

ULTRAFINE PARTICLES IN AMBIENT AIR AND HEALTH

Sen. Consultant and Sen. lecturer Dr. Ivan Eržen, M.D., specialist on public health, Inštitut za varovanje zdravja RS [Health protection institute of Slovenia], Trubarjeva cesta 2, Ljubljana, Ivan.Erzen@ivz-rs.si

Petre Otorespec, M.D., specialist on public health, Inštitut za varovanje zdravja RS, Trubarjeva cesta 2, Ljubljana

Vesna Lesjak, M.D., Zavod za zdravstveno varstvo Maribor [Institution for health protection], Prvomajska 1, Maribor

Airborne particles as pollutants

Air pollution is a problem which is dealt with by all societies on all development levels, whereas urban population is at special risk by it (1, 2). Studies over the last 30 years have shown that there is a connection between short-term and long-term exposure to fine particles (PM) in ambient air and an increased mortality and more frequent admissions to hospitals due to cardiac and respiratory illnesses. It is established that airborne particles are a complex compound which comprises of particles of different size and chemical compounds. What is less known is that some characteristics of these particles are more harmful for the health of the people exposed than other, so it is more important that we reduce their number in ambient air as much as possible.

It is known that there are different distinctions of particles by size. The most frequent is the division to coarse and fine particles, where the boundary is 2.5 μm . Fine particles are smaller than 2.5 μm , and coarse particles are bigger. Ultrafine particles are defined as particles smaller than 0.1 μm (3). The characteristics of particles depend on their origin. Particles of different sizes only rarely come from one source; usually they are generated within different processes. Fine particles occur in natural processes (eruptions of volcanoes, water aerosols, erosion), or they are a product of man's activities – a consequence of traffic, industry and firing systems (so called primary particles), secondary particles occur as a consequence of various physicochemical processes in the polluted atmosphere (3). Due to different characteristics particles can form compounds, can form flakes and can be withdrawn from air due to their increased mass. Bigger particles fall faster onto soil and relatively close to their source. When inhaled, particles bigger than 10 μm are deposited in the upper respiratory tract. Fine particles are complex mixtures of solid and liquid parts which are suspended in gaseous form. They reach the distal lung parts and can transfer into the blood stream. Next to size, the chemical composition of the particles and their morphology are also of importance.

The chemical composition of the particles depends on the source and on later processes. The most important chemical characteristics of the particles are defined by their elementary structure, inorganic ions and carbon compounds. The elementary structure is important due to potential effects on health, e.g. lead, mercury or cadmium and the possibility to use individual elements as indicators for emission sources.

Ultrafine particles

In the last fifteen years ultrafine particles (UFP) have received more and more attention. It became a priority to know and understand the role of these extremely small particles for health. It was agreed that UFP are particles whose diameter is 100 nanometres or less (100 nm). Considering their small size UFP account for very little in the total mass of fine particles in ambient air (4.5), but their share in the total number of all particles is substantial. Primary UFP occur at burning processes, but also secondary UFP are important as they originate from particles occurring in the atmosphere. Because of a heterogeneous formation of UFP, the concentration (number) of UFP differs in various locations, observation, time and season. The highest concentrations can be expected in a city environment, especially near traffic routes, as motorised cars and especially those with diesel engines are one of the most important sources of UFP-emissions and relevant for human exposure. It was established that although diesel engines are most important as regards emissions the absolute and relative contributions of different types of vehicles to UFP is practically impossible to define. The reason is a constant change of emissions of cars which on one hand is due to regulations that are intended to lower the exhausts and this also affects a decrease in UFP-emissions and on the other hand this reduction is less successful because new technical solutions for a better utilisation of fuels have been introduced. The role played by these new rules, as well as ethanol or mixtures of biodiesel and natural gas, is still poorly defined. The total effect of all these changes has not been studied in detail and it is understandable that it differs from area to area. Also important are the use of fossil fuels and UFP of natural origin.

UFP can occur as autonomous parts or as aggregates. When in aggregates, they change their deposit characteristics, as they have a bigger diameter than autonomous particles. If they are smaller in size then the number of atoms on surface increases relative to particle volume. The result of this is a higher reactivity of particles of nano-metric size (6). They can deposit in the lung parenchyma as autonomous particles or as aggregates (7). Nowadays we still know relatively little of their exact structure, respectively of their physical and chemical characteristics (8).

Effects of ultrafine particles on human health

For many decades now, fine airborne particles and their influence to health are occupying the expert world. Considering the findings of numerous studies – as well experimental as epidemiological – we can conclude that there is an independent correlation between fine particles, especially PM_{2.5} and PM₁₀, and negative impacts on the respiratory system and to the cardiovascular system in humans. These evidences were also the basis for regulatory decisions on restricting pollution and on ambient air pollution with these particles. Also the question occurs what is the role of UFP at adverse consequences of fine particles to human health. A concern due to the effects of UFS is connected with findings in animal studies. The studies show that these parts penetrate deeper into the lungs and can be more toxic than bigger parts. This presupposition is justified with their extremely high number and small diameter. UFP can cause inflammations in the alveolus, besides which they have a big potential for a translocation into the blood and through blood to various organs. At the given

mass ultrafine particles have an area which is between 100- and 1000-times greater than that of particles with a diameter between 0.1 and 2.5 μm and approx. 105-times greater area than particles with a diameter between 2.5 and 10 μm (9). In a big area, UFP can absorb various toxins from the environment and the particles transfer these deep into the lung alveoli and then into the body. Special physical characteristics of UFP, their interaction with tissues and cells and their potential to reach other organs beside lungs raised expectations between researchers that UFP have different, more toxic effects than other fine particles and that their harmful effects reach also other organs and not just the respiratory and cardiovascular system. Provisional research in this respect has not yet offered any conclusions. Toxicological studies on animals, experimental studies of exposure with humans and epidemiological studies so far have not given any conclusive data on the exposure effects of UFP in ambient air on human health (10-12).

Extraction of fine particles from alveoli is difficult, If they are soluble in water they transfer directly into the circulatory system. If they are insoluble then they are transported by macrophages into the lymphatic system where they are stored for months or years. Donaldson et al. conclude that macrophages have difficulties recognising smaller UFP (size < 65 nm), especially at high numbers of particles and deposit them in the lung epithelium (13). After entering the blood system through the epithelium they can travel through the whole body. They enter the cells through caveolae, a kind of surface invaginations on cell membranes. Their size is between 40 to 100 nm, and their function is the transduction of signals and endocytosis. UFP can even transfer through the placenta (8).

Conducted research shows that there are three main types of impact of UFP to the health of the exposed people:

1. Parts which are deposited in the bronchial tree can change the autonomic balance which leads into a decrease of the parasympathetic tone and/or increased tone of the sympathetic tone. This can be provoked directly with triggering the pulmonary neural reflexes or indirectly as a consequence of an oxidative stress and inflammation in the lungs. Oxidative stress is an important part of the pathogenic activity of UFP and it can lead to an inflammation and thus to increased body temperature, fibrosis, bronchitis, and it also contributes to carcinogenesis.
2. Circulating, pro-oxidative and pro-inflammatory mediators, which are realised in lungs, can cause a systemic chain reaction. Mediators, reactants in acute inflammation phases and vasoactive hormones can lead to an endothelial dysfunction and a pro-coagulatory state with a development of blood clots and encouraging arteriosclerotic lesions.
3. After inhaling, UFP can translocate into the circulation and enter into a direct interaction with the cardiovascular system. They affect the endothelium of the blood vessels and arteriosclerotic plaque, and also they can cause local inflammation and oxidative stress (14).

Some population groups are receptive to the effects of polluted air. These groups can feel the consequences at lower concentrations as the general population, and the severity of the effects can also be greater. Individuals with respiratory illnesses (acute bronchitis, chronic obstructive pulmonary disease) and with cardiovascular diseases (e.g. ischemic heart

disease, arteriosclerosis) have a higher risk for premature death and hospitalisation. People with infectious respiratory diseases (e.g. pneumonia) have a higher risk for premature death and risk for diseases (increased respiratory symptoms), also exposure to particles increases the predisposition of individuals for infections. With elderly, a higher risk for premature death and risk for cardiovascular diseases was ascertained, while children have a higher risk for respiratory illnesses and decreased lung functions. With asthmatic patients it was established that the probability for aggravation of the disease and an increase in anti-asthma medication is indicated when they are exposed to particles (3).

Toxicological and epidemiological research

Current data does not show that merely exposure to UFP could lead to consequences which were researched in the case of exposure to PM_{2.5}. Considering that PM_{2.5} and UFP occur simultaneously further research will be needed in order to find out to what extent health consequences can be connected with UFP and how much to other fine particles (8). Some of the newer studies tied acute effects of polluted air with changes in the blood vessels. Severe cardiovascular health problems can also be caused by a disruption of the arteriosclerotic plaque and occurrence of blood clots. Also they can be a consequence of a disrupted autonomous imbalance, which leads into arrhythmia resp. to sudden cardiac death (14). As it appears chronic effects are a consequence of an aspect induced by particles or a worsening of arteriosclerosis. Here an important role is played by inflammation, release of cytokines and chemokines, products of leucocytes, occurrence of free radicals in lungs and stimulation of some receptors (15).

Results of experimental studies enable the assumption that harmful health effects caused by exposure to UFP differ from those which are connected to an exposure to bigger particles. Due to their physical characteristics UFP are reacting differently in the human body as are bigger and heavier particles. They differ in their art of depositing, release from the airways, transformation capability to other organs and also in the types of mechanisms for toxic activities in the cells itself (16). Some experiments show that UFP can reach the brain also through the olfactory nerve.

Experimental research in animals as well as with humans shows that UFP are influencing the respiratory tract and the cardiovascular system. The effects of UFP include: changes of the respiratory function, a more intensive response in case of an allergic reaction, thrombogenic effects, changed function of the endothelia, changes of the heartbeat, an increased development of arteriosclerotic changes and increased markers, which indicate inflammatory changes of the central nerve system. Similar changes, except for the changes of the central nerve system, are also found in cases of exposure to an increased concentration of fine particles.

The number of research which studied the effect of UFP on health after a short-term exposure is limited, thus the results and conclusions from them are for now less reliable. The number of epidemiologic studies aimed at the study of UFP-effect to human health is increasing in the last years and they are pointing to a harmful influence on human health due to short-term exposure. This can be observed as an increased mortality and higher risk for

cardiovascular and respiratory diseases. The results are quite variable which is connected with the already mentioned fact that these epidemiologic studies are weak, as the data on actual exposure is highly unreliable. For now UFP in the inhaled air is not part of a routine monitoring; besides the techniques for measuring these particles in ambient air differ. The consequence is of course a higher probability of errors in exposure, and most of all it is a lot less reliable than in the case of PM_{2.5} and other pollutants, where the data on their concentrations in ambient air is much more exact. A lower reliability is probably also associated with the fact that the conducted epidemiological studies could not clearly show whether an exposure to UFP leads to health consequences which are independent of those caused by other pollutants. According to the data of these studies the effects of UFP could not be consistently separated from effects of other pollutants with which they normally occur simultaneously.

Despite that the mechanisms of UFP-impact are not totally clarified, it is established that the main targets of these particles are the respiratory and cardiovascular systems (8). The main consequences of the impact of fine particles on the population are: premature death, worsening of respiratory and cardiovascular illnesses, which shows itself by increased hospitalisation, absence from class, loss of working days. Also changes in the functioning of the autonomous nerve system can occur, changes in blood-pressure C-reactive protein (CRP), dysfunction of the endothelia, changes in the systemic blood markers, changes of the lung function and increased respiratory symptoms, changes of the lung tissue and changed respiratory defence mechanisms.

Challenges at the research of UFP-influence on human health

When researching the influence of UFP to human health we face numerous challenges. One of the main challenges at researching the effect of UFP to human health is the definition of exposure of the population. The exposure evaluation of the population to UFP is significantly less reliable than in the case of pollutants which we monitor regularly, as for example PM₁₀ and PM_{2.5}. The areal concentration of UFP is highly volatile, it reduces fast with distance from the road, thus the measurements of UFP differ substantially, if we compare them to locations in the same town. Regarding their small contribution to mass, UFP are not adequately measured with methods based on measuring particle mass. Besides, routine measurements are carried out only on few locations in the world.

UFP studies are founded on various measuring methods for the presence of these particles in ambient air. Most frequently they measured the numerical concentration (number of particles on air volume). Besides, the presence of UFP is in close correlation with other pollutants at burning processes as are carbon monoxide and nitrogen oxide. These correlations need to be considered when evaluating the exposure to sources as are traffic and of course at planning epidemiologic research and the interpretation of results. When we define the exposure of the population on basis of the results given by the central measuring points, the probability for a false evaluation of UFP-exposure is high – considering also that this is the most frequent approach in epidemiologic studies which research the consequences of long-term exposure to PM_{2.5} and other pollutants. Despite the high areal variability of UFP, the concentrations which were measured on various points, show a certain

connectivity over time, as the patterns of increase and decrease of concentrations during the day are alike in different locations.

We have monitored slightly moderate time correlations between the numeric concentrations of UFP, taken at the central measuring points and in housing environment and even in closed rooms in flats. The correlation was not always as strong as for PM_{2.5}, yet in some places it was enough to support epidemiologic studies on the influence of short-term fluctuations in the numeric concentration on human health. The fact that time variability of a numeric concentration of UFP is similar to other particles and to some cases of gaseous pollutants complicates a distinction between UFP-effects and health effects of other pollutants.

UFIREG (Ultrafine particles - An evidence based contribution to the development of regional and European environment)

For now we do not have any data on the consequences of a long-term exposure to UFP, that would be based on epidemiological research. The reason lies in the fact that epidemiologic studies which are dealing with long-term exposure are exploring geographical differences in exposure. As a difference to PM_{2.5} for UFP we do not have models on areal pollution expansion which could be used for defining areas of increased or decreased pollution which would enable us to carry out epidemiological research.

In July 2011 the project UFIREG, financed by the EU, started on this topic and it aims at establishing the characteristics of UFP-pollution in an urban environment and at researching the short-term influences of UFP of various sizes to the occurrence of illnesses and mortality. By the end of 2014 the experts in the field of air and environment pollution will define together with experts who research characteristics of illness occurrence in the population new findings in the field of UFP-pollution and the influence of this pollution to health and thus they will contribute to designing an appropriate European environmental policy within the so called programme Clean Air for Europe, which main aim is to prevent ambient air pollution. Also it is highly important that the public is informed with all dimensions of UFP-pollution of ambient air and with the health consequences of exposure to UFP, future decision-makers need to be aware of this and need to contribute to decrease ambient air pollution with these particles.

The classification of ultrafine particles in ambient air according to their quantity and size is carried out in five European cities: Dresden and Augsburg (Germany), Prague (Czech Republic), Ljubljana (Slovenia) and Chernivtsi (Ukraine). All measuring stations are set up in an urban environment. The points are not in the direct vicinity of highly frequented roads, yet they are representative of a substantial part of the city population. The measurements of ultrafine particles till now were never based on regulation law. The definition of the mass for fine dust (sizes PM₁₀ and PM_{2.5}) is not a suitable method for ultrafine particles because of the early mentioned small size and low mass. For airborne particles with a diameter of less than 1 micrometre a better indicator is to specify the number of particles on a unit of air (numeric concentration). With the appropriate measuring devices it is possible to specify the proportion of the particles by size. This means we can see how many particles of a specific

size are in one cubic centimetre of air. As a first step in the measuring equipment small particles of a size between 10 and 800 nanometres are charged up. Then these particles are classified according to different charge and diameter. The measurements are carried out constantly 24/7/365. Parallel to the measurement we conduct a monitoring of health consequences and the rate of admissions to hospitals and also the mortality due to respiratory and cardiovascular diseases. The linking of the data on health consequences and the rate of UFP-pollution will enable to conclude whether short-term exposure of UFP influences the degree of admissions to hospitals and the mortality rate caused by respiratory and cardiovascular diseases.

Conclusion

Fine particles are everywhere where people live. Mankind is producing it with its activities as are traffic, industry and residential heating. In recent years they represent a severe environmental problem, not only in Slovenia but also elsewhere in the world. UFP are due to their specific characteristics, e.g. capability of migrating from the lungs into blood and a higher oxidative potential due to their big area according to volume, more dangerous than bigger particles. Most frequently, here are mentioned effects on the respiratory and cardiovascular system and also in recent times effects on other organ systems. Although epidemiologic and toxicological research has revealed some important effects on human health further research is necessary in order to fully understand how ultrafine particle function.

For the purpose of science and research work we expect to receive data also within the UFIREG project which aims at studying the influence of UFP on the health of the exposed people.

Literature

1. Eržen I. et al. Zdravje in okolje: Izbrana poglavja. Maribor: Univerza v Mariboru, Medicinska fakulteta; 2010. [Health and environment: Selected chapters]
2. Oberdörster G. Pulmonary effects of inhaled ultrafine particles. *Int Arch Occup Environ Health* 2001; 74: 1-8.
3. HEI Perspectives 3 Understanding the Health Effects of Ambient Ultrafine Particles. HEI Review Panel on Ultrafine Particles 2013. Information gained on 30.05.2013 from the website: <http://pubs.healtheffects.org/getfile.php?u=893>
4. Donaldson K. Li XY. MacNee W. Ultrafine (nanometre) particle mediated lung injury. *J Aerosol Sci* 1998; 29(5-6): 553-60.
5. Penttinen P. et al. Number concentration and size of particles in urban air: effects on spirometric lung function in adult asthmatic subjects. *Environ Health Perspect* 2001; 109(4): 319-23.

6. Drašler B. Vpliv nanodelcev C60 in CoFe2O4 na umetne fosfolipidne membrane. Dipl. delo. Ljubljana, Univ. v Ljubljani, Biotehniška fakulteta, Odd. za biologijo, 2010. [Thesis: Influence of nanoparticles C60 and CoFE2O4 on artificial phospholipid membranes]
7. K Donaldson V Stone, A Clouter, L Renwick, W MacNee. Ultrafine particles. *Occup Environ Med* 2001; 58: 211-6.
8. Howard CV. Particulate Emissions and Health. Statement of Evidence. Proposed Ringaskiddy. Waste-to-Energy Facility Information gained on 30.05.2013 from the website: <http://www.durhamenvironmentwatch.org/Incinerator%20Health/CVHRingaskiddyEvidenceFinal1.pdf>
9. Harrison R. et al. Measurement of number, mass and size distribution of particles in the atmosphere. *Philos Trans R Soc A* 2000; 358: 2567–79.
10. Li N. et al. Ultrafine particulate pollutants induce oxidative stress and mitochondrial damage. *Environ Health Perspect*, 2003. 111(4): 455-60.
11. Wahlin P. et al. Pronounced decrease of ambient particle number emissions from diesel traffic in Denmark after reduction of the sulphur content in diesel fuel. *Atmospheric Environ* 2001; 35(21): 3549-52.
12. Donaldson K. Tran L. Jimenez LA. et al. Combustion-derived nanoparticles: A review of their toxicology following inhalation exposure. *Part Fibre Toxicol*. 2005 Oct 21; 2: 10.
13. Donaldson K. Stone V. MacNee W. The toxicology of ultrafine particles. In *Particulate matter: properties and effects upon health*. Editors Maynard RL. Howard CV. Oxford: BIOS Scientific Publishers; 199: 115-29.
14. Rückerl R. Schneider A. Breitner S. et al. Health effects of particulate air pollution: A review of epidemiological evidence. *Inhal Toxic* 2011; 23(10): 555-92.
15. Nel AE. Diaz-Sanchez D. Ng D. Hiura T. Saxon A. Enhancement of allergic inflammation by the interaction between diesel exhaust particles and the immune system. *J Allergy Clin Immunol* 1998; 102: 539-54.
16. WHO Regional Office for Europe. Review of evidence on health aspects of air pollution – REVIHAAP: First Results. Copenhagen: WHO; 2013a. Information gained on 30.05.2013 from the website: http://www.eurowho.int/_data/assests/pdf_file/0020/182432/e96762-final.pff