



Regional Deposition of Submicrometer Aerosol in the Human Respiratory System Determined at 1-s Time Resolution of Particle Size Distribution Measurements

Pasquale Avino^{1*}, Francesco Lopez², Maurizio Manigrasso¹

¹ *DIPIA, INAIL Settore Ricerca, via IV Novembre 144, I-00187 Rome, Italy*

² *Department of Agriculture Environment Food, University of Molise, via De Sanctis, I-86100 Campobasso, Italy*

ABSTRACT

Submicrometer aerosol size number distributions have been measured in downtown Rome with 1 s time resolution. From these data, the particle deposition in the human respiratory system has been assessed for infants, children and adults under different exercise levels. The estimates are reported as size segregated percentages and as total particle numbers deposited. The greatest percentages of particles are deposited in the alveolar interstitial region. Deposited doses, expressed per unit body weight or per unit alveolar surface area, indicate that children and infants are more at risk than adults. Following vehicle exhausts, nucleation particle concentrations increase within a few seconds and decrease in the time scale of tens of seconds. In accordance with traffic cycles, such particles are very common during the day, and decrease at night, when accumulation mode particles are more prevalent. As a consequence, the exposure scenario, in proximity to traffic, may be represented by a sequence of short-term peak exposures. The appraisal of such brief exposures depends on the time resolution of measurements, being underestimated if aerosol measurements are performed with resolutions on the time scale of minutes. The health relevance of such exposure patterns needs to be investigated, and the relevant measurement averaging time should also be defined.

Keywords: Ultrafine Particles; Submicrometer aerosol; FMPS; Respiratory system; Regional deposition.

INTRODUCTION

Among the different pollutants present in urban air (Monod *et al.*, 2001; Avino and Manigrasso, 2008), an important role is played by the urban aerosol (Avino *et al.*, 2000, 2002, 2003a, b; Lepore *et al.*, 2003; Avino and Manigrasso, 2006; Avino *et al.*, 2006; Avino and Manigrasso, 2007; Avino *et al.*, 2008; Movassaghi *et al.*, 2008; Manigrasso *et al.*, 2010). It can be classified in three modes: PM₁₀, PM_{2.5} and Ultrafine Particles (UFPs, particles with sizes less than about 100 nm). PM₁₀ and PM_{2.5} are well-known and studied as well whereas the data on the UFPs are very few. These particles derive from combustion and gas-to-particle conversion processes. UFPs can be further divided into nucleation mode particles (< 30 nm), formed directly from the gas/vapor phase and Aitken mode particles (30 nm < dp < 100 nm) that have aged and grown somewhat. UFPs can grow into accumulation-mode, by coagulation and condensation of low volatility compounds.

Recently, several studies on aerosol particle number

concentrations and size distribution have been published (Manigrasso *et al.*, 2009; Fanizza *et al.*, 2010; Avino *et al.*, 2011; Manigrasso and Avino, 2012) evidencing that particles in the ultrafine size range (< 100 nm) pose special problems to the lungs due to their high efficiency of deposition. Several epidemiological studies have shown associations among ambient ultrafine particles and human respiratory or cardiovascular diseases (Delfino *et al.*, 1998; Donaldson *et al.*, 2001; Peters *et al.*, 2001; Von Klot *et al.*, 2002; Brook *et al.*, 2002; Avino *et al.*, 2004; Avino and Brocco, 2004; Petraccia *et al.*, 2005; Dominici *et al.*, 2006; Simkhovich *et al.*, 2008; Oliva *et al.*, 2010). High UFPs deposition efficiency in the pulmonary region was demonstrated in healthy subjects (Brown *et al.*, 2002) and an increased deposition was observed in patients with asthma (Delfino *et al.*, 1998; Von Klot *et al.*, 2002) or chronic obstructive lung disease (Brown *et al.*, 2002; Avino *et al.*, 2004; Petraccia *et al.*, 2005; Dominici *et al.*, 2006). The health relevance of short-time peak exposures is an issue of particular attention especially in urban areas due to the fast-changing characteristics of urban aerosols (Zhang and Wexler, 2004). The importance of particle dimensions is emphasized by many recent studies (Michaels and Kleinman, 2000; Donaldson *et al.*, 2001) focusing their attention on Ultra Fine Particles (UFPs < 0.1 µm). UFPs penetrate efficiently into the respiratory system and are capable of translocating from the airways into the

* Corresponding author.

Tel.: +39 06 97893035; Fax: +39 06 97893004

E-mail address: p.avino@inail.it

blood circulation (Oberdörster, 2000).

Within this context, the aim of this study is the assessment of the exposure of human population to submicrometer aerosol in an urban environment. To such purpose, we have carried out aerosol measurements fulfilling two fundamental requisites: the first is size resolution, since the deposition of particles into the human respiratory system is strictly related to their dimensions, the second is time resolution, comparable with the time scale of variation of aerosols deriving from combustion exhausts.

MEASUREMENTS AND METHODS

Aerosol Measurements

A set of measurements was performed to study the size number distribution of submicrometer aerosol and its fast evolution peculiarities in urban area. These data have been used to estimate the particle deposition in the respiratory tract of different subjects exposed. Aerosol size number distributions were measured by means of a TSI Fast Mobility Particle Sizer (model 3091, FMPS, Shoreview, MN, USA). The instrument counts and classifies particles, according to their electrical mobility, in 32 size-channels, in the range from 5.6 to 560 nm, with 1 s time resolution.

The aerosol measurements were carried out at the ISPESL's Pilot Station in downtown Rome (near S. Maggiore Cathedral). The site (41°53'46''N, 12°29'46''E) is located in an area characterized by high density of automotive traffic, in a narrow double lane street (street width, *W*, of about 8 m), with high buildings on the sides (average height, *H*, of about 25 m). Such street can be considered a street canyon, as the aspect ratio *H/W* is about 3:1.

Number of Deposited Particles

Particle regional deposition in human respiratory tract estimates have been carried out using 1 h aerosol concentration data, on a weekday, during the morning traffic peak hour. Estimates have been carried out with the deposition model of International Commission on Radiological Protection (ICRP, 1994). All the methodology along with relative literature is deeply reported and described in two previous papers (Manigrasso and Avino, 2012; Manigrasso *et al.*, 2013). Briefly, the ICRP model was published 1994 in Human Respiratory Tract Model for Radiological Protection, ICRP publication 66. In this model the respiratory tract is divided into five parts, the anterior nasal passages ET1, all the other extrathoracic airways ET2, the trachea bronchi BB, the bronchioles bb and the alveolus (AI). In the model each part of the respiratory tract is represented by a filter and each breath is modeled by a tidal airflow. The filters are described by two parameters, their volume and their efficiency for removing particles. The deposition of aerosol particles is derived from the combined effect of settling, impaction and diffusion in the modelled airways. The effect of settling is calculated from the physical airway dimensions as is the effect of diffusion in the conducting and respiratory bronchioles and the alveoli, where the airflow is laminar. In the bronchial airways where the flow is more complex the calculated diffusion is corrected

empirically for the increased particle deposition observed in hollow airway casts under realistic flow conditions. The effect of impaction is based on empirical observation in hollow casts of the human bronchi. On inhalation a successively smaller fraction of inhaled air passes through each filter and on exhalation the volume of air returning through each filter equals the volume that passed on inhalation. Particle number deposition data are reported as the total particles deposited in a 1 h exposure in each anatomical region of respiratory tract.

So, the ICRP morphometric model divides the respiratory system in five anatomical regions. Two regions constitutes the extrathoracic airways: one is the anterior nasal passages (ET1) and the other includes the posterior nasal passages, the naso- and oropharynx and the larynx (ET2). Three regions represent the thoracic airways: the bronchial (BB), the bronchiolar (bb) and the alveolar interstitial (AI) regions. The filtration efficiency (η) of each region is described by the equation

$$\eta = 1 - \exp(-aR^p) \quad (1)$$

where *a* and *p* are parameters and *R* is a function of both volumetric flow rate and particle diameters.

The particle diameters are the aerodynamic (inertial deposition and gravitational settling) and the thermodynamic (equivalent volume diameter, d_{ve} , for Brownian deposition) diameters.

FMPS measurements furnish aerosol concentrations as function of electrical mobility diameters (d_m). Thus, conversion from d_m to d_{ve} has been performed with the equations (DeCarlo *et al.*, 2005)

$$\frac{d_m}{C(d_m)} = \frac{d_{ve} \times \chi}{C(d_{ve})} \quad (2)$$

$$C(d) = 1 + \frac{2}{\lambda d} \left[1.142 + 0.058 \exp\left(\frac{-0.999}{2\lambda/d}\right) \right] \quad (3)$$

where *C*(*d*) is the Cunningham slip correction factor, λ is the mean free path of gas molecules, that is about 0.065 μm for normal temperatures and pressures, χ is the dynamic shape factor. The following values of χ have been used on combustion generated soot aerosols (Slowik *et al.*, 2004; Park *et al.*, 2004; Manigrasso *et al.*, 2013): $\chi = 1$ ($d_m = 6\text{--}50$ nm); $\chi = 1.5$ ($d_m = 50\text{--}100$ nm); $\chi = 1.7$ ($d_m = 100\text{--}150$ nm); $\chi = 2$ ($d_m = 150\text{--}200$ nm); $\chi = 2.5$ ($d_m = 200\text{--}520$ nm).

RESULTS AND DISCUSSION

Ultrafine Particle Determination in Downtown Rome

The starting point of this study was to define what the relevant part of aerosol and its measure to be in Rome considering that in such urban area combustive sources represent the main contributors to submicrometric aerosol (Manigrasso *et al.*, 2009; Fanizza *et al.*, 2010; Avino *et al.*, 2011). The Fig. 1 shows the typical particle size

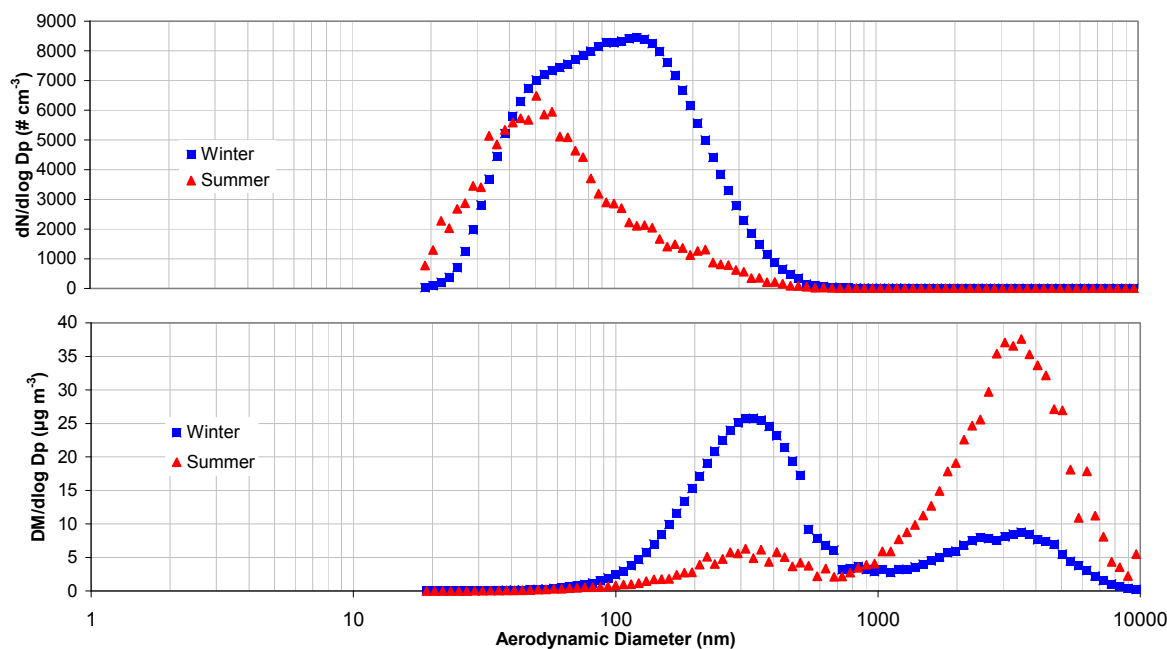


Fig. 1. Average size distributions expressed as number and mass in winter and summer periods. Data obtained using SMPS and APS.

distributions during winter and summer periods in downtown Rome expressed as numerical and mass determinations (determinations performed by means of Scanning Mobility Particle Sizer, SMPS, and Aerodynamic Particle Sizer, APS, TSI).

Firstly, it can be seen how the *fine* mode (fraction $< 2.5 \mu\text{m}$) is described by a distribution below $1 \mu\text{m}$. This suggests that it is appropriate to measure the PM_{10} compared to $\text{PM}_{2.5}$ as a descriptor of the *fine* mode (PM_{10} explains a significant and notable portion of $\text{PM}_{2.5}$). Basically the particles in excess of 500–600 nm have a negligible influence on the distribution if expressed on a numerical basis, while if we refer to the concentrations in mass, they have a considerable importance not only in the accumulation mode but also, and especially, in the *coarse* mode.

The number size distribution of the *fine* mode has a maximum aerodynamic diameters lower in summer. The explanation is searchable in the greatest contribution in the summer due to photochemical processes leading to the formation of particles from the gas phase. However, on mass basis, maximum aerodynamic diameter value in the coarse mode are at about $3 \mu\text{m}$ both in winter and in summer: the shape of the coarse mode is heavily influenced by dust mass transport from Sahara that occurred in both seasons (Manigrasso et al., 2012).

Fig. 2 shows another example of mean distribution of measurements with resolution time of 5 minutes, making a distinction between working days and weekends. In particular, looking at the Fig. 2(b) where the particle cumulative concentrations are reported, the particle concentration is less (about $25000 \#/\text{cm}^3$) during the week ends whereas during the work days they are about $35000 \#/\text{cm}^3$ following the trend related to the cycles of the traffic. In a previous paper (Avino et al., 2011) we described

extensively the temporal evolution of particle number size distribution in downtown Rome using 1 Hz resolution FMPS data points. Briefly resuming, three intense modes in the 10–30 nm range, are present during rush traffic hours whereas a fourth mode at about 100 nm is preeminent when traffic levels were very low because of removal processes.

Fig. 3 shows the information that can be derived from a measurement performed by a time resolution of 1 s. Data obtained using a FMPS, show the total particle number from 6 to 520 nm and the channels at 10 nm and 45 nm. For comparison the total particle numbers (6–523 nm) averaged over a period of 5 minutes, have also shown. It is evident that within few seconds an abrupt numerical concentration increase occurs, approximately an order of magnitude. The intensity of this episode is considerably reduced on the average of 5 minutes and most likely it would be unnoticed with a measure based on scanning technique. It is not possible to observe phenomena articulated by sampling the relevant signal with a frequency of one datapoint per minute or even lower (e.g., every 5 min). Fig. 4 shows and underlines such information. In fact, the blue curve describes a trend measured every second: it can be seen how Geometric Mean Diameter (GMD) collapses twice within few seconds. The two episodes have a duration of about 1.5–2 minutes: with measurements taken every 5 minutes, these episodes are virtually lost. It is also noted that a GMD reduction involves a contribution increase of the particles with lower diameters that are numerically the most relevant ones.

Particles undergo transformations that lead to the modifications of the size distribution curves, in particular the nucleation mode disappears or becomes a minor component. The implications of such time scale on the particle deposition into the human respiratory tract are fundamental and will be discussed in the next section.

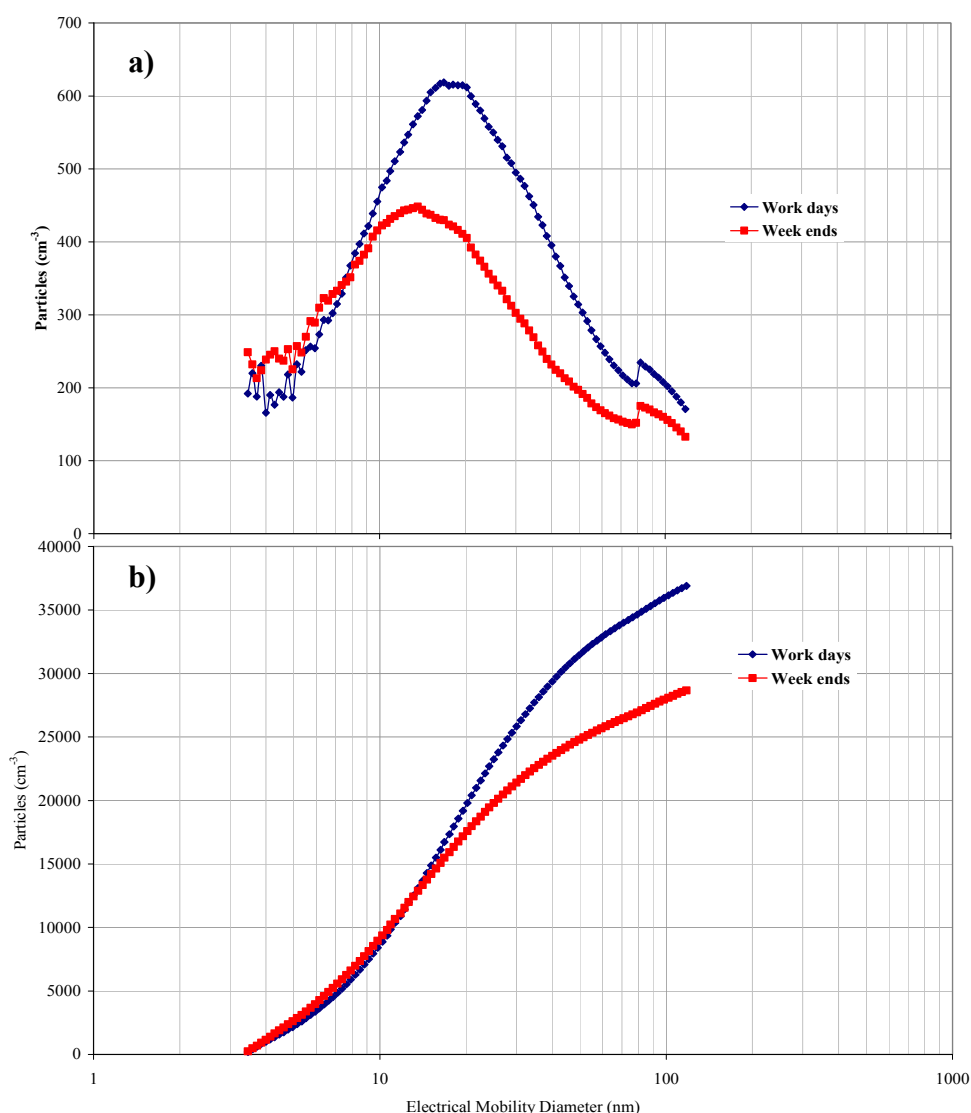


Fig. 2. Average dimensional distribution expressed as number and mass during weekends and work days (resolution time 5 min) (April–May, 2012).

Regional Particle Deposition in the Respiratory System

The number of particles deposited in the five regions of the ICRP deposition model are reported in Fig. 5(a), for 3 months old infants, 1 and 5 years children, adult males and females, performing light exercise.

Due to their higher ventilation rates (Table 1), by far, more particles are deposited in the respiratory systems of adults, in comparison with infants and children (1 and 5 y). However, children have lower body weight (bw) and smaller lungs than adults, consequently, a given fixed dose of deposited particles may elicit increased toxicity in children than in adults. We can assume average body weights of 87 kg for 30–40 y males, 74.8 kg for 30–40 y females, 5.9 kg for 1–3 months infants, 9.2 kg for 6–12 months infants and 18.6 kg for 3–6 years children (US EPA, 2009). Then, if calculated for unit bw (Fig. 5(b)), for the same PM concentration the total doses of particles deposited in the respiratory systems of infants and children are about twice as much as in adults.

Activity level is an important parameter for determining the dose of aerosol deposited in the respiratory tract. ICRP (1994) considers two exercise levels for adults: 1/3 (light exercise) of the maximum workload completed (W_{\max}) and 2/3 (heavy exercise) of W_{\max} (Godfrey *et al.*, 1971). As a result of increasing workload from light to heavy, ventilation rate increases from 1.5 to 3.0 m³/h and from 1.25 to 2.7 m³/h, respectively in adult males and females. Consequently, total deposited particles increase of 85% and 98%, respectively in males and females (Fig. 5(c)). The main contribution to such increments is due to the alveolar-interstitial region (Fig. 5(c)).

Fig. 6 compares the % particle regional deposition as a function of particle sizes, in adult females performing light exercise (the curves for adult males are substantially similar) with infants 3 months old, sleeping or under light exercise condition. In all cases, the major share of % particle deposition occurs in the AI regions, although some differences are observed. AI % depositions are lower in

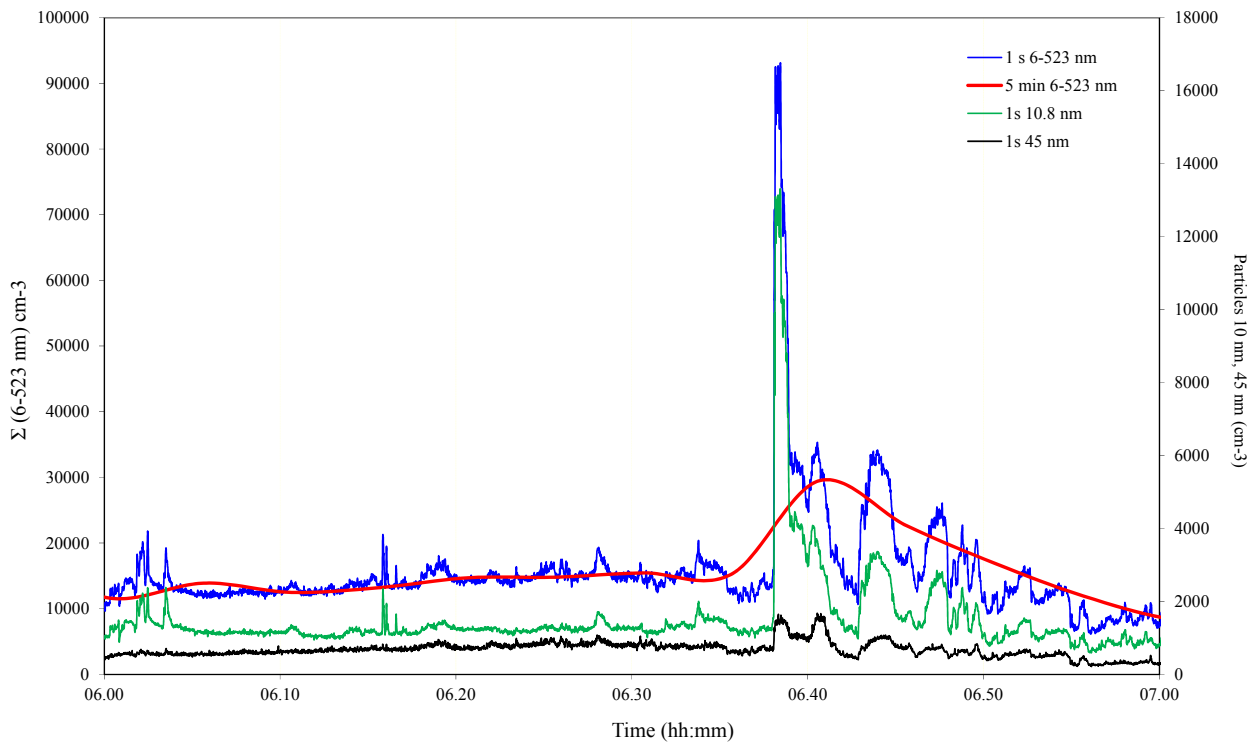


Fig. 3. Comparison of measurements performed at fast (1 s) time resolution (green, blue and black lines) and the relative 5 min-average trend (red line).

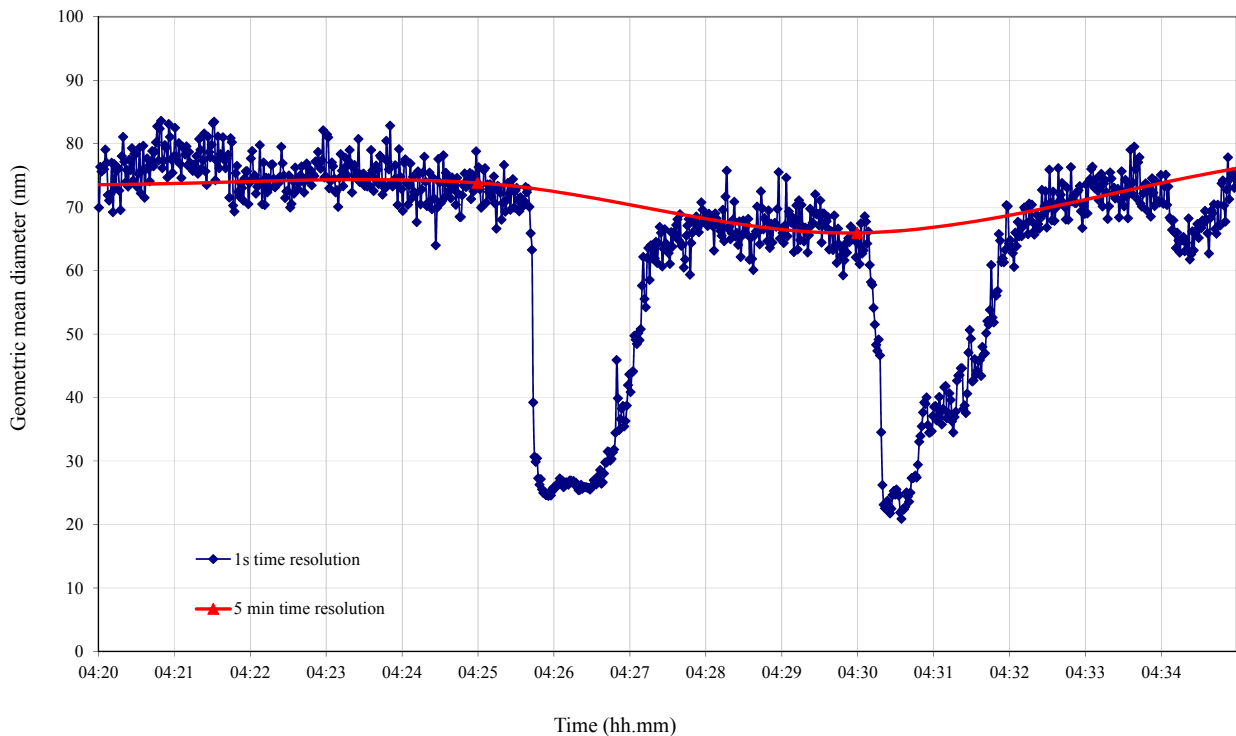


Fig. 4. Evolution of submicrometer aerosol number geometric mean diameter (GMD) described by measurements at 1 s resolution time (blue line) and averaged every 5 min (red line).

infants than in adults, while the contribution due to the bronchiolar region is higher. For small particle size, the main contribution in infants comes from the bb region, with

a cross-over point of the AI and bb curves that is higher in the sleeping (about 13 nm) than in the light exercise (about 9 nm) condition.

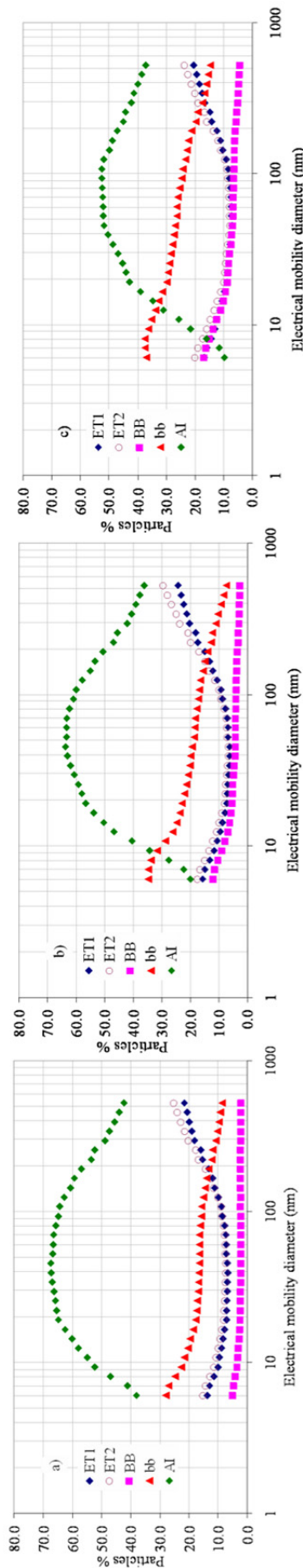
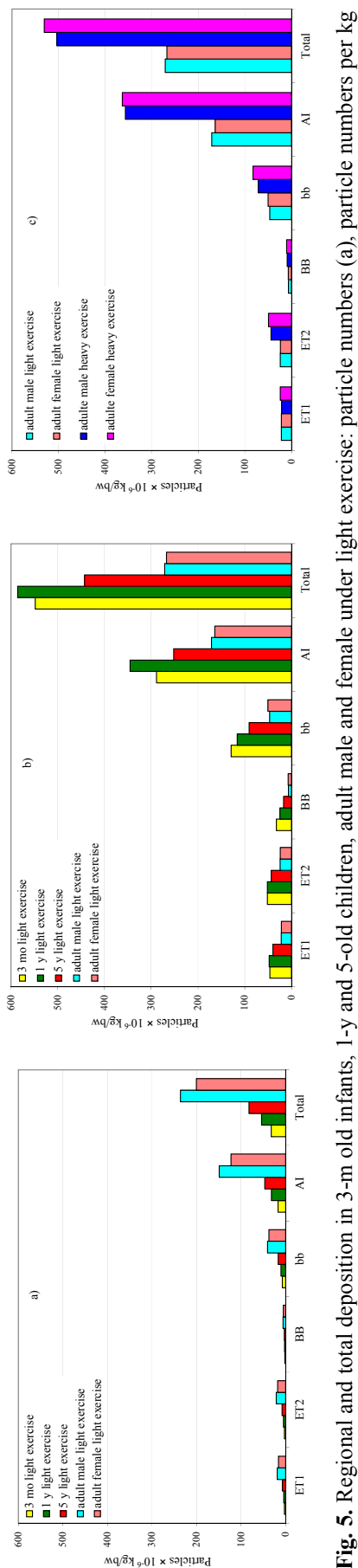


Table 1. Anatomical and physiological parameters for the subjects considered (Caucasian, nasal augmenters). Light Exercise (LE), Heavy Exercise (HE), Functional residual capacity (FRC); Extratoracic, Bronchial and Bronchiolar dead spaces ($V_{D(ET)}$, $V_{D(BB)}$, $V_{D(bb)}$); Scaling factors for ET and BB (SF_t , SF_b) and AI regions (SF_a); Ventilation rate (B); Tidal volume (V_T); Volumetric flow rate (V_{fr}); Fraction breathed through the nose (F_n).

	Adult male		Adult female		Infant 3 mo	Child 1y	Child 5y	
	LE	HE	LE	HE	Sleeping	LE	LE	
FRC (cm^3)	3301	3301	2681	2681	148	148	244	767
$V_{D(ET)}$ (cm^3)	50	50	40	40	2.6	2.6	4.7	13.3
$V_{D(BB)}$ (cm^3)	49	49	40	40	4.5	4.5	6.8	15.5
$V_{D(bb)}$ (cm^3)	47	47	44	44	6.8	6.8	8.7	16.7
SF_t	1	1	1.08	1.08	2.68	2.68	2.20	1.55
SF_b	1	1	1.04	1.04	1.67	1.67	1.55	1.30
SF_a	1	1	1.07	1.07	2.58	2.58	2.30	1.63
B (m^3/h)	1.5	3	1.25	2.7	0.09	0.19	0.15	0.24
V_T (cm^3)	1250	1920	992	1364	39	66	74	174
V_{fr} (cm^3/s)	833	1670	694	1500	50	106	83	133
F_n	1	0.5	1	0.5	1	1	1	1

The results of several studies in which rats were exposed to particles of different-sizes (15–20 nm, 80 nm, 0.5 μm , 3 μm , 10 μm) indicate that nanoparticles inhaled and deposited as singlets in the alveolar space are not as efficiently phagocytised by alveolar macrophages as occurs for larger particles (Oberdörster *et al.*, 2005). UFPs, rather interact with epithelial cells and translocate to the interstitium (Oberdörster, 2000). From the pulmonary interstitial sites, particles can translocate to the blood circulation on a way dependent on their size (nanoparticles are favored), charge and surface coating (Oberdörster *et al.*, 2005; Nemmar *et al.*, 2002). Once in blood circulation, particles can directly affect the cardiovascular system (Peters *et al.*, 2001; Brook

et al., 2002; Simkhovich *et al.*, 2008) and can be distributed to other organs (Takenaka *et al.*, 2001; Oberdörster *et al.*, 2002). For particles deposited in the AI region, their number per unit alveolar surface may represent a more suitable metric, than per unit body weight. Estimates of alveoli present at birth vary widely from 17 to 71 million, with a mean of about 55 million. This value in the adult lung varies from 200 to 600 million. At birth, the alveolar surface area is approximately 3 m^2 ; while in adults, the alveolar surface area is 75 m^2 (Clewell *et al.*, 2002).

Considering such values of alveolar surface area, Fig. 7 compares particle depositions in the AI region for adult males and infants, under light exercise condition.

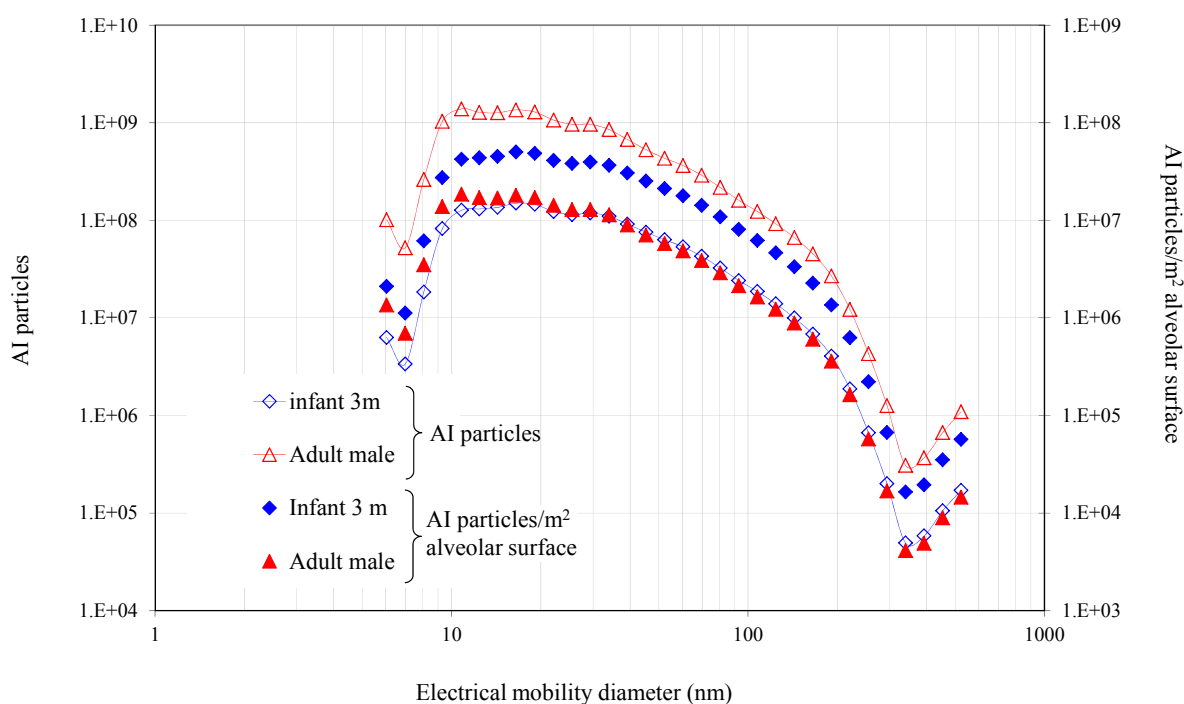


Fig. 7. Alveolar interstitial deposition: a) particle number (\diamond) and particle number per m^2 alveolar surface area (\blacklozenge) for 3-month infants; b) particle number (Δ) and particle number per m^2 alveolar surface area (\blacktriangle) for adult males.

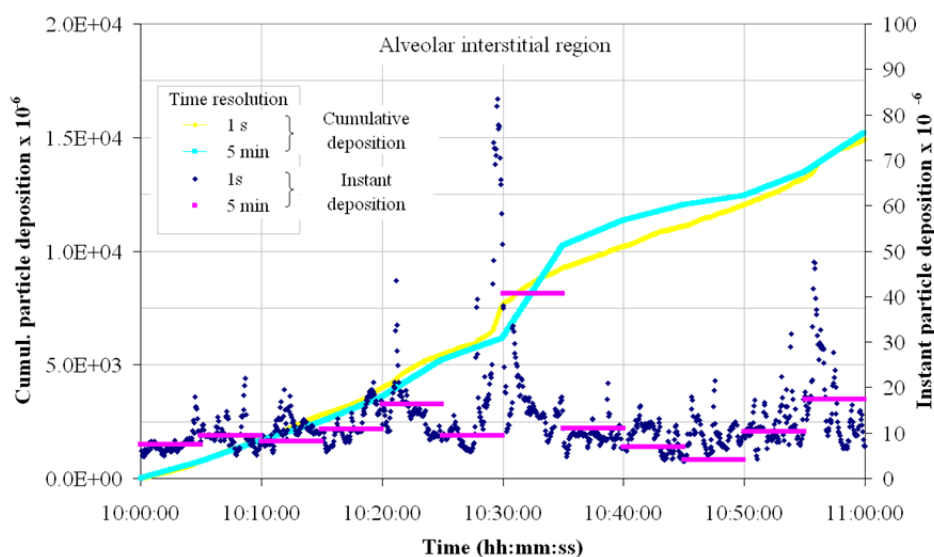


Fig. 8. Cumulative and instant AI particle deposition for an adult male under light exercise (1s vs 5 min time resolution).

It can be seen that, even if the number of deposited particles is greater in adults than in infants (from 6 to 16 times, depending on particle size), are infants that receive a greater dose per unit alveolar surface area (from 1.5 to 4 times). Moreover, this occurs in a critical period of lung development, that, on the ground of limited experimental and epidemiologic studies, has been addressed, as a window of high susceptibility for lung damage created by exposure to environmental toxicants (Gauderman *et al.*, 2002; Finkelstein and Johnston, 2004; Soto-Martinez and Sly, 2010). Such effects have been considered irreversible by some authors (Plopper and Fanucchi, 2000).

In urban areas, a sequence of short term peak exposures to vehicle exhaust is a recurrent scenario for people spending long periods in streets or driving in the traffic. Epidemiological studies have addressed the adverse effects on health of short duration exposures to high particle concentrations (Delfino *et al.*, 1998; Michaels and Kleinman, 2000; Peters *et al.*, 2001; Brook *et al.*, 2002). Hence, the importance of time resolution of aerosol measurements, particularly in urban environment, due to the fast changing characteristic of traffic aerosol. How such feature reflects into the respiratory exposure pattern is shown in Fig. 8 reporting the particle deposition in the Alveolar Interstitial (AI) region for an adult male under light exercise, estimated with 1 s and 5 min time resolution aerosol concentration data. Cumulative particle deposition at the end of 1 h exposure is almost the same with the two datasets. However, short-time peak exposures are clearly underestimated with 5 min time resolution data. Thus the need arise to assess the health relevance of such exposure pattern, whether there is any difference in receiving the same aerosol daily dose, with or without peak exposures.

ACKNOWLEDGMENTS

This work was supported by INAIL under the grants P20L09 and P20L01.

REFERENCES

- Avino, P., Brocco, D., Lepore, L. and Ventrone, I. (2000). Distribution of Elemental Carbon (EC) and Organic Carbon (OC) in the Atmospheric Aerosol Particles of Rome. *J. Aerosol Sci.* 31: S364–S365.
- Avino, P., Brocco, D., Cecinato, A., Lepore, L. and Balducci, C. (2002). Carbonaceous Components in Atmospheric Aerosol: Measurements Procedures and Characterization. *Ann. Chim.* 92: 333–341.
- Avino, P., Brocco, D., Pareti, S. and Scalisi, G. (2003a). Description of the Carbonaceous Particulate Matter Evolution in an Urban Area. *Ann. Chim.* 93: 21–26.
- Avino, P., Brocco, D., Lepore, L. and Pareti, S. (2003b). Interpretation of Atmospheric Pollution Phenomena in Relationship with the Vertical Atmospheric Remixing by means of Natural Radioactivity Measurements (Radon) of Particulate Matter. *Ann. Chim.* 93: 589–594.
- Avino, P., De Lisio, V., Grassi, M., Lucchetta, M.C., Messina, B., Monaco, G., Petracchia, L., Quartieri, G., Rosentzweig, R., Russo, M.V., Spada, S. and Valenzi, V.I. (2004). Influence of Air Pollution on Chronic Obstructive Respiratory Diseases: Comparison between City (Rome) and Hillcountry Environments and Climates. *Ann. Chim.* 94: 629–636.
- Avino, P. and Brocco, D. (2004). Carbonaceous Aerosol in the Breathable Particulate Matter (PM₁₀) in Urban Area. *Ann. Chim.* 94: 647–653.
- Avino, P. and Manigrasso, M. (2006). Vertical Distribution of Carbonaceous Material in Urban Atmosphere. *Fresenius Environ. Bull.* 15: 866–877.
- Avino, P., Capannesi, G. and Rosada, A. (2006). Characterization and Distribution of Mineral Content in Fine and Coarse Airborne Particle Fractions by Neutron Activation Analysis. *Toxicol. Environ. Chem.* 88: 633–647.
- Avino, P. and Manigrasso, M. (2007). Caratterizzazione della Frazione Carboniosa dell'inquinamento Particellare nell'area Urbana di Roma. Parte I. *Med. Lav.* 98: 192–

- 203.
- Avino, P. and Manigrasso, M. (2008). Ten-year Measurements of Gaseous Pollutants in Urban Air by an Open-Path Analyser. *Atmos. Environ.* 35: 4138–4148.
- Avino, P., Capannesi, G. and Rosada, A. (2008). Heavy Metal Determination in Atmospheric Particulate Matter by Instrumental Neutron Activation Analysis. *Microchem. J.* 88: 97–106.
- Avino, P., Casciardi, S., Fanizza, C. and Manigrasso, M. (2011). Deep Investigation of Ultrafine Particles in Urban Air. *Aerosol Air Qual. Res.* 11: 654–663.
- Brook, R.D., Brook, J.R., Urch, B., Vincent, R., Rajagopalan, S. and Silverman, F. (2002). Inhalation of Fine Particulate Air Pollution and Ozone Causes Acute Arterial Vasoconstriction in Healthy Adults. *Circulation* 105: 1534–1536.
- Brown, J.S., Zeman, K.L. and Bennett, W.D. (2002). Ultrafine Particle Deposition and Clearance in the Healthy and Obstructed Lung. *Am. J. Respir. Crit. Care Med.* 166: 1240–1247.
- Clewell, H.J., Teeguarden, J., McDonald, T., Sarangapani, R., Lawrence, G., Covington, T., Gentry, R. and Shipp, A. (2002). Review and Evaluation of the Potential Impact of Age- and Gender-specific Pharmacokinetic Differences on Tissue Dosimetry. *Crit. Rev. Toxicol.* 32: 329–389.
- DeCarlo, P.F., Slowik, J.G., Worsnop, D.R. and Davidovits, P. (2005). Particle Morphology and Density Characterization by Combined Mobility and Aerodynamic Diameter Measurements. Part 1: Theory. *Aerosol Sci. Technol.* 38: 1185–1205.
- Delfino, R.J., Zeiger, R.S., Seltzer, J.M. and Street, D.H. (1998). Symptoms in Pediatric Asthmatics and Air Pollution: Differences in Effects by Symptom Severity, Anti-Inflammatory Medication Use and Particulate Averaging Time. *Environ. Health Perspect.* 106: 751–761.
- Dominici, F., Peng, R.D., Bell, M.L., Pham, L., McDermott, A., Zeger, S.L. and Samet, J.M. (2006). Fine Particulate Air Pollution and Hospital Admission for Cardiovascular and Respiratory Diseases. *J. Am. Med. Assoc.* 295: 1127–1134.
- Donaldson, K., Stone, V., Seaton, A. and MacNee, W. (2001). Ambient Particle Inhalation and the Cardiovascular System: Potential Mechanisms. *Environ. Health Perspect.* 109: 523–527.
- Fanizza, C., Casciardi, S., Avino, P. and Manigrasso, M. (2010). Measurements and Characterization by Transmission Electron Microscopy of Ultrafine Particles in the Urban Air of Rome. *Fresenius Environ. Bull.* 19: 2026–2032.
- Finkelstein, J.N. and Johnston, C.J. (2004). Enhanced Sensitivity of the Postnatal Lung to Environmental Insults and Oxidant Stress. *Pediatrics* 113: 1092–1096.
- Gauderman, W.J., Gilliland, G.F., Vora, H., Avol, E., Stram, D., McConnell, R., Thomas, D., Lurmann, F., Margolis, H.G., Rappaport, E.B., Berhane, K. and Peters, J.M. (2002). Association between Air Pollution and Lung Function Growth in Southern California Children. Results from a Second Cohort. *Am. J. Respir. Crit. Care Med.* 166: 76–84.
- Godfrey, S., Davies, C.T.M., Wozniak, E. and Barnes, C.A. (1971). Cardio-Respiratory Response to Exercise in Normal Children. *Clin. Sci.* 40: 419–431.
- ICRP (1994). *Human Respiratory Tract Model for Radiological Protection*. International Commission on Radiological Protection (ICRP), Publication 66, Elsevier Science, Oxford, U.K.
- Lepore, L., Brocco, D. and Avino, P. (2003). Carbonio Organico e Carbonio Elementare nelle Particelle Atmosferiche. *Ann. Ist. Super. Sanità* 39: 365–369.
- Manigrasso, M., Avino, P. and Fanizza, C. (2009). Ultrafine Particles in the Urban Area of Rome. *Fresenius Environ. Bull.* 18: 1341–1347.
- Manigrasso, M., Abballe, F., Jack, R.F. and Avino, P. (2010). Time-resolved Measurement of the Ionic Fraction of Atmospheric Fine Particulate Matter. *J. Chromatogr. Sci.* 48: 549–552.
- Manigrasso, M. and Avino, P. (2012). Fast Evolution of Urban Ultrafine Particles: Implications for Deposition Doses in the Human Respiratory System. *Atmos. Environ.* 51: 116–123.
- Manigrasso, M., Febo, A., Guglielmi, F., Ciambottini, V. and Avino, P. (2012). Relevance of Aerosol Size Spectrum Analysis as Support to Qualitative Source Apportionment Studies. *Environ. Pollut.* 170: 43–51.
- Manigrasso, M., Stabile, L., Avino, P. and Buonanno, G. (2013). Influence of Measurement Frequency on the Evaluation of Short-Term Dose of Sub-Micrometric Particles during Indoor and Outdoor Generation Events. *Atmos. Environ.* 67: 130–142.
- Michaels, R.A. and Kleinman, M.T. (2000). Incidence and Apparent Health Significance of Brief Particle Airborne Excursions. *Aerosol Sci. Technol.* 32: 93–105.
- Monod, A., Sive, B.C., Avino, P., Chen, T., Blake, D.R. and Rowland, F.S. (2001). Monoaromatic Compounds in Ambient Air of Various Cities: a Focus on Correlations between the Xylenes and Ethylbenzene. *Atmos. Environ.* 35: 135–149.
- Movassaghi, K., Campanella, L. and Avino, P. (2008). The first investigation on PM₁₀ and SO₂ Levels in an Iranian Megacity, Isfahan, and a Relative Comparison with Rome. *Fresenius Environ. Bull.* 17: 786–792.
- Nemmar, A., Hoet, P.H.M., Vanquickenborne, B., Dinsdale, D., Thomeer, M., Hoylaerts, M.F., Vanbilloen, H., Mortelmans, L. and Nemery, B. (2002). Passage of Inhaled Particles into the Blood Circulation in Humans. *Circulation* 105: 411–414.
- Oberdörster, G. (2000). Toxicology of Ultrafine Particles: in vivo Studies. *Philos. T. Roy. Soc. B.* 358: 2719–2740.
- Oberdörster, G., Sharp, Z., Atudorei, V., Elder, A., Gelein, R., Lunts, A., Kreyling, W. and Cox, C. (2002). Extrapulmonary Translocation of Ultrafine Carbon Particles following Whole-Body Inhalation Exposure of Rats. *J. Toxicol. Environ. Health Part A* 65: 1531–1543.
- Oberdörster, G., Oberdörster, E. and Oberdörster, J. (2005). Nanotoxicology: an Emerging Discipline Evolving from Studies of Ultrafine Particles. *Environ. Health Perspect.* 113: 823–840.
- Oliva, G., Perri, F., Vernale, C., Galasso, V., Manigrasso,

- M., Fanizza, C., Bailardi, F., Pellegrini, A.L., Giannico, C. and Avino, P. (2010). Impact of Lachrymal Film's Alterations and Corneal Sensibility on Fine Particle Exposure. *Fresenius Environ. Bull.* 19: 2123–2132.
- Park, K., Kittelson, D.B. and McMurry, P.H. (2004). Structural Properties of Diesel Exhaust Particles measured by Transmission Electron Microscopy (TEM): Relationship to Mass and Mobility. *Aerosol Sci. Technol.* 38: 881–889.
- Peters, A., Dockery, D.W., Muller, J.E. and Mittleman, M.A. (2001). Increased Particulate Air Pollution and the Triggering of Myocardial Infarction. *Circulation* 103: 2810–2815.
- Petraccia, L., Maciullo, S.G., Grassi, M., Pace, A., Lucchetta, M.C., Valenzi, V.I., Avino, P. and Fraioli, A. (2005). Spa and Climate Therapy in Chronic Obstructive Pulmonary Diseases. *Clin. Ther.* 156: 23–31.
- Plopper, C.G. and Fanucchi, M.V. (2000). Do Urban Environmental Pollutants Exacerbate Childhood Lung Diseases? *Environ. Health Perspect.* 108: A252–A253.
- Simkhovich, B.Z., Kleinman, M.T. and Kloner, R.A. (2008). Air Pollution and Cardiovascular Injury Epidemiology, Toxicology, and Mechanisms. *J. Am. Coll. Cardiol.* 52: 719–726.
- Slowik, J.G., Stainken, K., Davidovits, P., Williams, L.R., Jayne, J.T., Kolb, C.E., Worsnop, D.R., Rudich, Y., DeCarlo, P.F. and Jimenez, J.L. (2004). Particle Morphology and Density Characterization by Combined Mobility and Aerodynamic Diameter Measurements. Part 2: Application to Combustion-Generated Soot Aerosols as a Function of Fuel Equivalence Ratio. *Aerosol Sci. Technol.* 38: 1206–1222.
- Soto-Martinez, M. and Sly, P.D. (2010). Relationship between Environmental Exposures in Children and Adult Lung Disease: the Case for Outdoor Exposures. *Chron. Resp. Dis.* 7: 173–186.
- Takenaka, S., Karg E., Roth, C., Schulz, H., Ziesenis, A., Heinzmann, U., Schramel, P. and Heyder, J. (2001). Pulmonary and Systemic Distribution of Inhaled Ultrafine Silver Particles in Rats. *Environ. Health Perspect.* 109: 547–551.
- US EPA (2009). *Exposure Factors Handbook*, External Review Draft July 2009 EPA/600/R-09/052A. United States Environmental Protection Agency, Washington, DC; <http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=209866>.
- Von Klot, S., Wölke, G., Tuch, T., Heinrich, J., Dockery, D.W., Schwartz, J., Kreylingz, W.G., Wichmann, H.E. and Peters, A. (2002). Increased Asthma Medication Use in Association with Ambient Fine and Ultrafine Particles. *Eur. Respir. J.* 20: 691–702.
- Zhang, K.M. and Wexler, A.S. (2004). Evolution of Particle Number Distribution near Roadways-Part I: Analysis of Aerosol Dynamics and Its Implications for Engine Emission Measurement. *Atmos. Environ.* 38: 6643–6653.

Received for review, June 8, 2013

Accepted, August 27, 2013