Biotic Impacts: Adverse Effects of Air Pollution on Biota (Human Health/Environment) and Practical Measures for Prevention

B. N. OKAFOR[1], H. N. OGBOKE[2], C. A. OBIORA-OKEKE[3], A. O. ANIAGBOSO[4]
[1, 2, 3, 4]*Department of Electrical Engineering, Nnamdi Azikiwe University Awka, Nigeria.*

Abstract- ***Air pollution is a major concern of new civilized world, which has a serious toxicological impact on human health and the environment. It has a number of different emission sources, but motor vehicles and industrial processes contribute the major part of air pollution. According to the World Health Organization, six major air pollutants include particle pollution, ground-level ozone, carbon monoxide, sulfur oxides, nitrogen oxides, and lead. Long and short term exposure to air suspended toxicants has a different toxicological impact on human including respiratory and cardiovascular diseases, neuropsychiatric complications, the eyes irritation, skin diseases, and long-term chronic diseases such as cancer. Several reports have revealed the direct association between exposure to the poor air quality and increasing rate of morbidity and mortality mostly due to cardiovascular and respiratory diseases. Air pollution is considered as the major environmental risk factor in the incidence and progression of some diseases such as asthma, lung cancer, ventricular hypertrophy, Alzheimer's and Parkinson's diseases, psychological complications, autism, retinopathy, fetal growth, and low birth weight. In this review article, we aimed to discuss toxicology of major air pollutants, sources of emission, and their impact on human health. We have also proposed practical measures to reduce air pollution in the environment.***

Indexed Terms- ***Air Pollution, Cardiovascular Diseases, Environment, Human Health, Respiratory Tract Diseases, Toxicology***

I. INTRODUCTION

Air pollution is a major problem of recent decades, which has a serious toxicological impact on human health and the environment. The sources of pollution vary from small unit of cigarettes and natural sources such as volcanic activities to large volume of emission from motor engines of automobiles and industrial activities. Long-term effects of air pollution on the onset of diseases such as respiratory infections and inflammations, cardiovascular dysfunctions, and cancer are widely accepted; hence, air pollution is linked with millions of death globally each year. A recent study has revealed the association between male infertility and air pollution.

Air pollution has now emerged in developing countries as a result of industrial activities and also increases the quantity of emission sources such as inappropriate vehicles. About 4.3 million people die from household air pollution and 3.7 million from ambient air pollution, most of whom (3.3 and 2.6 million, respectively) live in Asia. In developing country, the level of air pollutants has increased gradually since the beginning of industrialization in the 1970s, but it has reached a very harmful level in some countries such as Nigeria, and other developing countries over the past two decades. Africa is the world's main polluted continent in the world, which results in over 16 billion $ annual loss. In fact, four of the top ten air-polluted cities are in Iran. Ahvaz is the most air polluted city in the world with microdust blowing in from neighboring countries, and particulate levels three times that of Beijing, and nearly 13 times that of London. Air pollution caused almost 4460 deaths in 2013 only in Tehran although the reality seemed higher and is getting worse every year. Therefore, it is of great importance to describe the problem, particularly its toxic effects on human health and provide recommendations as a basis for environmental guidelines and standard protocols in the field of air pollution in Africa.

The present article is neither a systematic review nor a descriptive, educational study. It is a problem-based descriptive review in which the authors try to explain a problem which is the major health and ecological problem in developing countries like Nigeria. In this review, we have tried to summarize the toxicology of air pollutants and related diseases with a possible mechanism of action and appropriate management of the patients. Therefore, it shall be useful for the environmental and health professionals particularly policy makers, emergency physicians, and other clinicians who may be involved in air pollution and related diseases. In this paper, we also discuss sources of air pollution and proposed some feasible solutions which may be beneficial for the environmental legislators and decision makers.

II. DEFINITIONS

Air pollution is defined as all destructive effects of any sources which contribute to the pollution of the atmosphere and/or deterioration of the ecosystem. Air pollution is caused by both human interventions and/or natural phenomena. It is made up of many kinds of pollutants including materials in solid, liquid, and gas phases. Air pollutions of indoors will not be specifically considered in this article.

The Pollutant Standard Index (PSI) is a numerical value and indicator of pollutants that is normally used to facilitate risk assessment. It is a numeric value between zero to 500. PSI is a guideline for reporting air quality which was first introduced by Thom and Ott in 1974. Hence, it would provide a method of comparing the relative contribution of each pollutant to total risk. The calculation of PSI is based on the concentration of five major air pollutants including particulate matters (PMs), sulfur dioxide (SO_2), nitrogen dioxide (NO_2), carbon monoxide (CO), and ozone (O_3) in the air.

According to Johnson *et al*., "air quality index (AQI) is defined as a measure of the condition of air relative to the requirements of one or more biotic species or to any human need." AQI is divided into ranges, in which they are numbered, and each range is marked with color codes. It provides a number from healthy standard level of zero to a very hazardous level of above 300 to indicate the level of health risk associated with air quality. Based on PSI, air quality is classified into six major indices, which is marked by color codes and each color corresponds to a different level of health concerns. Principally, green is defined as a color indicator for healthy air quality; while yellow, orange, red, purple, and maroon colors indicate as moderate, unhealthy for sensitive groups, unhealthy, very unhealthy, and hazardous air quality, respectively. These ranges and codes may differ in the different methods of classifications in different countries.

III. TOXICOLOGY OF AIR POLLUTION

Effects of air pollutants on living organism will not only be limited to the human and animal health but also include the whole environment. Different geographical conditions, global climate changes, and the environmental variations affect the human health and the environment including the animal life.

Environmental damages

Ecologically, air pollution can cause serious environmental damages to the groundwater, soil, and air. It is also a serious threat to the diversity of life. Studies on the relationship between air pollution and reducing species diversity clearly show the detrimental effects of environmental contaminants on the extinction of animals and plants species. Air suspended toxicants may also cause reproductive effects in animals. Acid rain, temperature inversion, and global climate changes due to the emissions of greenhouse gasses to the atmosphere are other major ecological impacts of air pollution.

Air pollutants and their toxicities

Every material in the air which could affect human health or have a profound impact on the environment is defined as air pollutants. According to the World Health Organization (WHO), particle pollution, ground-level O_3, CO, sulfur oxides, nitrogen oxides, and lead (Pb) are the six major air pollutants which harm human health and also the ecosystem. There are many pollutants of suspended materials such as dust, fumes, smokes, mists, gaseous pollutants, hydrocarbons, volatile organic compounds (VOCs), polycyclic aromatic hydrocarbons (PAHs), and halogen derivatives in the air which at the high concentrations cause vulnerability to many diseases

including different types of cancers. The most important air pollutants and their toxic effects on different human body organs and related diseases have been briefly described below.

Particle pollutants

Particle pollutants are major parts of air pollutants. In a simple definition, they are a mixture of particles found in the air. Particle pollution which is more known as PM is linked with most of pulmonary and cardiac-associated morbidity and mortality. They have varied in size ranging mostly from 2.5 to 10 μm ($PM_{2.5}$ to PM_{10}).

The size of particle pollutants is directly associated with the onset and progression of the lungs and heart diseases. Particles of smaller size reach the lower respiratory tract and thus have greater potential for causing the lungs and heart diseases. Moreover, numerous scientific data have demonstrated that fine particle pollutants cause premature death in people with heart and/or lung disease including cardiac dysrhythmias, nonfatal heart attacks, aggravated asthma, and decreased lung functions. Depending on the level of exposure, particulate pollutants may cause mild to severe illnesses. Wheezing, cough, dry mouth, and limitation in activities due to breathing problems are the most prevalent clinical symptoms of respiratory disease resulted from air pollution.

Long-term exposure to current ambient PM concentrations may lead to a marked reduction in life expectancy. The increase of cardiopulmonary and lung cancer mortality are the main reasons for the reduction in life expectancy. Reduced lung functions in children and adults leading to asthmatic bronchitis and chronic obstructive pulmonary disease (COPD) are also serious diseases which induce lower quality of life and reduced life expectancy. Strong evidence on the effect of long-term exposure to PM on cardiovascular and cardiopulmonary mortality come from cohort studies.

Ground-level ozone

O_3 with the chemical formula of O_3 is a colorless gas which is the major constituent of the atmosphere. It is found both at the ground level and in the upper regions of the atmosphere which is called troposphere. Ground-level ozone (GLO) is produced as a result of chemical reaction between oxides of nitrogen and VOCs emitted from natural sources and/or due to human activities. GLO is believed to have a plausible association with increased risk of respiratory diseases, particularly asthma.

As a powerful oxidant, O_3 accepts electrons from other molecules. There is a high level of polyunsaturated fatty acids in the surface fluid lining of the respiratory tract and cell membranes that underlie the lining fluid. The double bonds available in these fatty acids are unstable. O_3 attacks unpaired electron to form ozonides and progress through an unstable zwitterion or trioxolane (depending on the presence of water). These ultimately recombine or decompose to lipohydroperoxides, aldehydes, and hydrogen peroxide. These pathways are thought to initiate propagation of lipid radicals and auto-oxidation of cell membranes and macromolecules. It also increases the risk of DNA damage in epidermal keratinocytes, which leads to impaired cellular function.

O_3 induces a variety of toxic effects in humans and experimental animals at concentrations that occur in many urban areas. These effects include morphologic, functional, immunologic, and biochemical alterations. Because of its low water solubility, a substantial portion of inhaled O_3 penetrates deep into the lungs but its reactivity is scrubbed by the nasopharynx of resting rats and humans in around 17% and 40%, respectively. On ecological aspect, O_3 can reduce carbon assimilation in trees leading to deforestation which may affect global food security in long-term exposure.

Carbon monoxide

CO is a colorless and odorless gas, which is produced by fossil fuel, particularly when combustion is not

appropriate, as in burning coal and wood. The affinity of CO to hemoglobin (as an oxygen carrier in the body) is about 250 times greater than that of oxygen. Depending on CO concentration and length of exposure, mild to severe poisoning may occur. Symptoms of CO poisoning may include headache, dizziness, weakness, nausea, vomiting, and finally loss of consciousness. The symptoms are very similar to those of other illnesses, such as food poisoning or viral infections.

No human health effects have been showed for carboxyhemoglobin (COHb) levels lower than 2%, while levels above 40% may be fatal. Hypoxia, apoptosis, and ischemia are known mechanisms of underlying CO toxicity.[48] The mechanism of such toxicity is the loss of oxygen due to competitive binding of CO to the hemoglobin heme groups. Cardiovascular changes also may be observed by CO exposures that create COHb in excess of 5%. In the early 1990s, Health Effects Institute performed a series of studies associated with cardiovascular disease to determine the potential for angina pectoris with COHb levels in the range of 2–6%.[49] The results showed that premature angina can occur under these situations but that the potential for the occurrence of ventricular arrhythmias remains uncertain. Thus, the reduction in ambient CO can reduce the risk of myocardial infarction in predisposed persons.

Sulfur dioxide

SO_2 is a colorless, highly reactive gas, which is considered as an important air pollutant. It is mostly emitted from fossil fuel consumption, natural volcanic activities, and industrial processes. SO_2 is very harmful for plant life, animal, and human health. People with lung disease, children, older people, and those who are more exposed to SO_2 are at higher risk of the skin and lung diseases.

The major health concerns associated with exposure to high concentrations of SO_2 include respiratory irritation and dysfunction, and also aggravation of existing cardiovascular disease. SO_2 is predominantly absorbed in the upper airways. As a sensory irritant, it can cause bronchospasm and mucus secretion in humans. Residents of industrialized regions encountered with SO_2 even at lower concentrations (<1 ppm) in the polluted ambient air might experience a high level of bronchitis.

The penetration of SO_2 into the lungs is greater during mouth breathing compared to nose breathing. An increase in the airflow in deep, rapid breathing enhances penetration of the gas into the deeper lung. Therefore, people who exercise in the polluted air would inhale more SO_2 and are likely to suffer from greater irritation. When SO_2 deposits along the airway, it dissolves into surface lining fluid as sulfite or bisulfite and is easily distributed throughout the body. It seems that the sulfite interacts with sensory receptors in the airways to cause local and centrally mediated bronchoconstriction.

According to the Environmental Protection Agency (EPA) of the USA, the level of annual standard for SO_2 is 0.03 ppm. Due to its solubility in water, SO_2 is responsible for acid rain formation and acidification of soils. SO_2 reduces the amount of oxygen in the water causing the death of marine species including both animals and plants. Exposure to SO_2 can cause damages to the eyes (lacrimation and corneal opacity), mucous membranes, the skin (redness, and blisters), and respiratory tracts. Bronchospasm, pulmonary edema, pneumonitis, and acute airway obstruction are the most common clinical findings associated with exposure to SO_2.[50]

Nitrogen oxide

Nitrogen oxides are important ambient air pollutants which may increase the risk of respiratory infections.[50] They are mainly emitted from motor engines and thus are traffic-related air pollutants. They are deep lung irritants that can induce pulmonary edema if been inhaled at high levels. They are generally less toxic than O_3, but NO_2 can pose clear toxicological problems. Exposures at 2.0–5.0 ppm have been shown to affect T-lymphocytes, particularly $CD8^+$ cells and natural killer cells that play an important role in host defenses against viruses. Although these levels may be high, epidemiologic

studies demonstrate effects of NO_2 on respiratory infection rates in children.

Coughing and wheezing are the most common complication of nitrogen oxides toxicity, but the eyes, nose or throat irritations, headache, dyspnea, chest pain, diaphoresis, fever, bronchospasm, and pulmonary edema may also occur. In another report, it is suggested that the level of nitrogen oxide between 0.2 and 0.6 ppm is harmless for the human population.[51]

Lead

Pb or plumb is a toxic heavy metal that is widely used in different industries. Pb pollution may result from both indoor and outdoor sources. It is emitted from motor engines, particularly with those using petrol containing Pb tetraethyl. Smelters and battery plants, as well as irrigation water wells and wastewaters, are other emission sources of the Pb into the environment. Evaluation of the blood Pb level in traffic police officers shows that environmental pollution may be considered as a source of Pb exposure. Fetuses and children are highly susceptible to even low doses of Pb. Pb accumulates in the body in blood, bone, and soft tissue. Because it is not readily excreted, Pb can also affect the kidneys, liver, nervous system, and the other organs.

Pb absorption by the lungs depends on the particle size and concentration. Around 90% of Pb particles in the ambient air that are inhaled are small enough to be retained. Retained Pb absorption through alveoli is absorbed and induces toxicity. Pb is a powerful neurotoxicant, especially for infants and children as the high-risk groups. Mental retardation, learning disabilities, impairment of memory, hyperactivity, and antisocial behaviors are of adverse effects of Pb in childhood. Therefore, it is very important to reduce the Pb level of ambient air.

Pb exposure is often chronic, without obvious symptoms. It can affect the different parts of the body including cardiovascular, renal, and reproductive systems, but the main target for Pb toxicity is the nervous system. Pb disrupts the normal function of intracellular second messenger systems through the inhibition of N-methyl-D-aspartate receptors. Pb may also replace calcium as a second messenger resulting in protein modification through various cellular processes including protein kinase activation or deactivation.

Abdominal pain, anemia, aggression, constipation, headaches, irritability, loss of concentration and memory, reduced sensations, and sleep disorders are the most common symptoms of Pb poisoning. Exposure to Pb is manifested with numerous problems, such as high blood pressure, infertility, digestive and renal dysfunctions, and muscle and joint pain.

Other air pollutants

Other major air pollutants that are classified as carcinogen and mutagen compounds and are thought to be responsible for incidence and progression of cancer in human include VOCs such as benzene, toluene, ethylbenzene, and xylene, PAHs such as acenaphthene, acenaphthylene, anthracene, and benzopyrene, and other organic pollutants such as dioxins, which are unwanted chemical pollutants that almost totally produced by industrial processes and human activity.

In Table 1, the standard level of some conventional air pollutants is presented in which the values were defined as air quality standards that provide public welfare protection.

Table 1

Standard level of criteria air pollutants and their sources with health impact based on the United States Environmental Protection Agency

Standard level of criteria air pollutants and their sources with health impact based on the United States Environmental Protection Agency

Air pollutants*	Major source of emission	Averaging time	Standard level	Health impact target organs
Particle pollutants				
$PM_{2.5}$	Motor engines, industrial activities, smokes	24 h	35 μg/m³	Respiratory and cardiovascular diseases, CNS and reproductive dysfunctions, cancer
PM_{10}		24 h	150 μg/m³	
Ground-level ozone	Vehicular exhaust, industrial activities	1 h	0.12 mg/m³	Respiratory and cardiovascular dysfunctions, eye irritation
Carbon monoxide	Motor engines, burning coal, oil and wood, industrial activities, smokes	1 h	35 mg/m³	CNS and cardiovascular damages
Sulfur dioxide	Fuel combustion, burning coal	1 h	75 μg/m³	Respiratory and CNS involvement, eye irritation
Nitrogen dioxide	Fuel-burning, vehicular exhaust	1 h	100 μg/m³	Damage to liver, lung, spleen, and blood
Lead	Lead smelting, industrial activities, leaded petrol	3 months average	0.15 μg/m³	CNS and hematologic dysfunctions, eye irritation
Polycyclic aromatic hydrocarbons*	Fuel combustion, wood fires, motor engines	1 year	1 ng/m³	Respiratory and CNS involvement, cancer

*Air quality standards according to the European Union. *$PM_{2.5}$ is stand for PM of 2.5 μ or less. PM_{10} is stand for PM of 10 μ or more. PM = Particulate matter, CNS = Central nervous system

As it can be easily understood, fossil fuel consumption shares the largest part of air contamination. Air pollutants can also be classified into anthropogenic and natural according to their source of emission. From anthropogenic aspect, air contamination occurs from industrial and agricultural activities, transportation, and energy acquisition. While from natural contaminant has different sources of emission such as volcanic activities, forest fire, sea water, and so on.

Health hazards

In terms of health hazards, every unusual suspended material in the air, which causes difficulties in normal function of the human organs, is defined as air toxicants. According to available data, the main toxic effects of exposure to air pollutants are mainly on the respiratory, cardiovascular, ophthalmologic, dermatologic, neuropsychiatric, hematologic, immunologic, and reproductive systems. However, the molecular and cell toxicity may also induce a variety of cancers in the long term. On the other hand, even small amount of air toxicants is shown to be dangerous for susceptible groups including children and elderly people as well as patients suffering from respiratory and cardiovascular diseases.

Respiratory disorders

Because most of the pollutants enter the body through the airways, the respiratory system is in the first line of battle in the onset and progression of diseases resulted from air pollutants. Depending on the dose of inhaled pollutants, and deposition in target cells, they cause a different level of damages in the respiratory system. In the upper respiratory tract, the first effect is irritation, especially in trachea which induces voice disturbances. Air pollution is also considered as the major environmental risk factor for some respiratory diseases such as asthma and lung cancer. Air pollutants, especially PMs and other respirable chemicals such as dust, O_3, and benzene cause serious damage to the respiratory tract. Asthma is a respiratory disease which may be developed as a result of exposure to air toxicants. Some studies have validated associations between both traffic-related and/or industrial air pollution and increasing the risk of COPD. Treatment of respiratory diseases due to air pollution is similar to the other toxic chemical induce respiratory disorders.

Cardiovascular dysfunctions

Many experimental and epidemiologic studies have shown the direct association of air pollutant exposure and cardiac-related illnesses. Air pollution is also associated with changes in white blood cell counts which also may affect the cardiovascular functions. On the other hand, a study on animal models suggested the close relationship between hypertension and air pollution exposure. The traffic-related air pollution, especially exposure to high levels of NO_2, is associated with right and left ventricular hypertrophy. In addition to the antidote therapy that exists only for a few cardiotoxic substances like CO, usual treatment of cardiovascular diseases should be carried out.

Neuropsychiatric complications

The relationship between exposure to air suspended toxic materials and nerve system has always been argued. However, it is now believed that these toxic substances have damaging effects on the nervous system. The toxic effect of air pollutants on nerve system includes neurological complications and psychiatric disorders. Neurological impairment may cause devastating consequences, especially in infants. In contrast, psychiatric disorders will induce aggression and antisocial behaviors. Recent studies have reported the relationship between air pollution and neurobehavioral hyperactivity, criminal activity, and age-inappropriate behaviors. Studies have also revealed the association between air pollution and higher risk of neuroinflammation, Alzheimer's and

Parkinson's diseases. Some studies showed that aggression and anxiety in megacities are in close relationship with the high level of air pollutants.

Other long-term complications

Skin is the body's first line of defense against a foreign pathogen or infectious agent and it is the first organ that may be contaminated by a pollutant. The skin is a target organ for pollution in which the absorption of environmental pollutants from this organ is equivalent to the respiratory uptake. Research on the skin has provided evidence that traffic-related air pollutants, especially PAHs, VOCs, oxides, and PM affect skin aging and cause pigmented spots on the face.

Theoretically, toxic air pollutants can cause damage to organs when inhaled or absorbed through the skin. Some of these pollutants are hepatocarcinogen chemicals. There are some proven data which highlighted the role of air pollutants, especially traffic-related air pollution on the incidence of autism and its related disorders in fetus and children. Disrupting endocrine by chemical components of pollutants has been described as a possible mechanistic pathway of autism or other neurological disorders. Some studies showed that there are relationships between air pollution exposure and fetal head size in late pregnancy, fetal growth, and low birth weight.

Many of the diseases that are linked to immune system dysfunction can be affected by several environmental factors such as poor air quality. Poor air quality can cause serious complications in the immune system such as an abnormal increase in the serum levels of the immunoglobulin (Ig); IgA, IgM, and the complement component C_3 in humans as well as chronic inflammatory diseases of the respiratory system. Exposure to these immunotoxicants may also cause immune dysfunction at different stages which can serve as the basis for increased risks of numerous diseases such as neuroinflammation, an altered brain innate immune response. Air pollutants modify antigen presentation by up-regulation of costimulatory molecules such as CD80 and CD86 on macrophages.

The eye is a neglected vulnerable organ to the adverse effects of air suspended contaminants even household air pollution. Clinical effects of air pollution on the eyes can vary from asymptomatic eye problems to dry eye syndrome. Chronic exposure to air pollutants increases the risk for retinopathy and adverse ocular outcomes. In addition, there are now evidence suggesting the association between air pollution and irritation of the eyes, dry eye syndrome, and some of the major blinding. According to data, the level of air pollution is linked to short-term increases in the number of people visiting the ophthalmological emergency department.

CONCLUSIONS AND RECOMMENDATIONS

Air pollutions have major impacts on human health, triggering, and inducing many diseases leading to high morbidities and mortalities, particularly in the developing continents such as Africa. Therefore, air pollutions control is vital and should be on the top of priority list of the governments. The policy makers and legislators in these continents must update all laws and regulations related to air pollutions. Coordination between different departments involving in air pollutions must be leaded by a powerful environmental protection organization. An effective environmental protection organization should have enough budgets for administration, research, development, monitoring, and full control of the environment including air pollution.

REFERENCES

[1] Robinson DL. Air pollution in Australia: Review of costs, sources and potential solutions. *Health Promot J Austr.* 2005; 16:213–20. [PubMed] [Google Scholar]

[2] Habre R, Coull B, Moshier E, Godbold J, Grunin A, Nath A, et al. Sources of indoor air pollution in New York city residences of asthmatic children. *J Expo Sci Environ Epidemiol.* 2014; 24:269–78. [PubMed] [Google Scholar]

[3] Rumana HS, Sharma RC, Beniwal V, Sharma AK. A retrospective approach to assess human health risks associated with growing air pollution in urbanized area of Thar Desert, Western Rajasthan, India. *J Environ Health Sci*

Eng. 2014; 12:23. [PMC free article] [PubMed] [Google Scholar]

[4] Yamamoto SS, Phalkey R, Malik AA. A systematic review of air pollution as a risk factor for cardiovascular disease in South Asia: Limited evidence from India and Pakistan. *Int J Hyg Environ Health.* 2014; 217:133–44. [PubMed] [Google Scholar]

[5] Zhang W, Qian CN, Zeng YX. Air pollution: A smoking gun for cancer. *Chin J Cancer.* 2014; 33:173–5. [PMC free article] [PubMed] [Google Scholar]

[6] Brucker N, Charão MF, Moro AM, Ferrari P, Bubols G, Sauer E, et al. Atherosclerotic process in taxi drivers occupationally exposed to air pollution and co-morbidities. *Environ Res.* 2014; 131:31–8. [PubMed] [Google Scholar]

[7] Biggeri A, Bellini P, Terracini B. Meta-analysis of the Italian studies on short-term effects of air pollution – MISA 1996-2002. *Epidemiol Prev.* 2004;28(4-5 Suppl):4–100. [PubMed] [Google Scholar]

[8] Vermaelen K, Brusselle G. Exposing a deadly alliance: Novel insights into the biological links between COPD and lung cancer. *Pulm Pharmacol Ther.* 2013; 26:544–54. [PubMed] [Google Scholar]

[9] Kan H, Chen B, Zhao N, London SJ, Song G, Chen G, et al. Part 1. A time-series study of ambient air pollution and daily mortality in Shanghai, China. *Res Rep Health Eff Inst.* 2010; 154:17–78. [PubMed] [Google Scholar]

[10] Zhou N, Cui Z, Yang S, Han X, Chen G, Zhou Z, et al. Air pollution and decreased semen quality: A comparative study of Chongqing urban and rural areas. *Environ Pollut.* 2014; 187:145–52. [PubMed] [Google Scholar]

[11] Chen B, Kan H. Air pollution and population health: A global challenge. *Environ Health Prev Med.* 2008; 13:94–101. [PMC free article] [PubMed] [Google Scholar]

[12] Molina MJ, Molina LT. Megacities and atmospheric pollution. *J Air Waste Manag Assoc.* 2004; 54:644–80. [PubMed] [Google Scholar].