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PM10 and the Respiratory Tract: What Do We Know?

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Abstract

The present review deals mainly with recent developments in research on the impact of PM10 (particulate matter below 10 μm) air pollution on the respiratory system and the possibly oxidant reactions that occur as a result of breathing these particles.

Keywords: PMIO, free radicals, respiratory tract, antioxidants.

PMK) and Particulate Air Pollution

Particulate air pollution refers to an air-suspended mixture of solid and liquid particles that vary in size, composition, origin, and effects. The term "aerosols" refers to a stable mixture of suspended particles and gases and therefore implies small-sized particles. Such particles can remain suspended in air for hours or even days until they are removed by gravitation, diffusion or rain. Particulate air pollution is formed by condensation of gases or vapors, or by direct generation through mechanical processes such as diesel exhaust emissions.

Particle size is expressed in terms of its aerodynamic diameter, defined as the diameter of a unit-density sphere that has the same settling velocity as the particle in question. The size distribution of suspended particles in the atmosphere is bimodal. Large particles are 10 to 30 micrometers aerodynamic diameter and most often have a basic pH. These large particles are derived from uncontrolled combustion and mechanical breakup of soil and other crustal materials. Biological particles such as pollens and spores are also found in this large-particle range **[11].**

PM10 are particulates which have aerodynamic diameter smaller than 10 micrometers or, more strictly, particles which pass through a size selective inlet with a 50% efficiency cut-off at 10 micrometers aerodynamic diameter. The term PM10 includes fine mode particles which are smaller than 2.5 micrometers aerodynamic diameter (fPM2.5) and ultrafine particles with diameters less than 50 nanometers (ufPMlO). Fine and ultrafine particles include soot and acid-condensates derived from vehicle emissions, manufacturing, power generation, and agricultural burning.

In Poland, problems of tiny particulate matter suspended in air are of increasing concern. The studies conducted by Chorąży's group and others on ambient air pollution in the highly industralized region of Upper Silesia indicate that the residents of the polluted region are at higher risk of health hazard than residents from rural areas. The great excess of particulate matter above the permitted level is probably one of the major contributing factors to negative effects on health [9].

The upper exposure limit of PM10, established by the World Health Organisation, is 70 $\mu g/m^3$ when the concentration of sulfur dioxide (SO_2) is smaller than 48 ppb. Background levels of PM10 may vary from day to day and with time of day, depending on local pollution sources, weather conditions and traffic emissions.

Diesel Exhaust Particles (DEP)

Diesel engines are employed in light-duty applications such as passenger cars and light trucks, and in heavy-duty usage in larger trucks, buses, locomotives, and ships as well as agricultural and construction equipment. Diesel usage is popular due to its cheaper cost than conventional gasoline. Diesel engines also have several advantages over gasoline or spark-ignition engines. These include increased fuel efficiency, decreased emissions of carbon monoxide and hydrocarbons, and 10% to 25% less emission of carbon dioxide, which has implications for reducing global warming [20].

Examinations of diesel exhaust particles show that the majority are ultrafine with diameters of between 20 and 200 nm. The numbers of particles of this size increase during air pollution episodes and remain airborne for longer periods of time than larger particles. Diesel exhaust materials have been estimated to contribute some 20-80 % of the mass of the particle fraction of PM10 [38]. Diesel vehicles emit some 2 to 20 times more nitrogen oxides and some 30 to 100 times more particles than do gasoline engine cars. Gases and hydrocarbons are absorbed or condensed on a carbonaceous core of submicron particles. The amounts of the components in the exhaust vary considerably from vehicle to vehicle [39] and also depend on physical and chemical characteristics of diesel fuels. It has been shown that fuels with biologically less hazardous potentials have a high cetane number and contain less polycyclic aromatic compounds (PAC) and sulfur [42]. The carbon nuclei of diesel exhaust particles absorb a vast number of organic compounds, such as polyaromatic hydrocarbons, nitroaromatic hydrocarbons, heterocyclics, quinones, aldehydes, and aliphatic hydrocarbons [14]. Some of this compounds are strong mutagens and carcinogens [26].

Epidemiological Evidence of PM10

Links have been proposed between increases in asthma symptoms, hospital visits and mortality and increases in PM10 concentration in air [8]. A series of time-series analyses of the associations of daily mortality with particulate air pollution has shown a ~ 1.0% increase in total deaths/day associated with each 10 μg/m^3 increase in PM10 concentration. Stronger associations were observed with cardiovascular disease (1.4% per 10 μg/m^3 PM10) and respiratory disease (3.4% per 10 μg/m^3 PM10) [11]. The respiratory symptom reports are often aggregated into upper respiratory symptoms (including symptoms such as runny or stuffy nose, sinusitis, sore throat, wet cough, head cold, hayfever, and burning or red eyes) and lower respiratory symtoms (including wheezing, dry cough, phlegm, shortness of breath, and chest discomfort or pain) [12, 47, 22, 18,4,48,32].

Sceptics argue against a role of PM10 in producing mortality and suggest that changes in temperature or viral infections are responsible. To refute or validate either of these views, we now need to examine the biological evidence which has accumulated.

Biological Evidences

At the present time, there are limited studies in animals, humans and in vitro systems on the effects of urban air particles and diesel exhaust particles. The findings of these studies strongly support the hypothesis that PM10 particles induce an oxidant stress, causing inflammation and injury to airway epithelium [27]. It has also been hypothesised that PM10 particles, along with other pathogenic particles, generate free radicals at their surface in reactions involving iron, and that this is a factor in the pathogenicity of PM10 particles [19]. The contribution of free radical reactions was also proposed by Sagai and co-workers who showed that diesel exhaust particles (DEP) produce superoxide radical anions (O_2^-) and hydroxyl radicals (OH) in vitro in the absence of any biological activating system. In this reaction system, O_2^- and OH production was inhibited by addition of superoxide dismutase (SOD) and dimethylsulfoxide (DMSO), respectively. DEP washed with methanol could no longer produce O_2^- and OH, indicating that the active components were extractable with organic solvents [40]. These organic active components may include primarily oxygenated polycyclic aromatic hydrocarbons (PAH) derivatives such as compounds with hydroxy, ketone, quinone, acid anhydride, and acid substituents on parent PAH. They are thought to be mutagenic and/or carcinogenic as well as cytotoxic to bacteria and mammals [24]. Indeed, long - term overload doses of diesel exhaust, which contained particles, produces lung tumours in rats. In contrast, animal exposed under identical conditions to petrol exhaust gases (which were scrubbed with a catalytic convector) or diesel exhaust gases from which the particles were removed by filtration did not develop any lung tumours [5]. However, studies performed by Belinsky and co-workers [3] showed that prolonged inhalation of either diesel engine exhaust or carbon black particles by rats did not cause any detectable mutations in selected cancer-associated genes in rat lung tumors. This finding however precludes reaching any definitive conclusions about mechanism by which these substances induce lung tumors. The possibility exists that tumor induction by both diesel exhaust and carbon black particles proceeds by a nongenotoxic mechanism, probably brought on by the burden of these particles in the lung, rather than by the genotoxic mechanism that might be expected from mutagenic organic compounds present only in diesel exhaust. It was also shown that urban air particles (UAP) over a range of noncytotoxic concentrations of particles strongly induced tumor necrosis factor (TNF) and interleukin 6 (IL-6) production from human and rat alveolar macrophages (AM) in vitro. The AM cytokine response to UAP was partly inhibitable by polymyxin B, but not by the iron chelator deferoxamine [2]. Moreover, morphological and biochemical responses of the respiratory tract after intratracheal instillation of PM10 in animals have been conjugated with an influx of neutrophils into the alveolar space, increased lactate dehydrogenase (LDH), and decreased the level of reduced glutathione and activity of superoxide dismutase, glutathione peroxidase and glutathione S-transferase [27, 40].

Factors Which Can Make a Significant Contribution to Health Outcome

On the given evidences it can be concluded that the following factors are important in defining biological activity of PM10:

- size of origin and soure of origin [31, 33]
- number of particles and total mass [37]
- their available reactive surface area [13]
- nature of surface chemistry and bulk chemistry [1, 28,25]
- clearance from and durability in biological tissues [15, 16, 10]

The available reactive surface area is strongly connected with particle size and is a very important factor, when we consider possibility reactions of PM10 with protective lung lining fluids or with many types of epithelial cells lining the respiratory tract [38].

Surface and bulk chemical analysis of PM10 indicates that it is a complex mixture of inorganic compounds and organic micropollutants, the composition of which may vary from city to city or between urban and rural environments. The elemental and organic carbon, some of the metal ions (Al, Ba, Ca, Cu, Fe, Mg, Mn, Zn, Ti) and many of organic micropollutants, are very common in ultrafine particles. These complexes may act as carriers for minute fragments from animal and plant sources which may be potentially alergenic.

One of the most important distinctions to be drawn in relation to airborne particles reflects their origin. They may be either: primary - these are emitted directly from sources such as non-nuclear power stations, motor vehicles and cement factories; or secondary - particles formed within the atmosphere from condensation of vapours, or as a result of chemical reaction processes. The most abundant secondary constituent is frequently ammonium sulphate, formed from the reaction of ammonia gas with sulphuric acid, itself a product of atmospheric oxidation of SO_2 gas.

The biological effects of a particle are determined by the physical and chemical nature of the particle itself, particularly its solubility. In addition, the physics of deposition, its distribution in the respiratory tract, and the physiological events, including chemical and biochemical reactions of PM10 with components of lung lining fluid layer, that occur in response to the particle's presence are important factors to consider. Particle size is the most important characteristic influencing deposition in the respiratory system [16, 15]. Models of inhaled particle deposition relate aerodynamic particle diameter to the size of deposition. Most inhaled particles above 5 micrometers diameter deposit in the upper airways or larger lower airways. Particles below 2.5 micrometers diameter deposit in the lower airways and alveoli; however, ultrafine particles deposit in the alveoli and alveolar tissue (Figure 1).

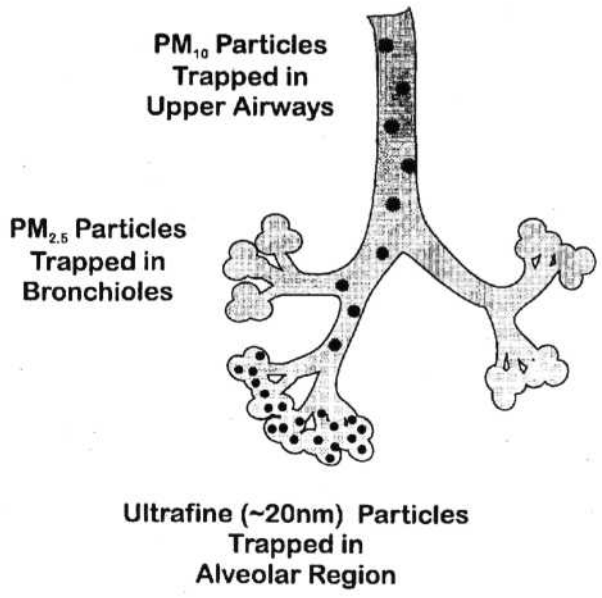

Fig. 1. Deposition of PM10 in the respiratory tract.

Particle clereance is achieved by several mechanisms. Particles deposited in the trachea and bronchioles rise on the mucociliary ladder to be expelled by coughing or to be swallowed. Particles deposited beyond the terminal bronchioles are cleared largely by lung macrophages that, in turn, transport the ingested particles onto the mucociliary ladder or into the lymphatic system. A small fraction of these distally deposited particles migrate throught alveolar tissue directly into the lymphatic circulation. So, it is not suprising that suspicion of the toxicological events which occur in the respiratory system has centered on ultrafine particles produced by natural, industrial and traffic activities.

The Antioxidant Defensive Screen in Human Respiratory Tract Lining Fluid

The first physical interface encountered by inspired ultrafine PM10 is the respiratory tract lining fluid (RTLF), an aqueous layer which overlays the respiratory epithelium of the lung. Several investigators have shown that RTLF contains a wide spectrum of antioxidants [7, 21, 23, 34, 35, 36, 43]. The RTLF of the lower respiratory tract contains the proteins, ceruloplasmin and transferrin [35] and abundant amounts of the low molecular weight antioxidants, reduced glutathione (GSH) [7], vitamin C [43], uric acid [36] and a-tocopherol [34]. All these compounds form the antioxidant defensive screen in lung lining fluid. Although not yet shown experimentally, breathing PM10 and the oxidant reactions that will occur will have an impact on this screen and may be a key to understanding the mechanisms by which PM10 cause biochemical damage in the lung.

Thus, one of the most important question that remains unresolved is what happens in the respiratory tract after deposition of ultrafine particles. What kind of chemical or biochemical reaction between PM10 and protective components of RTLF will be the most important or if any physiological response should be prevailing. It is possible that adsorption of antioxidants onto the surface of PM10 may be very important. Such a process would decrease the activation energy for reactions of low molecular antioxidants with oxygen and then may produce superoxide radical anions, which undergo dismutation to give hydroxy] radicals [13]. Additionally, iron released from PM10 into RTLF could generate free radicals by the Fenton reaction or via a metal-catalyzed Haber-Weiss reaction [6]. These are very likely mechanisms because it was shown that dimethylsulfoxide (DMSO), which is hydroxyl radical scavenger, and desferal, which inhibits hydroxyl radical production by chelating of iron ion were effective in protecting the diesel exhaust particle-promoted DNA scission in vitro [25, 19].

The important source of free radicals may be diesel exhaust particle components having a quinoid structure (or nitro functions). These can undergo one-electron reduction to yield anion radical species, which, in turn can result DNA damage [17]. Indeed, it has been shown that superoxide radical anion was produced during metabolism of benzo(a)pyrene and 1-nitropyrene in the presence of lung microsomes [45, 29]. These compounds are known to be highly mutagenic and they have been identified as a component of diesel exhaust particles [24, 41].

An additional source of free radicals may be phagocyto-

sis of PM10 by alveolar macrophages [30]. It has been hypothesized that surfactant components modulate phagocytosis of environmental particulates by acting as particle opsonins, or by direct activation of alveolar macrophages [44, 2]. During this process, polymorphonucleocytes (PMNs) are marginated into epithelial lining fluid and provide an additional source of reactive oxygen species, which further impinge upon the oxidative burden experienced in this microenvironment [46].

Conclusion

Given that the majority of PM10 reacts within the epithelial lining fluids via free radical mechanisms, the antioxidant composition of this fluid may be critically important in determining an individual's sensitivity to air PM10 pollution. For this reason:

- The role of metals in surface layer of ultrafine partic les should be defined. There is a need to know whether they catalyse chemical reactions, interact with tissue, or induce toxicological sequelae.
- The toxicological properties of ultrafine particles should be studied. The possible toxicological interactions between such particles and gaseous pollutants are especial ly worth consideration.
- The effects of co-exposure to allergens and ambient particles should be studied.
- The practicability of carrying out controlled human exposures to a broader range of suspended particulate mat ter components, observing short-term effects on lung func tion or symptoms, should be considered.
- The effects of biological active compounds or extracts with antioxidant properties originating from plant materials in the food chain, should be considered as a potentially beneficial factors against air pollution induced oxidative stress in the lung.

Hence it is evident that many unresolved questions require resolution before the observations of the epidemiologists can be confirmed with a possible mechanism of action of PM10.

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