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THE EFFECTS OF PARTICULATE MATTER AIR POLLUTION ON RESPIRATORY HEALTH AND ON THE CARDIOVASCULAR SYSTEM

VPLIV PRAŠNIH DELCEV NA BOLEZNI DIHAL IN SRČNO-ŽILNEGA SISTEMA

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Abstract

Particulate matter (PM) is a major component of urban air pollution and has a significant effect on human health. Natural PM sources are volcanic eruptions, dust storms, forest and grassland fires, living vegetation and sea spray. Traffic, domestic heating, power plants and various industrial processes generate significant amounts of anthropogenic PM. PM consists of a complex mixture of solid and liquid particles of organic and inorganic substances suspended in the air. The chemical composition of particles is very complex and depends on emission sources, meteorological conditions and their aerodynamic diameter. Several epidemiological studies have demonstrated that exposure to PM of varying size fractions is associated with an increased risk of respiratory and cardiovascular diseases. Adverse health effects have been documented from studies of both acute and chronic exposure. The most severe effects in terms of overall health burden include a significant reduction in life expectancy by a several months for the average population, which is linked to long-term exposure to moderate concentrations of PM. Nevertheless, numerous deaths and serious cardiovascular and respiratory problems have also been attributed to short-term exposure to peak levels of PM. Although many studies attribute greater toxicity to smaller size fractions, which are able to penetrate deeper into the lung, the molecular mechanisms and the size fractions of the PM that are responsible for the observed diseases are not completely understood.

Key words: particulate matter, air pollution, respiratory diseases, cardiovascular diseases, exposure

Pregledni znanstveni članek
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Izvleček

Prašni delci so eden najpogostejših onesnaževal zraka in imajo velik vpliv na zdravje ljudi. Kemijska sestava prašnih delcev je zelo zapletena in je odvisna od vira emisij, meteoroloških okoliščin in od aerodinamskega premera delcev. Naravni izvori prašnih delcev so vulkanski izbruhi, puščavski pesek, naravni požari in morska sol. Promet, domača kurišča, termoelektrarne in industrijski obrati pa so glavni vir antropogenih prašnih delcev. Prašni delci so sestavljeni iz zapletene mešanice trdnih in tekočih delcev, sestavljenih iz organskih in anorganskih snovi. Številne epidemiološke študije so pokazale, da je izpostavljenost prašnim delcem različnih velikosti povezana s povečanim tveganjem za razvoj dihalnih in srčno-žilnih obolenj. Škodljiv učinek na zdravje je bil ugotovljen na osnovi raziskav, ki so proučevale akutno, in na osnovi raziskav, ki so proučevale kronično izpostavljenost prašnim delcem. Najbolj škodljiv učinek prašnih delcev je skrajšanje življenjske dobe povprečne populacije za nekaj mesecev, kar je povezano z dolgoročno izpostavljenostjo prašnim delcem zmernih koncentracij. Kljub temu pa so vzroki za številne smrti in resne dihalne ter srčno-žilne bolezni povezane s kratkoročno izpostavljenostjo visokim koncentracijam prašnih delcev. Številne raziskave pripisujejo večje negativne učinke na zdravje ljudi manjšim prašnim delcem, ker lahko globlje prodrejo v pljuča. Kljub številnim raziskavam še ni popolnoma pojasnjeno, kateri prašni delci so ključni za povzročene neželene učinke in prek katerih molekularnih mehanizmov sprožajo neželene učinke.

Ključne besede: prašni delci, onesnaževala, bolezni dihal, bolezni srca in ožilja, izpostavljenost

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1 INTRODUCTION

Air pollutants are a heterogeneous mixture of gaseous and particulate matter (PM). The main gaseous components of air pollution include NO_2, SO_2, CO, O_3, NH_3, carbonyl compounds, and organic solvents (1, 2, 3, 4). On the other hand, PM is made of solid and liquid particles from traffic, industry, domestic heating and various natural sources.

Air pollution, both indoors and outdoors, is a major environmental health problem affecting the majority of the population on Earth. It is estimated that air pollution causes 3.1 million premature deaths worldwide every year (5). Adverse health effects have been documented after short-term exposure to peak levels of PM, as well as after long-term exposure to moderate concentrations. Long-term exposure to moderate levels of fine PM has been estimated to reduce life expectancy by as much as several months (5). Nevertheless, numerous deaths and serious cardiovascular and respiratory problems have been attributed to short-term exposure to peak levels. The scientific literature on PM epidemiology suggests an association between ambient PM exposures and various acute health outcomes, including hospital admissions, inflammatory responses in the respiratory tract, the exacerbation of asthma and decreased lung functions (6, 7).

A number of groups within the population have potentially increased vulnerability to the effects of exposure to PM. Groups that develop increased sensitivity include the elderly (8), those with pre-existing heart and lung disease (6) or diabetes (9), children (10), those who are exposed to other toxic materials that interact with PM and those who are socioeconomically deprived (8). Another group within the population includes those members who are simply exposed to unusually large amounts of PM. The literature of the findings indicates that sensitive populations are susceptible to more severe symptoms, including coughs, phlegm, wheezing, shortness of breath, bronchitis, increased asthma attacks and the aggravation of lung or heart disease (6, 9, 10).

In developing countries, exposure to pollutants from the indoor combustion of solid fuels on open fires or traditional stoves increases the risk of acute lower respiratory infections and associated mortality among young children; indoor air pollution is also a major risk factor for chronic obstructive pulmonary disease and lung cancer among adults (5). On the other hand in developed countries, the human respiratory tract has to deal with a much wider variety of ambient particles and gasses. An increase in the prevalence of respiratory diseases, such as rhinosinusitis and bronchial asthma and also in chronic obstructive pulmonary diseases (COPD) has been observed in developed countries over the last 3 decades (11, 12, 13, 14, 15, 16). The adverse effect of PM on respiratory health has a quantifiable impact, not only on the morbidity but also on the mortality of respiratory diseases (17, 18).

On the other hand the possible association between cardiovascular diseases (CVD) and exposure to airborne PM has only recently been addressed. As reviewed in several papers (19, 20, 21), exposure to PM as a result of outdoor air pollution has become a recognized risk factor for adverse cardiovascular events including cardiovascular mortality, cardiac arrhythmia, myocardial infarction (MI), myocardial ischemia, and heart failure (22, 23, 24, 25).

Additionally, the mortality in cities with high levels of air pollution exceeds that observed in relatively cleaner cities by 15–20 %. Even in the EU, the average life expectancy is 8.6 months lower due to exposure to PM produced by human activities (5, 26).

In the present review, the components of air pollution are presented and the effect of PM exposure on the cardiovascular and respiratory system is analysed.

2 THE COMPONENTS OF AIR POLLUTION

PM is a major component of urban air pollution and has a major effect on human health, nature and atmosphere. PM10 means PM that passes through a size-selective inlet with a 50 % efficiency cut-off at 10 µm aerodynamic diameter (27). Likewise PM2.5 means particles that pass through a size-selective inlet with a 50 % efficiency cut-off at 2.5 µm aerodynamic diameter. The limit value for the annual average concentration for PM10 is 40 µg/m^3. The limit value for 24 h averages, which may be exceeded 35 times per year, is 50 µg/m^3 for PM10. For air quality monitoring purposes, PM10 measurements are most widely used at present. EU Member states were also obliged to gather information on the concentrations of fine PM2.5 particles. The target value of 25 µg/m^3 for PM2.5 entered into force on 01/01/2010 and the limit value enters into force on 01/01/2015 (28). The World Health Organization (WHO) recommended limits for the concentration of PM10 is 20 µg/m^3 and 10 µg/m^3 for PM2.5 (29).

2.1 Natural and anthropogenic sources

Sources of PM can be classified as natural or anthropogenic. Natural sources include volcanic eruptions, dust storms, forest and grassland fires,

living vegetation and sea spray. For some natural primary emissions, a strong annual cycle is typical (30, 31). Human activities, such as traffic, domestic heating, power plants and various industrial processes also generate significant amounts of anthropogenic aerosols. Regulators in both the United States of America and Europe have required significant emission reductions from land-based emission sources, while air pollution from ships went largely unregulated until recently (32, 33). The diesel used by ships is usually very dirty fuel that cannot be used for land-based transport. Projections show that by the year 2020, the SO_2 emissions from international shipping are expected to equal or even exceed land-based sources (34).

2.2 Primary and secondary aerosols

Airborne suspended PMs can be also classified as primary or secondary. Primary particles are emitted directly into the atmosphere formed by friction, fossil fuel burning and wind erosion, whereas secondary particles are formed in the atmosphere by the transformation of different gaseous precursors, e.g. SO_2, NO_X, NH_3 (35, 36, 37, 38, 39, 40), see Figure 1. Gaseous precursors are transformed in to secondary PMs in complex photochemical reactions in the air. The common components of atmospheric particles, such as sulphate, nitrate, ammonium, organic compounds, crustal material and water, reach a particulate phase through several photochemical processes (41). A major fraction of the ambient PM arises from atmospheric gas-to-particle conversion.

2.3 The size and chemical composition of Particulate Matters

PM consists of a complex mixture of solid, liquid or solid and liquid particles of organic and inorganic substances suspended in the air. Besides the varying emission sources, PM also differs in chemical composition and size. Size properties govern the transport and removal of particles from the air; they also govern their deposition within the respiratory system and are associated with the chemical composition and sources of particles. In this way, particles are usually sampled and described on the basis of their aerodynamic diameter. Three separate size groups of particulate matter are distinguished:

- PM10: diameter <10 µm (coarse fraction)
- PM2.5: diameter <2.5 µm (fine fraction)
- Diameter <0.1 µm (ultra-fine fraction)

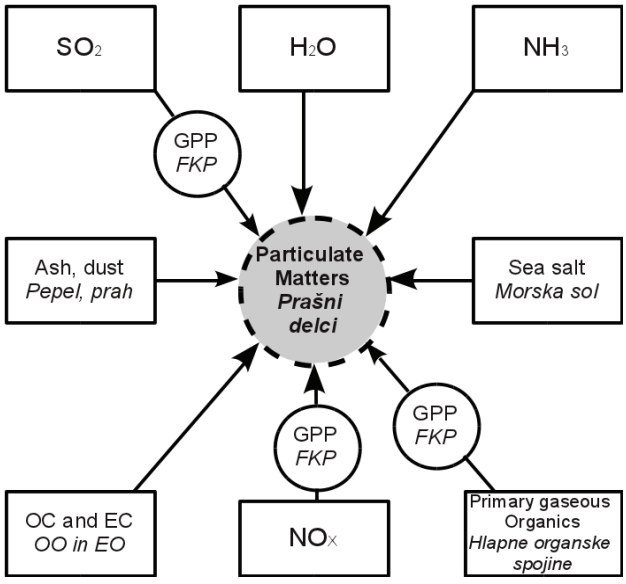

Figure 1. The major components of particulate matters. Particles such as ash, dust, sea salt, water (H2O), organic carbon (OC) and elemental carbon (EC) are directly emitted into the atmosphere. The common components of atmospheric particles are sulphate (SO2), nitrate (NOx) and primary gaseous organics. These components reach the particulate phase through several gas-phase-photochemical (GPP) processes.

Slika 1. Sestava prašnih delcev. Prašni delci, kot so pepel, prah, morska sol, voda (H2O), organski ogljik (OO) in elementarni ogljik (EO) so v ozračje emitirani neposredno. Zelo pogosti prašni delci v zraku so delci sulfatov (SO2), nitratov (NOx) in hlapnih organskih spojin, ki nastanejo preko številnih fotokemičnih (FKP) procesov.

Particles with different aerodynamic diameters come from different emission sources. Coarse particles are mainly formed by mechanical processes, while fine and ultrafine particlesare directly emitted (e.g. biomass burning, diesel soot) and formed by chemical reactions from gaseous precursors. Fine and ultra-fine particles contain secondarily formed aerosols (gas-to-particle conversion), combustion particles and recondensed organic and metal vapours. Coarse particles usually contain dust from roads, industry and earth crust materials. The fine fraction contains most of the acidity and mutagenic activity of PM (42). The largest number of particles can be found in the fine and ultra-fine fractions – i.e. with an aerodynamic diameter less than 2.5 µm (43, 44).

The chemical composition of particles is very complex and depends on the emission sources, meteorological conditions and their aerodynamic diameter. Airborne PM constituents are a mixture of organic and inorganic substances (45, 46, 47, 48, 49, 50). Studies show that the major components of PM include: geological material (metal oxides), organic carbon, elemental carbon, sulphate (SO_2), nitrate (NO_X) and ammonium (NH_3). PM10 sources vary by geographic latitude and longitude. Traffic in urban places and industrial activities are the most important PM10 sources. The variation of PM10 concentrations is controlled by the rate of emission in PM10 sources and by the meteorological conditions. Calm conditions with a low mixing height in a cold season usually lead to higher concentrations than during the summer period. As reported by various research studies (51, 52, 53, 54, 55, 56), the main meteorological factors are wind (speed and direction), temperature, monsoon, rain effect and dust storms.

3 PARTICULATE MATTER AND HEALTH EFFECTS

Exposure to PM has been linked to a number of different health outcomes, including lung inflammatory reactions, reduction in lung function, adverse effects on the cardiovascular system, visit to the hospital emergency department, admission to hospital, and death. Adverse health effects have been documented by studies of both acute and chronic exposure. The most severe effects in terms of overall health burden include a significant reduction in life expectancy of the average population by a several months, which is linked to long-term exposure to moderate concentrations of PM (57). Nevertheless, numerous deaths and serious cardiovascular and respiratory problems have also been attributed to short-term exposure to peak levels of PM. In particular, pulmonary function studies are suggestive of short-term effects resulting from ambient PM exposures. Such outcomes include hospital admissions, inflammatory responses in the respiratory tract, the exacerbation of asthma and decreased lung functions (58).

3.1 Particulate matter exposure and respiratory morbidity

The association between increased levels of air pollution and the mortality and morbidity rates from respiratory diseases is well-established (22, 59). Positive associations have been observed between urban air pollution (especially road traffic) and respiratory symptoms in children (60, 61, 62, 63, 64, 65). Gauderman et al. have demonstrated that PM can negatively influence lung development in children and adolescents. They have shown that exposure to ambient air pollution is correlated with significant deficits in respiratory growth over an eight-year period, leading to clinically important deficits in lung function at the age of 18 (66, 67). PM has also been significantly associated with emergency department visits due to asthma, wheezing, bronchitis and lower respiratory tract symptoms, as well as with the use of anti-asthma medication and physician visits concerning asthma (13, 17, 68, 69). Respiratory morbidity and mortality have also been related to admissions for pneumonia, pulmonary emboli and COPD (70). Strong epidemiological evidence additionally suggests that exposure to PM causes an exacerbation of pre-existing lung conditions, such as COPD, resulting in increased morbidity and mortality (16).

There is also some evidence to indicate that high levels of PM are correlated with the rising trend in allergic respiratory diseases and bronchial asthma. Laboratory studies have confirmed epidemiologic evidence that air pollution may facilitate the access of inhaled allergens to the cells of the immune system, thus promoting the sensitization of the airway (13).

3.2 Particulate matter exposure and cardiovascular morbidity

The increase in risk of adverse clinical cardiovascular outcomes associated with particulate air pollution is relatively small compared to the traditional risk factors such as smoking, as well as diet, obesity, diabetes and metabolic syndrome. But particulate air pollution exposes a much larger number of individuals in the population and over an entire lifetime. Thus the relatively small cardiovascular effects of PM translate into a serious and major public health impact.

A review of the findings (71) has shown that several epidemiological studies have demonstrated that exposure to ambient air pollutants is a major cause of increase in hospital admissions for cardiovascular diseases. Some studies have confirmed that an increase in PM10 or PM2.5 results in an increased risk of hospitalization for myocardial infarction (MI), dysrhythmias, heart failure and cardiac arrest (72, 73, 74, 75, 76, 77, 78). With regard to non-fatal outcomes, the risk of MI has been estimated to be 1.48 times greater for a small increase in particulate air pollution (25 $\mu g/m^3$ in the preceding two hours) (23). In comparison, the risk of MI was recently reported to be nearly 3-times higher in current smokers compared to non-smokers (79). Studies have described an

association between the increase of air pollutants and the development of atherosclerosis. The increase of PM2.5 has been described in humans as coinciding with the incidence of atherosclerosis processes and carotid intima-media thickness (80, 81). Additional research has suggested that there is a link between exposure to PM and heart rate variability (82). Studies show that a temporary increase in PM concentrations may lead to an increased risk of ischemic stroke, cardiac ischemia and coronary artery disease, as well as variations in systolic and diastolic blood pressure values (20, 76, 83, 84). It has been proposed that PM inhalation can increase deep vein thrombosis and coagulation (85, 86, 87). Additionally, it has been demonstrated that PM exposure can induce changes in numerous proteins associated with coagulation, which increases C-reactive protein (88), plasminogen activator inhibitor-1 (89), fibrinogen (90), and the von Willebrand factor (88). Brook et al. proposed in 2004 that PM components might induce endothelial dysfunction, platelet activation and alterations in coagulation. These events may elicit plaque rupture and thrombosis by increasing atherosclerotic plaque instability, conditions that will lead to either MI or stoke (19).

3.3 Association between particulate matter and mortality

Since most of the world's population is potentially exposed to PM in its entire possible fraction, WHO has estimated that 3.1 million deaths are caused each year by PM (5). Most of the currently available epidemiological studies on the health effects of PM use mortality as the indicator of health, because of the relatively easy access to information on population mortality. Some studies have shown a significant association between daily mortality from respiratory and cardiovascular diseases and PM (18, 24, 91). The Health Effects Institute re-analysis has shown an increase in cardiovascular mortality with an increase in fine PM (92). Medina et al. estimated in 2004 that a reduction in PM10 concentrations by only 5 $\mu g/m^3$ would prevent approximately 3300 to 7700 deaths per year (93). Aphekom's projects have shown that a decrease to 10 $\mu g/m^3$ of long-term exposure to PM2.5 could add up to 22 months of life expectancy for persons 30 years of age and older (94). Pope et al. reported in 2004 that a 10 $\mu g/m^3$ elevation of PM2.5 is associated with an increased risk of mortality ranging from 8 % to 18 % (95). The results from the APHENA study reported that a 10 $\mu g/m^3$ elevation of PM10 is associated with an increased risk of mortality from all causes across all ages ranging from 0.2 % to 0.6 % (7). Approximately one million individuals are at risk of death from CVD related to particulate air pollution exposures worldwide each year (96).

3.4 Possible mechanisms of particulate matters that leads to cardio- respiratory diseases

The effect of PM on lung function depends on the type of pollutant and its environmental concentration, the duration of exposure, the total ventilation of the exposed individuals and the interaction between air pollution and aeroallergens such as pollens and fungal spores (13). The main mechanisms of deposition of PM in the lungs are impaction, sedimentation and diffusion (97). Impaction is thought to be the principal mechanism of large PM deposition. Sedimentation happens to particles that are allowed to fall under their own force of gravity. And diffusion affects the smallest particles as they are displaced by random gas motion and will principally occur in the small airways and gas exchange regions of the lung.

The respiratory tract is lined with a thin liquid layer (ELF), composed of various agents such as antioxidants, lipids and proteins (98). The main component of the ELF is surfactants, which reduce surface tension and displace PM less than 6 μm in diameter (99). Also proteins in the surfactant help macrophages target and clear PM (98). So, lung phagocytes are the first line of defence in the cellular response of the lungs to inhaled PM (100). While human lung parenchyma retains PM2.5, particles larger than 6 μm only reach the proximal airways, where they are eliminated by mucociliary clearance if the airway mucosa is intact. The alveolar macrophages (AM) and bronchial and alveolar epithelial cells are the principle cells that process inhaled airborne particles in the lung. They produce pro-inflammatory mediators that have the ability to elicit both a local inflammatory response in the lung tissues and also a systemic inflammatory response (101, 102).

The exposure of AMs to PM influences their phagocyte activity, increases their oxidant production and releases pro-inflammatory mediators such as tumour necrosis factor-α and interleukin-1β that are important in mediating the local and systemic inflammatory response (102). Lung epithelial cells, which have a large surface area, are also important in processing inhaled particles due to the production of several pro-inflammatory mediators (103, 104, 105). In summary AMs and lung epithelial cells determine the profile and the magnitude of the mediator response in the lung following exposure to PM.

The major conduit for the translocation of PM into body is the respiratory tract (Figure 2). The majority of the coarse PM fraction are deposited in the nasal, pharyngeal and laryngeal regions (106). On the other hand, particles in the size fraction PM2.5-0.1 are deposited in the alveolar ducts and sacs (106) and have been shown to be especially toxic (25, 107, 108) (Figure 2).

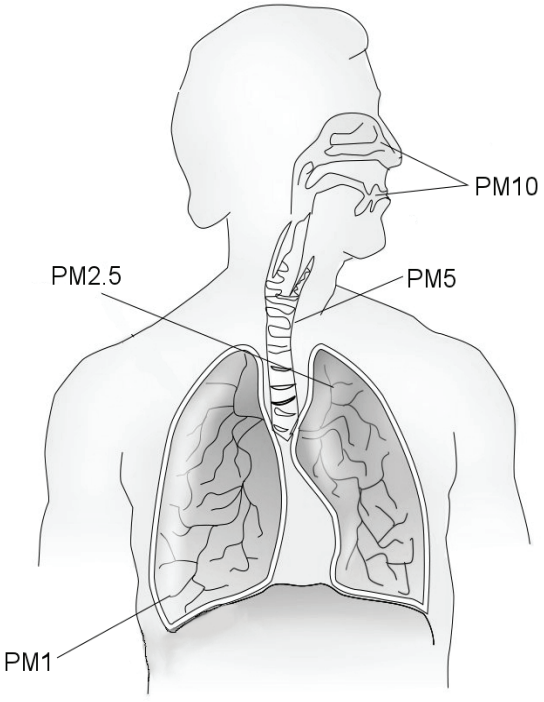

Figure 2. PM deposition in the respiratory system. The major conduit for the translocation of PM into body is the respiratory tract. The majority of the coarse PM (PM10) fractions are deposited in the nasal, pharyngeal and laryngeal regions, PM5 are deposited in the tracheas, while fine and ultrafine particles (PM2.5-0.1), due to their small size, are deposited deep into the lungs, in the alveolar ducts and sacs.

Slika 2. Odlaganje prašnih delcev v dihalnem sistemu. Prašni delci v telo vstopajo preko dihalnega sistema. Večji delci (PM10) se v dihalnem sistemu ustavijo v nosni sluznici, v grlu in v žrelu. Nekoliko manjši prašni delci (PM5) se lahko odložijo v sapniku, frakcije manjših prašnih delcev (PM2.5-0.1) pa lahko zaradi izjemno majhne velikosti pridejo in se odložijo v pljučne mešičke.

While the precise biological mechanisms linking PM exposure to CVD is yet unclear, likely mechanisms include systemic inflammation subsequent to pulmonary inflammation, alterations of the autonomic nervous system that lead to changes in heart rate and heart ratevariability, and the translocation of particles (specifically UFP) or soluble components (e.g., transition metals) from the lungs directly into systemic circulation (21).

Several studies have shown that UFPs are able to move across the blood barrier of the lung and enter into the bloodstream (109, 110). Two studies showed that the UFPs can spread beyond the lungs and cause damage to other organs, such as the brain (111, 112). However, several studies have shown that the translocation to systemic circulation is negligible (113, 114, 115). Regarding the effect of PM on the autonomic nervous system, it has been suggested that PM deposited in the pulmonary tree can stimulate sensory nerve reflexes that alter the systemic autonomic balance (21).

4 CONCLUSIONS

Several epidemiological and experimental studies have identified that air pollution with PM, and especially its fine fraction, affects the health of most of the population, leading to a wide range of acute and chronic health problems and to a reduction in life expectancy. Although many studies attribute greater toxicity to the smaller size fractions, evidence that these particles make up part of the internal constituents of PM10 has to be taken into consideration. Health effects associated with PM exposure are generally known, though the molecular mechanisms and size fractions of the PM that are responsible for the observed diseases are less known. It has also been proposed that the number of ultra-fine particulates is more relevant than the mass of PM (116). There is no clear, direct evidence identifying which of the many sources of PM are responsible for the effects and, in particular, to what extent these effects are caused by PM from the long-range transport of pollution. Also there remain some uncertainties as to the precise contribution of pollution from regional versus local sources in causing the effects observed in both short- and long-term epidemiological studies. It would also be necessary to distinguish between the long and short-term effects of PM on health and to clarify the molecular mechanisms underlying the effects of PM on the cardiovascular system. It is necessary to determine the nature of the components of PM in all the size fractions and to investigate the incidence and

effects of PM10 on health, alongside PM2.5, PM1 and nanoparticles. In research work published in the Journal of Molecular Cell Biology (117) data provides a molecular explanation for nanoparticle-induced lung injury and raised concern about the safety of some nanomaterials.

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