseases. As air pollution also is a cause of obesity, obese individuals who are chronically exposed to polluted air are particularly at risk for the onset of disease. Both air pollution and obesity also have evolutionary effects on the human species with unknown consequences for the future.

8. CONCLUSIONS

Air pollution and obesity are known causative agents for many of the same diseases, acting via identical oxidative stress-mediated mechanisms. Both AP and OBS contribute to the early onset of numerous non-communicative diseases. As air pollution also is a cause of obesity, obese individuals who are chronically exposed to polluted air are particularly at risk for the onset of disease. Both air pollution and obesity also have evolutionary effects on the human species with unknown consequences for the future.

Conflict of Interest

Author declares no conflict of interest.

REFERENCES


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