Chapter 15
Outdoor Air Pollutants

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15.1 When Did the Air Pollution Start?

Although it is a common idea that "air pollution" started in our planet concomitant with the Industrial Revolution, there are documents showing that pollution started well before the eighteenth century. A recent study by Sapart et al. [1] from the Utrecht University in the Netherlands, shows that methane emissions, a gas implicated in climate changes, increased significantly already more than 2000 years ago, during the Roman Empire. The increase was not correlated to increased warming but with human activities. It should be mentioned that metallurgy and large-scale agriculture started around 100 B.C. During the Roman Empire, the population kept domesticated livestock – cows, sheep and goats – which excrete methane gas, a byproduct of digestion. At the same time, in Asia, the Han dynasty expanded its rice fields, which harbor methane-producing bacteria. Also, blacksmiths in both empires produced methane and CO_2 gas when they burned wood to fashion metal weapons.

In the third Century B.C., Theophrastus (a student of Aristotle) wrote "smell of burning coal was disagreeable and troublesome" and later the Roman philosopher Seneca, in 61 A.D., defined the air in Rome as heavy, a sign of air pollution.

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Furthermore, it was during this period that Romans started the use of beach houses as a way to escape from the city pollution.

In the Middle Ages, the use of coal in cities such as London was beginning to increase. In the latter part of the thirteenth century, in an effort to reduce air pollution, England's King Edward I threatened Londoners with harsh penalties if they did not stop burning sea-coal. However, the king's regulations–and those of subsequent leaders–had little effect. In the United Kingdom, the Industrial Revolution in the eighteenth century was based on the use of coal that dramatically increased urban air pollution. In this period, the word smog was coined, as in foggy condition, and pollution levels escalated when urban smog (smoke and fog) was formed. Reports of hazardous effects induced by smog reach as far back as the thirteenth century when, during the reign of Richard III (1377–1399), the first reports of human diseases were attributed to severe air pollution. The 1875 Public Health Act in England contained a smoke abatement section in an attempt to reduce smoke pollution in urban areas.

Starting from the eighteenth century, increased smog and soot levels had serious health impacts on the residents of growing urban centers. For example, in 1952, pollutants from factories and home fireplaces mixed with air condensation killed at least 4,000 people in London over a few days. A few years earlier, in 1948, severe industrial air pollution created a deadly smog that asphyxiated 20 people in Donora, Pennsylvania, and made 7,000 sick. Acid rain, first discovered in the 1850s, was another problem resulting from coal-powered plants. The release of human-produced sulfur and nitrogen compounds into the atmosphere negatively impacted plants, fish, soil, forests and some building materials.

Today, the leading cause of air pollution is motor vehicles, (which were first mass-produced in the U.S. by Henry Ford, in the early twentieth century); auto emissions also increase the amount of greenhouse gases in the atmosphere, which in turn contribute to global warming.

15.2 Air Pollution in Life

A good quality of life for humans and other living organisms is assured by low concentrations of air pollutants that must not exceed threshold limits, established by empirical and/or experimental methods. Atmospheric air is a mixture of nitrogen, oxygen, noble gases (such as Ar, Ne, He,), and carbon-dioxide. In addition, atmospheric air is a gas-mixture where solid and liquid particulates are present and thus could be considered as an aero-disperse system. The ideal composition of pure air can not be defined because, in nature, air is always polluted by various components (gases, solid particles and aerosols) that change the base composition of the atmosphere. Pollutants can be harmful to human health, living organisms, soil, water and other elements of the environment.

More than 3,000 substances that are not part of the base atmospheric composition can be considered air pollutants [2]. Some substances that are normally present in the atmosphere at nominal non-toxic concentrations can be considered pollutants if their concentration reaches much higher than usual levels. Also, some substances that are normally present in certain layers of the atmosphere (e.g. ozone in the stratosphere), when present in the troposphere, are considered pollutants. There is no an ideal method for defining a standard air quality index. In fact, in each country, or even within a country in different cities, the air quality index is determined following different methods and even simple air quality indices need skills in mathematical statistics [3]. Although there is not any unique and comprehensive classification of pollutants, generally they can be classified in several ways according to their origin (natural or anthropogenic, chemical or biological), phase (solid, liquid, gaseous), formation mechanism (primary and secondary), and their effect on human health (toxic, allergic or carcinogenic) (Fig. 15.1). Modern industrial and technical progress has resulted in a significant increase of the concentration of pollutants in the atmosphere and, consequentially, an ever-increasing frequency of allergic illnesses [4].

Pollutants may originate from natural or anthropogenic sources. Biogenic or natural sources include windborne dust, sea spray, wild fires, and volcanic eruptions. Hence, H_2S, SO_2, HCl, NO, NO_2, NO_3, CO, CO_2, CH_4, NH_3, dust, pollen, fungus spore, bacteria are natural pollutants [5]. Anthropogenic sources are mainly related to human activities, in particular combustion of fuels, both as industrial process or nonindustrial fugitive fonts such as exhaust gas of transportation vehicles [6]. Combustion engines produce nitrogen oxides, volatile organic chemicals

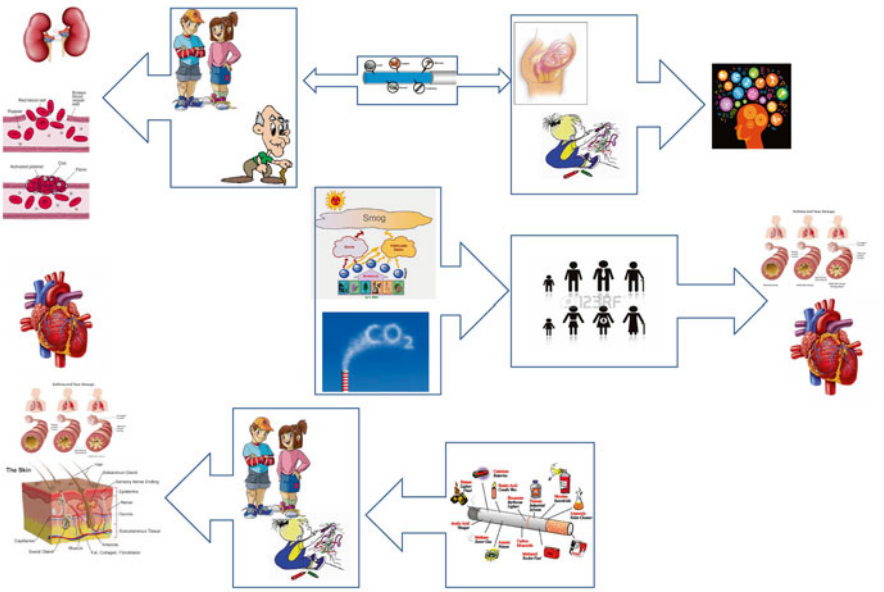


Fig. 15.1 Health effects of air pollutants

(VOCs), carbon monoxide, carbon dioxide, sulfur dioxide and particulates. Cars gas, stoves, incinerators, and farming activities produce carbon monoxide and dioxide, as well as particulates. Other human-made sources include aerosol sprays and solvent spills or leaks.

These anthropogenic pollutants are basically the same as natural pollutants except maybe the biological pollutants and some specific synthetic organic compounds (chlorofluorocarbon (CFC), dioxin and benzene derivatives), soot and ash [4]. According their physical state, air pollutants are classified into **gas forms** (such as oxidized and reduced forms of carbon (CO_2, CO, CH_4), of sulphur (SO_2), of nitrogen (NO_2, NO, N_2O_4, NH_3), O_3, halogens, benzene vapors, Hg, VOCs, **particles in suspension** (including heavy metals with toxic effect (Pb, Ni, Cd, As), polycyclic aromatic hydrocarbons (PAHs), PM_{10} and $PM_{2.5}$ particulate matter and different ionizing radiation.

Because it is not possible to discuss all the air pollutants in this chapter, the main air pollutants to which terrestrial life are exposed based on the EPA classification and for which EPA has set National Ambient Air Quality Standard, will be considered. These pollutants are found throughout the USA and are defined as "most common" or "criteria pollutants". They are (1) particulate pollution or particulate matter, (2) carbon monoxide, (3) sulfur oxides, (4) nitrogen oxides, (5) lead and (6) trophospheric ozone. Particulate matter and ground-level ozone are the most widespread health threats.

15.2.1 Particulate Matter

Particulate matter (PM) is defined as any substance (except pure water) that exists as a liquid or solid in the atmosphere under normal conditions and is microscopic or submicroscopic in size, but larger than molecular dimensions [7]. PM have both biogenic and anthropogenic origins. Biogenic or natural sources include windborne dust, sea spray, wild fires, and volcanic eruptions, while anthropogenic sources include combustion of fuels, industrial processes and transportation sources [6]. Particulate matter is generally classified as PM_{10} and $PM_{2.5}$; particles with aerodynamic diameters lower than 10 and 2.5 μm, respectively, that can induce morbidity and mortality [8–12]. It is further possible to discriminate particles as coarse particles, with diameters >2.5 μm, and fine particles with diameters <2.5 μm. The size of atmospheric particles plays an important role in their chemical and physical properties as well as their climatic and health effects, based on the number of particles, surface area, and volume distribution [13].

The concentrations of PM changes in urban sites as the result chemical and physical processes, vertical and/or horizontal transport, condensation, photochemical reactions [14].

Coarse particles typically originate from primary sources such as dust and traffic, while fine particles arise from secondary sources such as the reaction of gases in the atmosphere [15].

Four main source types for PM_{10} and $PM_{2.5}$ were identified in a recent study [16]:

- a vehicular source (traced by carbon/Fe/Ba/Zn/Cu);
- a crustal source (Al/Si/Ca/Fe);
- a sea salt source (Na/Cl/Mg);
- a mixed industrial/fuel oil combustion source (V/Ni/SO_4^{2-} and a secondary aerosol (SO_4^{2-}/ NO_3^-/NH_4^+).

Biomass combustion or shipping emissions were also identified, although their contribution to PM levels is less relevant.

The health risks related to inhaled airborne particles depends on both the penetration and deposition of particles in the various regions of the respiratory tract. The larger particles that are inhaled are usually removed in the extrathoracic region, while the smaller particles can easily reach and deposit in the alveolar region where gas exchange occurs. As this region is not coated with a protective mucus layer that is rapidly moved and eliminated, the residence time for the particles deposited in the alveolar region is more significant than in the extrathoracic region [15].

Epidemiologic studies have shown a direct correlation between increased mortality and levels of airborne particles, especially for $PM_{2.5}$ [17].

Of note is a recent work that assessed the association between long-term exposure to ambient air pollution and lung cancer incidence in European populations using seven cohort studies based in nine European countries. The study showed a statistically significant association between risk for lung cancer and PM exposure. Interestingly, an increase in road traffic of 4,000 vehicle-km per day within 100 m of a residence was associated with an increased risk for lung cancer. These data showed, for the first time, that particulate matter air pollution contributes to lung cancer incidence in Europe [18].

15.2.2 Carbon-Monoxide (CO)

Carbon-monoxide (CO) consists of one carbon atom and one oxygen atom, connected by a triple bond which consists of two covalent bonds as well as one dative covalent bond. It is the simplest ox-carbon and it is produced during incomplete combustion of organic matter due to insufficient oxygen supply to enable complete oxidation to carbon dioxide (CO_2). Worldwide, the largest source of carbon monoxide is natural in origin; due to photochemical reactions in the troposphere which generate about 5×10^{12} kg per year, other natural sources of CO include volcanoes, forest fires, and other forms of combustion [19].

Carbon monoxide is a colorless, odorless, tasteless, and initially non-irritating gas, and thus it is very difficult for people to detected [20]. In biology, carbon monoxide is naturally produced by the action of heme oxygenase 1 and 2 on the heme from hemoglobin breakdown [21]. Although it is produced in low quantities by animal metabolism and is involved in some normal biological functions, in higher quantities it is toxic to humans and animals. The affinity between hemoglobin and CO is approximately 230-fold higher than the affinity with oxygen so hemoglobin

binds preferentially to CO. This results in a proteic complex and squeezes out oxygen. Hemoglobin becomes carbon-monoxide hemoglobin, preventing blood oxygen transport through the body. This results in oxygen depletion of the heart, brains and blood vessels, eventually causing death if the exposure is severe or extended for long time [4]. CO also binds to the hemeprotein myoglobin, with a 60-fold higher affinity than oxygen, reducing its functionality [22]. This causes reduced cardiac output and hypotension, which may result in brain ischemia [23].

Acute CO poisoning brings on headache, heavy breathing, heart problems, in serious cases unconsciousness and even breath paralysis. Chronic symptoms are headache, dizziness, insomnia, heart ache, nervous system symptoms and increase of heart attack frequency.

15.2.3 Sulphur Dioxide (SO_2)

Sulphur dioxide (SO_2) is the most abundant among the highly reactive gasses known as "oxides of sulfur" (SO_x). SO_2 is a colorless gas with a pungent odor and dissolves readily in water. SO_2 in the air results primarily from activities associated with the combustion of coal and other fuels in industrial and domestic use. Minor sources of SO_2 include industrial processes such as extracting or smelting metal from ore. Once released into the environment, SO_2 can be converted to sulfuric acid, sulfur trioxide, and sulfates. Once dissolved in water, SO_2 can form sulfurous acid. Soil can absorb SO_2, but it is not known if or how it moves in soil. Humid weather promotes the transformation of the oxide into sulphuric acid causing acid rains and winter smog [4]. However, SO_2 concentrations in air have been decreasing over the past two decades due to the use of alternative energetic sources [24].

SO_2 is responsible for several adverse effects on the respiratory system. Short-term exposures to SO_2, ranging from 5 min to 24 h, are associated to bronchoconstriction and increased asthma symptoms especially during exercise or other hyper-ventilated conditions. Children, elderly people and asthmatics are more sensitive to the actions of SO_2. Furthermore, SOx can react with other compounds in the atmosphere generating small particles that reach deep sensitive parts of the lungs and can cause or worsen respiratory disease, such as emphysema and bronchitis, and can intensify existing heart disease, and induce premature death.

15.2.4 Nitrogen Oxides (NOx)

Nitrogen dioxide (NO_2) is one component of the complex mixture of different highly reactive gasses known as "oxides of nitrogen," or "nitrogen oxides (NO_x)." Other nitrogen oxides include nitrous acid and nitric acid. The Environmental Protection Agency (EPA) established NO_2 as the indicator for the larger group of nitrogen oxides. Nitrogen oxides are produced naturally (by bacterial and volcanic

action and lightning) but emissions from cars, trucks and buses, power plants, and off-road equipment represent the major sources of NO_2 [25].

NO_2, reacting with ammonia in the presence of moisture, is a precursor for a number of harmful secondary air pollutants, and other compounds to form small particles, that increase the formation of ground-level ozone. Fine particle pollution thus is responsible for severe effects on the respiratory system such as emphysema and bronchitis, and can aggravate existing heart disease [26].

Nitrogen-oxides irritate the mucous membrane, cause coughing, nausea, headache, and dizziness. These symptoms usually disappear in a few hours although with acute poisoning, after a few hours, pneumonia and pulmonary edema can emerge [27]. When NO_2 reaches the mucous membrane it forms nitrous or nitric acid, and induces local tissue damage. If it gets into the bloodstream, haemoglobin is converted to methehemoglobin, becoming unable to carry oxygen to the organs. Longer exposures reduce the resistance to infections, aggravate asthmatic diseases, causes frequent respiratory illnesses, and, later on, decreased lung-functions may occur [4]. Recent data from a 73,000 cohort study showed that NO_2 is associated with lung cancer and ischemic heart disease mortality confirming the theory that pollution exposure causes premature mortality [28].

15.2.5 Heavy Metals (Lead)

Some elements naturally present in the earth's crust, with metallic properties and an atomic number higher than 20, such as lead, mercury, cadmium, silver, nickel, vanadium, chromium and manganese, are considered heavy metals [29]. Combustion, waste water discharges and manufacturing facilities represent sources of such metals. As metals are not biodegradable (although organic forms can result from metabolism) they can enter into the food chain.

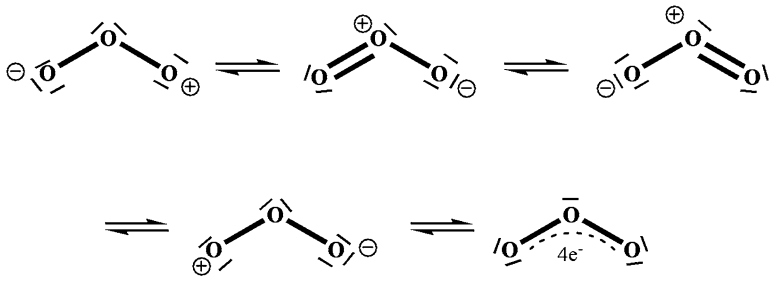
Some metals, such as zinc and iron, are indispensable as essential elements at very low concentrations. However, others, and all at higher doses and after prolonged exposure tend to bio-accumulate in the human body causing severe toxic effects disrupting the functions of vital organs such as brain, kidneys and liver [30]. The toxic effects of heavy metals are due to their ability to substitute or interfere with the actions of diverse polyvalent cations (calcium, zinc, and magnesium) that function as charge carriers, co-factors in catalyzed reactions, or as structural elements of protein.

Lead is one of the most toxic heavy metals and can cause serious adverse effects on different body tissues and organs. In particular, prolonged exposure to Pb even at low levels damage the nervous system. The toxic effects of Pb are mainly due to its capability to substitute for calcium in the body, altering its accumulation, transport, and thus all its physiological functions. Detrimental effects associated to lead exposure are directly related to a persons age. In particular, exposure to high lead levels during pregnancy is directly related to spontaneous abortion, low birth weight and

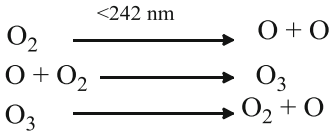
impaired neurodevelopment together with impairment of childhood cognitive functions [31–33]. Several studies also confirmed the carcinogenic properties of lead [31].

15.2.6 Ozone (O_3)

Ozone (O_3) or trioxygen, is a triatomic molecule consisting of three oxygen atoms. The word ozone derives from the Greek ὄζειν, which means "to give off a smell". It is an unstable gas of a soft sky-blue color, with a pungent, acrid smell already perceptible at a concentration of 0.01 ppb. The molecule has a molecular weight of 48 KD. Ozone does not have a stable structure but exists in several mesomeric states in dynamic equilibrium.



Ozone is naturally present in the atmosphere surrounding the earth. In the upper part of the atmosphere, the stratosphere, circa 20–30 Km from the earth² surface, the ozone layer can reach the concentration of 10 ppm. The ozone occurring in the stratosphere, where the majority of atmospheric ozone is found, forms a "filtering layer" that acts as a barrier to the dangerous radiation from the sun.



In contrast, O_3 present within the lower troposphere (10 miles from the ground level) is very noxious to the terrestrial health. It is a ubiquitous pollutant of the urban environment but it is not emitted directly by any man-made source in significant quantities. Ozone arises from chemical reactions in the atmosphere through the action of sunlight on oxygen molecules. Among the most common molecules that lead to O_3 formation at the ground level are nitric oxides (NO_x). NO_2 can be photolyzed by solar ultraviolet radiation (UV) resulting in NO and the atomic oxygen that can react with molecular oxygen leading the formation of O_3. Ozone can also be destroyed by nitric oxide; NO can react with O_3 to form NO_2 and O_2. Under these

steady-state conditions, the concentration of O_3 cannot increase until most of NO has been converted to NO_2 by additional reactions occurring within the complex. This accumulation occurs as the rate of NO_2 photolysis is much faster than that of O_3.

Other species in photochemical smog also undergo photodecomposition to yield free radicals that may participate either directly or indirectly in the conversion of NO to NO_2. Hydroxyl and hydroperoxyl radicals are an example of compounds that can react with nitrogen radicals with the destruction of O_3 by NO.

$$\begin{aligned} NO_2 &\xrightarrow{<310\ nm} NO + O \\ O + O_2 &\longrightarrow O_3 \\ O_3 + NO &\longrightarrow NO_2 + O_2 \end{aligned}$$

In large metropolises like Mexico City, but also European cities such as Rome, Milan and Paris, O_3 can reach toxic concentrations (0.8 ppm) especially during the summer. Anthropogenic emissions, mainly of NOx but also methane (CH_4), carbon monoxide (CO) and sulphuric compounds, have caused a progressive increase of ozone concentration over 1 ppm [34]. It has been estimate that the level of tropospheric O_3 will increase 5-fold at the end of this century because the increase of cars and industrial fumes, leading to dangerous consequences to terrestrial life [35].

Ozone is strongly toxic to human health especially the respiratory tract. O_3 reacts with the respiratory tract lining fluid (RTLF) components and may never directly reach the underlying respiratory tract epithelial cells, at least in areas where they are covered by RTLFs [36]. Therefore, the toxic effects of O_3 on the underlying epithelial cells may be mediated by products of its reaction with RTLF constituents. These products would include lipid hydroperoxides, cholesterol ozonization products, ozonides, aldehydes, and oxidation products proteins or even antioxidants themselves (e.g., thyol and thyol-derived radicals).

As O_3 is relatively insoluble in water, interactions of O_3 with RTLFs are primarily governed by reactive absorption (i.e., the more oxidizable substrate that is present in RTLFs, the more O_3 will be absorbed by the RTLFs). Therefore, inhaled O_3 may be effectively removed by antioxidants present in the more abundant, proximal RTLFs, thus delivering less inhaled O_3 to more distal and susceptible gas-exchanging regions of the lung [37]. This results in activation of cell defense systems or initiation of inflammatory–immune processes. Several researchers have shown that O_3 reacts readily with water-soluble antioxidants leading to a depletion of this defense at respiratory tract levels [37]. O_3 in sufficient amounts activates regulators of the expression of mediators of airway inflammation such as cytokines, chemokines, and adhesion genes [37]. Critical in this regard are investigations of the effects of O_3 in so called susceptible populations already known to have inflammatory airway diseases (e.g., subjects with asthma and cigarette smokers). Many of these subjects may actually have augmented RTLF antioxidant levels due to increased glandular secretions and plasma leakages and cellular adaptations to the oxidant stress provided by their chronic inflammatory states.

In addition, a the recent work by Jerrett et al. [38] has been shown for the first time that exposure to ozone increases the risk of death from ischemic heart disease, which accounts for more than 7 million deaths worldwide each year. These findings underline how not only the directly exposed organs are affected by air pollutants but once in contact with the toxicants there is a noxious systemic effect on our bodies [38]. Recently, the toxic effects of O_3 exposure have been shown also in other "target" organs, such as skin and eyes. One of the first studies on the effect of O_3 on skin, Thiele et al. demonstrated that O_3 induced significant antioxidants skin depletion and a clear increase in lipid peroxidation [39]. *In vivo* exposure to ozone depletes vitamins C and E and induces lipid peroxidation in epidermal layers of murine skin [40]. In addition to increased levels of oxidative stress markers, such as lipid peroxidation, aldehydes, and protein carbonyl, and decreased antioxidant levels, such as GSH and vitamins C and E, an induction of proinflammatory markers, such as cyclooxygenase-2 (COX-2), along with increased levels of heat shock proteins (HSP-32, −70, and −27) and activation of NF-κB, were observed in skin of hairless mice exposed to 0.8 ppm of O_3 [41]. The study by Valacchi et at. [41] was the first to show that O_3 exposure induces an active cellular response in the skin, and that O_3 can therefore alter skin physiology. Recently, Xu et al. have confirmed the cutaneous toxic effect of O_3 in humans [42], showing a clear correlation between ozone levels and skin conditions such as urticaria, eczema, contact dermatitis, rash/other nonspecific eruption, and infectious skin disease. Other pollutants such as particulates, SO_2, and NO_2, did not show an association with skin conditions. Furthermore, it has been proposed that the effects of O_3 on skin are mediated by the activation of the aryl receptor (AhR) and by the induction of the cytochrome P450 isoform CYP1, an enzyme in a detoxifying pathway usually activated in the cell by xenobiotics and carcinogens, suggesting that toxicological consequences follow the exposure of cutaneous tissues to O_3 [43].

Finally, although few reports have focused on the effect of ozone on eyes, there is a very early work that demonstrated that ozone exposure was able to affect tear protein stability thereby making the eye more susceptible to damage [44]. More recently, the work by Lee et al. [45] has elegantly shown the toxic effect of O_3 on ocular tissue using both *in vivo* and in *in vitro* models. This is the first report showing that ozone induced the breakdown of corneal epithelial integrity, decreased the number of mucin-secreting cells, and induced the production of inflammatory cytokines. This effect was mediated by the activation of NF-κB as also reported for lung and skin tissues [41].

15.2.7 Criteria Pollutants

Besides the "criteria pollutants" as classified by EPA, it is worth mentioning the so-called halogens and halogenated hydrocarbons, pollutants. They include: – Fluorine (F_2). Fluoride is present in air pollutant mixtures both as a gas (HF, SiF_6, CF_4 and F_2) and particulate (F_3AlF_6 (cryolite), CaF_2, NH_3F, AlF_6, CaSiF, NaF and Na_2SiF_6).

Aluminum factories, glassworks, steelworks, ceramic factories, phosphate fertilizer plants, uranium smelters and combustion of coal are the major sources of fluorine pollutants [46]. Fluoride air pollution can adversely affect human health and more than 90 % of fluoride ingested with food or water accumulates in the bodies through incorporation into the crystal structure of bone and tooth. Most of the fluorine that is not deposited in the bones, teeth, and other calcified tissues, is excreted in the urine within hours of ingestion.

Chlorine (Cl_2) Although chlorine concentrations change rapidly in the atmosphere due to atmospheric chemistry and light, rain can remove all the chlorine from the air in a very short time. The impact of chlorine pollution increases in bright sunlight and decreases in drought and low temperature.

Hydrogen chloride (HCl) This gas is released in large quantities through combustion of polyvinylchloride and other chlorinated hydrocarbon materials, and by incinerators. HCl gas is very hygroscopic and quickly reacts with atmospheric moisture and forms aerosol droplets.

Bromine (Br_2) and Iodine (I_2) At high temperatures, organo-bromine compounds are easily converted to free bromine atoms, a process which acts to terminate free radical chemical chain reactions. This makes such compounds useful fire retardants. Well-drilling fluids, as an intermediate in manufacture of organic chemicals, and in film photography represent the most important sources of such a gas. Volatile organic-bromine compounds, under the action of sunlight, form free bromine atoms in the atmosphere which are highly effective in ozone depletion.

In nature, iodine is a relatively rare element and its compounds are primarily used in nutrition, the production of acetic acid and polymers. Iodine's relatively high atomic number, low toxicity, and ease of attachment to organic compounds have made it a part of many X-ray contrast materials in modern medicine.

Halogenated Hydrocarbons Halogenated hydrocarbons are produced by reacting fluorine, chlorine, bromine, or iodine with a hydrocarbon molecule and are toxic for human health. They affect the stratospheric ozone layer tending to degrade into their component elements, which include halogen radicals having great affinity towards ozone. $CFCl_3$ and hydrochlorofluorocarbons HCFCs have been widely used as refrigerants, propellants and solvents, contributing to ozone depletion [47].

Polycyclic Aromatic Hydrocarbons (PAHs) More than 60 hydrocarbons and almost 20 aldehydes and ketones are emitted by incomplete combustion of solid fuel (i.e. wood, charcoal, peat, coal) as a complex mixture of particulate and gaseous species (benzene, formaldehyde, 1,3–butadiene, and styrene) that are known to be carcinogenic. The higher molecular weight polycyclic aromatic hydrocarbons (PAHs), PAH derivatives, methylated and alkylated PAHs, and nitrogen-containing heterocyclic aromatic compounds are emitted in the form of particles from the combustion of bituminous smoky coal that contains organic and inorganic materials including intrinsic concentrations of sulfur, arsenic, silica, fluorine, lead, nickel, chromium, and mercury. On combustion, these elements are released as such or in

the form of their oxides causing smog, soot, acid rains, and toxic air emissions. Microfibrous quartz can also be found in some smoky coals and the resulting coal smoke [48].

Volatile Organic Compounds (VOC) VOC are a complex mixture of many different contaminants such as carbohydrates, organic compounds and solvents, mainly derived from industrial processes and fuel combustion, paint and cleanser use, or agricultural activities. Depending of the nature of any components, VOC can cause different health problems, offensive odors, reduction of lung capacity and cancer. VOC also play an important role in raising ozone levels in the lower atmospheric layer, the main cause of smog.

15.3 The Singular Case Cigarette Smoke

Cigarette smoke is now considered part of the air pollutants. There are reports showing how cigarette smoke produces 10 times more particulates than diesel car exhaust [49]. Tobacco smoke is a complex aerosol, composed of several thousand chemical substances distributed between the gas and the particulate phases. Therefore, cigarette smoke can be classified as both a gaseous and particulate pollutant. The smoke emitted from a lit cigarette is a dense aerosol where microscopic droplets (particulate phase) are distributed in a vapor of air and other gases derived by burning tobacco. There are circa 10^{10} particles per cubic centimeter in fresh mainstream smoke (the combination of inhaled and exhaled smoke after taking a puff on a lit cigarette) and the particle sizes can reach 1 μm in diameter. Smoke particles can be collected using a filter paper (Cambridge filter pad) and are defined as total particulate matter (TPM) or tar. A small portion of the overall components of cigarette smoke are distributed between the gas and the particulate phases and are called "semivolatile components". The gas phase of cigarette smoke includes O_2, N, NO, CO_2, CO, etc.) and volatile compounds.

It has been calculated that mainstream cigarette smoke contains circa 5,000 chemicals suspended in the gaseous phase [50]. The presence of high levels of prooxidants, such as free radicals, in smoke is well-documented, and it is estimated that gas-phase smoke contains more than 10^{14} low-molecular-weight carbon- and oxygen- centered radicals per puff [51, 52]. In addition, as mentioned, the gas phase of smoke contains up to 500 ppm nitric oxide (NO), which slowly undergoes oxidation to nitrogen dioxide (NO_2) [53]; both these gases are radicals.

Radicals in gas-phase smoke have a very short life spam. The small organic radicals in gas-phase smoke are not produced in the flame: flame radicals are too short-lived to pass through the cigarette [52–54]. In addition, the radicals in tar phase are relatively stable and can reduce O_2 to generate superoxide, hydrogen peroxide and other ROS [52, 54, 55]. Although, cigarette smoke contains thousands of toxic chemicals including many carcinogens, a wealth of evidence supports the notion that a major part of the toxicity associated with cigarette smoking is related to

oxidative stress, caused by reactive oxidants and radical species in tobacco smoke itself, or by secondary oxidative events such as lipid peroxidation activated by smoke exposure [56, 57].

Both smokers and nonsmokers can incur adverse health effects from the smoke of burning cigarettes. Smokers inhale mostly mainstream smoke, which is drawn through the burning tobacco column and filter tip and exits through the mouthpiece of the cigarette. Nonsmokers inhale mostly sidestream (SS) smoke, which is emitted into the surrounding air between puffs from the end of the smoldering cigarette. Sidestream smoke is the major source of environmental tobacco smoke (ETS).

Numerous epidemiological studies covering the experience of millions of men and women over many years show that smokers' increased risks of developing cancer, cardiovascular diseases and COPD is related to the number of cigarettes smoked daily, the lifetime duration of smoking, and early age of starting smoking. Based on United States statistics, the lifetime risk that an individual (men and women combined) will develop lung cancer is 6.9 %, or 1 in 13 people. Clearly, this number would be higher for people who smoke and much lower for people who have never smoked.

In a 2006 European study, the risk of developing lung cancer was: 0.2 % for men who never smoked (0.4 % for women); 5.5 % for male former smokers (2.6 % in women); 15.9 % for current male smokers (9.5 % for women); 24.4 % for male "heavy smokers" defined as smoking more than 50 cigarettes per day (18.5 % for women). An earlier Canadian study quoted the lifetime risk for male smokers at 17.2 % (11.6 % in women) versus only 1.3 % in male non-smokers (1.4 % in female non-smokers).

From these statistical data it is easy to understand that, although CS is one of the main risk factors for lung cancer, only a percentage of smokers develop the disease, suggesting that, beside the different habits and the kind and number of cigarettes smoked, there is also a possible genetic predisposition. It should also be mentioned that about one nonsmoker dies from secondhand smoke exposure for every eight smokers who die from smoking, even though secondhand smoke doses (in terms of total mass inhaled) are substantially lower. Recent work by Schick and Glantz [58] showed that freshly generated sidestream CS is 3–4 times more toxic to laboratory animals than mainstream smoke (the smoke that the smoker inhales). In addition, the same group has very recently demonstrated that aged SS smoke is even more toxic than the fresh SS smoke. These are important data because in typical indoor spaces secondhand smoke lingers for 1.5–2.0 hours going through chemical transformations that make the smoke even more toxic for humans [59, 60].

15.4 Exposure and Toxicity of Air Pollutants

Airborne pollution can fall to the ground in precipitation, in dust, or simply due to gravity. These phenomena are defined "atmospheric deposition". Once deposited from the air, pollution can enter our bodies via direct deposition in water or indirect

deposition in land. Therefore, humans enter in contact with air pollutants not only via inhalation but also by ingestion and dermal contact. Once in our system, the pollutants can affect several organs, not only the one directly exposed to the toxicants. This explains the toxic effects that air pollutants can have at systemic levels. In addition to the respiratory tract system, chronic exposure to pollutants like CO can indirectly reduce the speed reflexes and induce dizziness and fatigue. Lung inflammation due to ozone or particulate matter exposure can affect blood coagulation [61] and even induce myocardial infraction. It is well-known that exposure to high levels of nitrogen oxides [62, 63] sulphur dioxide [64] and heavy metals promote an initial irritation of the first airways and, in particular in asthmatic individuals, a successive bronchoconstriction and dyspnea. Particulate matter and ozone can easily reach the alveolar epithelium [65] inducing lung irritation and inflammation [66] Analogous effects can be observed with long-term exposures to lower pollutant concentrations, while it is known that chronic exposure to ozone and heavy metals lead to a reduced functionality of lungs, including asthma, emphysema, and even lung cancer [67–70].

As mentioned before, pollutants are able to also reach organs that are not directly exposed to the pollutants. For example, the nervous system is mainly affected by heavy metals and several papers have shown symptoms like memory and sleep disorders, tremors, and blurred vision after lead exposure [71]. In particular, lead exposure causes the alteration of the dopamine system, glutamate system, and N-methyl-d-Aspartate (NMDA) receptor complex [72, 73]. Of note are also the effects of metals on the cardiovascular system; in fact mercury, nickel and arsenic can alter the blood pressure and inhibit hematopoiesis anemia [74]. Heavy metals can also affect the urinary system by damaging kidney tubular excretion and decreasing the glomerular filtration rate. Finally, maternal exposure to lead increases the risks of abortion and pre-term delivery, congenital malformations [75] and impairment in the nervous system development [76].

15.5 Pollution and Oxidative Stress

Most air pollutants act directly as prooxidants of lipids and proteins or as free radical generators. This common cellular mechanism promotes oxidative stress and induction of inflammatory responses [77, 78]. On the other hand, it is now confirmed that air pollutants play an important role in the initiation, promotion and progression of cancer.

Reactive oxygen and nitrogen species are very injurious inhibiting the normal functions of mitochondrial and nuclear DNA, cellular lipids, and proteins, in addition to their involvement in many signaling pathways [79]. During normal metabolism and in response to exogenous environmental exposures such as cigarette smoke, metals, ozone and free radicals are constantly produced leading to an “oxidative-stress” status. This oxidative state induces a wide variety of adverse effects in many organs and tissues, that easily can led to central nervous system

disorders such as Parkinson's, and Alzheimer's disease, atherosclerosis, or heart attacks, stroke, and even chronic inflammatory diseases such as rheumatoid arthritis. Heavy metals can also induce oxidative stress, but the negative effects are due generally due to their abilities to substitute calcium, magnesium and zinc cations in the maintenance of cellular functions and protein conformation. Heavy metals can also accumulate in cellular organelles leading to dysfunction. Lead, the most dangerous of the heavy metals, can accumulate in mitochondria causing a significant reduction of transmembrane potential [80]. Nickel enters the nucleus, silences the expression of genes such as tumor suppressor genes, interacting with chromatin and inducing carcinogenesis [81]. In conclusion, some metals interfere with various voltage-and ligand-gated ionic channels and cause neurotoxic diseases [82, 83].

15.6 Conclusion

Humans are exposed to not only one pollutant, but to several toxicants simultaneously and often this induces an additive if not a synergistic effect. For instance, in the work by Goldberg [84], the effect of exposure to three pollutants such as NO_2, O_3 and PM were analyzed. The exposure to fine particulate matter, O_3, and NO_2, was positively associated with ischemic heart disease mortality. NO_2 (a marker for traffic pollution) and fine particulate matter were also associated with mortality from all causes combined while only NO_2 had significant positive association with lung cancer mortality.

Not everybody that is exposed to toxicants develop diseases or the same diseases. This is a consequence not only of a genetic predisposition but also of the age, nutritional status and time of exposure. All these variables make the understanding of pollution effect in human health very difficult. Thus, the results of animal experiments are often difficult to be extrapolated for the benefit of humans.

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