ULTRAFINE PARTICLE DEPOSITION IN HUMANS DURING REST AND EXERCISE

Christopher C. Daigle, David C. Chalupa, F. Raymond Gibb, Paul E. Morrow, Günter Oberdörster, Mark J. Utell, Mark W. Frampton

Departments of Medicine and Environmental Medicine, University of Rochester School of Medicine and Dentistry, Rochester, New York, USA

Ultrafine particles (diameter < 100 nm) may be important in the health effects of air pollution, in part because of their predicted high respiratory deposition. However, there are few measurements of ultrafine particle deposition during spontaneous breathing. The fractional deposition for the total respiratory tract of ultrafine carbon particles (count median diameter = 26 nm, geometric standard deviation = 1.6) was measured in 12 healthy subjects (6 female, 6 male) at rest (minute ventilation 9.0 ± 1.3 L/min) using a mouthpiece exposure system. The mean ± SD fractional deposition was 0.66 ± 0.11 by particle number and 0.58 ± 0.13 by particle mass concentration, similar to model predictions. The number deposition fraction increased as particle size decreased, reaching 0.80 ± 0.09 for the smallest particles (midpoint count median diameter = 8.7 nm). No gender differences were observed. In an additional 7 subjects (2 female, 5 male) alternating rest with moderate exercise (minute ventilation 38.1 ± 9.5 L/min), the deposition fraction during exercise increased to 0.83 ± 0.04 and 0.76 ± 0.06 by particle number and mass concentration, respectively, and reached 0.94 ± 0.02 for the smallest particles. Experimental deposition data exceeded model predictions during exercise. The total number of deposited particles was more than 4.5-fold higher during exercise than at rest because of the combined increase in deposition fraction and minute ventilation. Fractional deposition of ultrafine particles during mouth breathing is high in healthy subjects, and increases further with exercise.

Particulate air pollution has been associated with increased morbidity and mortality from respiratory and cardiac disease (Utell et al., 2002). Particles less than 100 nm (0.1 µm) in diameter (ultrafine particles, UFP) are ubiquitous in ambient particulate pollution (Riesenfeld et al., 2000), dominate particle number and surface area concentrations because of their small size, and may be important in contributing to these health effects (Utell &
High numbers of UFP are emitted by internal combustion processes, including both diesel and gasoline-powered engines. In recent measurements made on roads in Minnesota, UFP concentrations were recorded as high as $1 \times 10^7$ particles/cm$^3$ (Kittelson et al., 2001). Animal exposure studies suggest UFP induce more intense airway inflammation than similar mass concentrations of larger particles (Oberdörster et al., 1995), and epidemiological data suggest that exposure to ambient UFP worsens respiratory disease (Peters et al., 1997). Enhanced pulmonary effects of UFP may be caused in part by the predicted high total respiratory and alveolar deposition of UFP, relative to larger particles (Cassee et al., 2002). For example, the International Commission on Radiological Protection model predicts that more than 70% of 20 nm particles would be deposited during mouth breathing at rest (ICRP, 1994).

The predominant mechanism of deposition for particles smaller than about 500 nm is diffusion (Schulz et al., 2000). The probability of deposition by diffusion increases as the particle size decreases (Stuart, 1973; Kim, 2000). In comparison with larger particles, diffusional deposition should be favored in the distal airways and alveoli because reduced airflow increases residence time in these regions. Therefore, distal respiratory deposition of UFP in the range of 20 to 40 nm would be expected to exceed that of larger particles.

The effect of exercise on UFP deposition is more difficult to predict. During controlled breathing experiments in a laboratory setting, increasing tidal volume ($V_T$) with flow rates held constant increases deposition for all respirable particles, and increasing flow rates with tidal volume held constant decreases diffusional deposition. Studies of the deposition of 1000- to 5000-nm particles (reviewed in Schulz et al., 2000) have shown either increases or no change with exercise. During exercise, tidal volume increases to a greater degree than respiratory rate, which may favor diffusional deposition mechanisms. Determining the influence of exercise on UFP deposition is important in understanding UFP dosimetry, because particle intake rate may be increased more than six- to eightfold during exercise on the basis of increased minute ventilation alone. Children and adults exercising outdoors may therefore be at increased risk for adverse health effects from UFP exposure (Dockery et al., 1989).

Few human experimental data exist that test predictions of UFP deposition during spontaneous breathing. Several studies measured UFP deposition in humans (Anderson et al., 1990; Brown et al., 2002; Wilson et al., 1985; Jaques & Kim, 2000; Schiller et al., 1988; Roth et al., 1994) using brief periods of controlled breathing at rest. Jaques and Kim (2000) found that UFP deposition was higher in women than men for 40- and 60-nm particles. No studies have measured UFP deposition in humans during exercise. The National Research Council listed particle dosimetry as one of the 10 highest priority research needs for particulate air pollution (National Research Council, 1998).
The objectives were to assess the deposition of a polydisperse carbonaceous UFP aerosol in healthy human subjects at rest and during exercise, and to test the accuracy of model predictions for UFP deposition. We hypothesized that the total respiratory deposition of UFP increases with decreasing particle size, and that deposition increases further with exercise. We also examined gender differences in UFP deposition during spontaneous breathing.

METHODS

Subjects and Experimental Design

Subjects were 24 healthy never-smoking men and women aged 18–55 yr, with normal spirometry, without a recent respiratory infection. The Research Subjects Review Board of the University of Rochester approved the study, and informed written consent was obtained.

Two sets of exposure studies were performed. All exposures were by mouthpiece with a nose clip for 2 h, with a 10-min break off the mouthpiece after the first hour. In the first set of exposures (Series 1), subjects \( n = 12 \) were exposed to 10 µg/m\(^3\) UFP at rest. In the second set of exposures (Series 2), subjects were exposed to 10 and 25 µg/m\(^3\) UFP on separate occasions. Exposures included 15 min of moderate exercise (target minute ventilation 25 L/min/m\(^2\) body surface area) on a bicycle ergometer, alternating with 15 min at rest, with a total of 4 exercise periods. In the initial exposures in Series 2, usable data were available for 7 of the 12 subjects. We found in the first few subjects that measurements of expiratory particle concentrations were inaccurate because of pressure changes associated with the subject's breathing; repositioning of the expiratory sampling port resolved this problem. For Series 2, there were no significant differences in deposition measured at 10 µg/m\(^3\) and 25 µg/m\(^3\); therefore, data were averaged.

Exposure System

The exposures were undertaken within an environmental chamber in the General Clinical Research Center at the University of Rochester Medical Center. We chose a mouthpiece exposure system in order to facilitate accurate measurement of respiratory deposition, which is predicted to be predominantly tracheobronchial and alveolar for the particle sizes in this study (ICRP, 1994; Cassee et al., 2002). Details of particle generation and the mouthpiece exposure system have been described elsewhere (Chalupa et al., 2002).

Briefly, the design is a one-pass, dynamic-flow exposure system. Particles are generated into diluting air and, when breathed, pass through one-way rebreathing valves (Hans Rudolph Inc., Kansas City, MO) at the mouthpiece; exhaled particles and excess aerosol are removed via an exhaust system. Particles are continuously generated, and the exposure concentration is moni-
tered and regulated during the exposure. All tubing is electrically conductive with lengths minimized to avoid particle loss. Dilution air is filtered through charcoal and high-efficiency particle air filters. Particle mass in the intake diluting air is undetectable, with particle numbers ranging from 0 to 10 particles/cm³. Particles pass through a charge neutralizer after generation, in order to achieve Boltzman’s equilibrium. The ionized particles then enter a 28.4-L mixing reservoir. Particles in the reservoir enter the circuitry to the mouthpiece according to the demands of the subject. An overflow line exhausts the excess aerosol.

The flow rate into the mixing chamber on the inspiratory side of the system is 120 L/min. The intake supply flow rate is monitored with a Magnahelic pressure gauge (Dwyer Instruments, Inc., Michigan City, IN), calibrated using a dry test meter (Singer American Meter Company Division, Wellesley, MA). On the expiratory side of the subject, a resilient reservoir is loosely coupled to a dedicated filter and exhaust system. The system is designed to keep both sides of the non-rebreathing valves at atmospheric pressure, unaffected by the subject’s respiration. Tubing on the expiratory side is heated to ~37°C to avoid condensation. A pneumotachograph provides a respired air flow signal that is electronically integrated to obtain volumetric data.

Ultrafine carbon particles were generated from pure graphite electrodes by spark discharge in anhydrous argon, using a commercial generator (Palas Co., Germany). The generator settings were adjusted to provide a nominal particle count median diameter (CMD) of 26 nm, with lognormal volume median diameter of 54 nm and geometric standard deviation (GSD) of 1.6. To determine particle losses, a reciprocal pump was used to simulate respiration. A resting minute ventilation of 10 L/min was simulated using a volume of 800 ml at 12.5 cycles/min. Mild exercise (22 L/min) was simulated using a volume of 1200 ml at 18.3 cycles/min. Continuous upstream and downstream measurements of particle number and volume were determined for the whole system, and for a respiratory valve alone. Mass losses were calculated using particle volume determined by the electrostatic classifier. During exercise simulation, losses were 0% for particles of 23.7 nm midpoint diameter and larger; maximum losses were 3.9% for 7.5-nm particles. At resting conditions, maximum losses were 13.2% for 7.5-nm particles.

The subject inhaled from a mouthpiece and wore a nose clip. Condensation particle counters (model 3220a, TSI, Inc., St. Paul, MN; flow rate 300 ml/min; response time <1 s) and a scanning mobility particle sizer (model 3071, TSI, Inc., St. Paul MN; flow rate 2 L/min, scan time 10 min) determined particulate number, surface area, and volume concentrations of the inspired and expired aerosols. The exposure mass concentrations were 10 and 25 µg/m³. The mass concentrations were determined by the use of a tapered-element oscillating microbalance (TEOM, Rupprecht and Patachnick, Albany, NY). Electronic integration (HPChem Integrating Software, Hewlett Packard, MD) of a pneumotachographic airflow transducer (E for M Co., White Plains,
NY) on the expiratory limb provided continuous measurements of $V_T$, respiratory rate, and minute ventilation.

**Particle Deposition**

The total respiratory deposition fraction (DF) was calculated for both particle number and mass concentrations. Inspiratory and expiratory UFP number concentrations were measured continuously and recorded every 5 s during the exposure. Particle number concentration was then averaged for the periods at rest and exercise. Particle size distribution from the inspiratory circuit was determined before each exposure and just after the exposure was completed. Particle size distribution from the expiratory circuit was measured during one rest and one exercise period each hour. For computational simplicity, data on particle size distribution from the scanning mobility particle sizer were grouped into 12 particle size bins. Four size bins each contained less than 1% of the total expired particle number (midpoint diameters <8.7 and >64.9 nm), and these were excluded, leaving a total of 8 size bins with midpoint CMD from 8.7 to 64.9 nm (particle CMD ranging from 7.5 to 75.0 nm), which included more than 98% of the particles. The mean size-specific inspiratory particle concentration was determined by multiplying the average inspiratory number concentration by the percentage of particles in each size bin in the inspiratory circuit. The mean size-specific expiratory particle concentration was determined by multiplying the average expiratory number concentration by the percentage of particles in each size bin in the expiratory circuit. The correction factors for system losses were subtracted from the measured inspired concentrations and added to the measured expired concentrations. The number DF was then calculated by subtracting the corrected expiratory number concentration from the corrected inspiratory number concentration and dividing the difference by the corrected inspiratory number concentration.

The particulate mass DF was calculated as follows. Inspired and expired particle volume concentrations were determined for each size bin from the scanning mobility particle sizer data. The percentage of inspired and expired particles by volume per bin was determined by dividing each bin volume concentration by the total volume concentration (sum of individual bins). The mean expired mass concentration was calculated by multiplying the ratio of the total expired volume concentration to the total inspired volume concentration, times the measured (TEOM) inspired mass concentration. The inspired mass concentration for each bin was calculated as the product of the inspired volume percentage of particles in each bin and the mean inspired mass concentration from the TEOM. The expired mass concentration for each bin was the product of the expired volume percentage for each bin and the calculated overall expired mass concentration. These mass data were corrected for system losses by multiplying each bin by the loss correction factor for that bin, then subtracting that product from the inspired data and adding...
to the expired data. Finally, a loss-corrected DF was calculated as the loss-corrected inspired mass concentration minus the loss-corrected expired mass concentration, divided by the loss-corrected inspired mass concentration.

Theoretical total respiratory deposition fractions were calculated using three models: (1) International Committee for Radiological Protection (ICRP) (ICRP, 1994), (2) National Committee for Radiological Protection (NCRP, 1997), and (3) the multiple path particle deposition model (MPPDep, Version 1.11, July 1999, Chemical Industry Institute of Toxicology) (Cassee et al., 2002). For the MPPDep model, predictions were calculated for each subject using measured functional residual capacity (FRC), respiratory frequency, and $V_T$ at rest and exercise. Default values entered for all subjects were: mouth breathing, upper respiratory tract volume 50 ml, inspiratory:expiratory ratio 1:2, and nominal particle density = 1.5 g/cm$^3$. Model predictions for 26-nm particles were not affected by changes in particle density or inspiratory:expiratory ratio.

Data means were compared using the two-tailed Student’s $t$-test (Brown, 1980), with $p < .05$ denoting significance.

RESULTS

The gender and mean age and spirometric values of the subjects are shown in Table 1. Table 2 shows the mean $V_T$, respiratory frequency, and minute ventilation during the exposures. Resting $V_T$ and total lung capacity (TLC) were slightly smaller in women compared with men, but the ratio $V_T$/TLC did not differ between men and women. In Series 2, exercise led to a doubling of $V_T$ and a 50% increase in respiratory frequency, giving an approximately 3.3-fold increase in minute ventilation.

Figure 1 shows the particle size distribution for inspired and expired aerosols from one resting exposure in Series 1. The expired aerosol showed a very slight rightward shift of particle CMD. Table 3 shows the deposition data from Series 1 with the subjects at rest. The individual total DF by particle number ranged from 0.46 to 0.79. The highest deposition fraction was seen with the smallest particles. The DF fell as particle size increased up to 48.7 nm and then leveled off (Table 3). Figure 2 shows the DF for the 19 subjects in both Series 1 and 2 breathing at rest.

**TABLE 1.** Subject demographics

<table>
<thead>
<tr>
<th></th>
<th>Series 1 ($n = 12$)</th>
<th>Series 2 ($n = 7$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr), mean (range)</td>
<td>30 (18–52)</td>
<td>24 (18–33)</td>
</tr>
<tr>
<td>Male/female</td>
<td>6/6</td>
<td>5/2</td>
</tr>
<tr>
<td>FVC (L)$^a$</td>
<td>4.13 ± 0.91</td>
<td>5.05 ± 1.16</td>
</tr>
<tr>
<td>FEV1 (L)$^a$</td>
<td>3.61 ± 0.70</td>
<td>4.38 ± 0.91</td>
</tr>
<tr>
<td>FEV1/FVC$^a$</td>
<td>0.88 ± 0.04</td>
<td>0.87 ± 0.06</td>
</tr>
</tbody>
</table>

$^a$Mean ± SD. FVC: forced vital capacity. FEV1: forced expiratory volume in 1 s.
The deposition data for Series 2, at both rest and exercise, are shown in Table 4. The individual total number DF ranged from 0.55 to 0.66 at rest and 0.76 to 0.88 with exercise. The results at rest were similar to Series 1, and DF increased with exercise in all size bins. The DF by particle size again plateaued in the larger size bins with exercise (Table 4 and Figure 3).

No significant gender differences were found. In the first set of exposures with subjects at rest, the mean ± SD number DF was 0.68 ± 0.13 for men (n = 6) and 0.65 ± 0.12 for women (n = 6) (p = .70). The corresponding mass DFs were 0.60 ± 0.13 and 0.59 ± 0.14, respectively (p = .89). There were not

### Table 2. Breathing parameters

<table>
<thead>
<tr>
<th>Subjects</th>
<th>Tidal volume (L)</th>
<th>Respiratory frequency (breaths/min)</th>
<th>Minute ventilation (L/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Series 1 (rest)</td>
<td>12</td>
<td>0.58 ± 0.13</td>
<td>16 ± 2.8</td>
</tr>
<tr>
<td>Series 2 (rest)</td>
<td>7</td>
<td>0.60 ± 0.11</td>
<td>20 ± 2.4</td>
</tr>
<tr>
<td>Series 2 (exercise)</td>
<td>7</td>
<td>1.33 ± 0.35</td>
<td>29 ± 5.4</td>
</tr>
</tbody>
</table>

Note: Data are means ± SD.

FIGURE 1. Inspiratory (circles) and expiratory (triangles) particle size distribution for one subject from Series 1.
TABLE 3. Particle number deposition fraction by particle size in 12 healthy subjects at rest (Series 1)

<table>
<thead>
<tr>
<th>Midpoint diameter (range, nm)</th>
<th>Deposition fraction (mean ± SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>8.7 (7.5–10.0)</td>
<td>0.80 (± 0.09)</td>
</tr>
<tr>
<td>11.6 (10.0–13.3)</td>
<td>0.78 (± 0.08)</td>
</tr>
<tr>
<td>15.4 (13.3–17.8)</td>
<td>0.74 (± 0.09)</td>
</tr>
<tr>
<td>20.5 (17.8–23.7)</td>
<td>0.70 (± 0.12)</td>
</tr>
<tr>
<td>27.4 (23.7–31.6)</td>
<td>0.66 (± 0.13)</td>
</tr>
<tr>
<td>36.5 (31.6–42.2)</td>
<td>0.59 (± 0.13)</td>
</tr>
<tr>
<td>48.7 (42.2–56.2)</td>
<td>0.55 (± 0.14)</td>
</tr>
<tr>
<td>64.9 (56.2–75.0)</td>
<td>0.55 (± 0.13)</td>
</tr>
<tr>
<td>Total DF by particle number</td>
<td>0.66 (± 0.11)</td>
</tr>
<tr>
<td>Total DF by particle mass</td>
<td>0.58 (± 0.13)</td>
</tr>
</tbody>
</table>

FIGURE 2. Observed and predicted total respiratory deposition of ultrafine particles in 19 healthy subjects at rest from exposure Series 1 and 2. Particle deposition was calculated separately for eight particle size bins. Circles represent experimental data (mean ± SD); squares represent predicted deposition for these subjects at rest using the multiple path particle deposition model (MPPDep, Version 1.11, July 1999, Chemical Industry Institute of Toxicology). Solid and dashed lines represent predicted total respiratory deposition using the ICRP (1994) (habitual mouth breathing reference workers breathing at 1.2 m³/h, Table F.1, p. 416) and NCRP (1997) (sum of naso-oropharyngo-laryngeal, tracheobronchial, and pulmonary deposition, \( V_t \) 770 cm³, breathing frequency 13; Table 5.2, p. 68) models, respectively.
enough subjects in Series 2 to make gender comparisons; analysis of all 19 exposures at rest from both Series 1 and Series 2 again showed no significant gender difference.

The predicted overall DF was determined using three models. For the ICRP and NCRP models, input data were chosen to match our exposure conditions as closely as model parameters would allow. For the MPPDep model, respiratory and lung function data (including functional residual capacity, tidal volume, and respiratory frequency) were entered for each of the subjects in these studies. Figures 2 and 3 compare the experimental DFs with predictions using the MPPDep model. Overall, the models predicted very little increase in DF with exercise, and experimental data significantly exceeded model predictions during exercise (Figure 3). For example, using the MPPDep model for 26 nm particles, breathing at 18 breaths/min with a $V_T$ of 722 ml, the predicted total DF is 0.624. With 25 breaths/min and $V_T$ of 1680 ml, the predicted DF increases slightly to 0.650. The tracheobronchial DF decreases from 0.232 to 0.170, and the alveolar DF increases from 0.333 to 0.428.

Figure 4 compares the rest and exercise values for the number DF and total particle number deposition over a 1-h period. The combined effect of increased minute ventilation, and an increase in DF with exercise, increased particle number deposition more than 4.5-fold.

**DISCUSSION AND CONCLUSIONS**

This study represents the first measurements of respiratory UFP deposition during spontaneous breathing (on a mouthpiece), at rest and exercise. The data confirm the relatively high predicted respiratory deposition of UFP, with increasing deposition as particle size decreases. Deposition increased further with exercise, to a degree greater than that predicted by modeling.

Resting deposition in this study is in general agreement with the results obtained by Wilson et al. (1985). They measured the total respiratory deposi-
tion of five different size fractions from a polydisperse aerosol of bis(2-ethyl-hexyl) sebacate particles (CMD 40 nm; GSD 1.93). Five healthy men took 10 breaths of 1 L $V_T$ at 12 breaths per minute, by mouth. The mean ± SE deposition ranged from 0.71 ± 0.06 for 24-nm particles, to 0.37 ± 0.06 for 240-nm particles, consistent with model predictions. Jaques and Kim (2000) studied 20 males and 20 females who inhaled, by mouth, monodisperse sebacate UFP with count median diameters from 40 to 100 nm (GSD ~1.3). $V_T$ and respiratory flow rates were controlled during exposure. Deposition increased with increasing $V_T$ and decreased with increasing flow rates, as predicted (both large $V_T$ and low flow rates increase particle time in the lung and make deposition by diffusion more probable). The total DF of 40 nm particles, for subjects breathing at a flow rate of 250 ml/s, was 0.44 ± 0.07 for a $V_T$ of 500 ml, and 0.59 ± 0.07 for a $V_T$ of 750 ml, comparable to our own findings for particles with midpoint diameter of 36.5 nm (Series 1: 0.59 ± 0.13; Series 2: 0.58 ± 0.05).

Jaques and Kim reported a higher DF for women than men with inhalation of 40- and 60-nm particles, by 6 to 15%. This finding is likely to be related to the effects of controlled breathing. In contrast to the current study

![Graph](image-url)
in which breathing was spontaneous and data averaged over time, in the
Jaques and Kim study, $V_T$ was fixed for each subject, and was the same for
men and women. Although the authors found no correlation between indi-
vidual body size and particle deposition, the ratio $V_T/TLC$ was likely higher
for women than men during particle inhalation, because of the smaller
average TLC in women. This would be expected to increase particle resi-
dence time and therefore deposition for women under these conditions.

Brown et al. (2002) measured deposition and clearance of 33-nm Technegas
particles, inhaled by mouthpiece in healthy subjects and patients
with chronic obstructive pulmonary disease. Subjects reproduced their
spontaneous breathing pattern during inhalation on the mouthpiece. For
healthy subjects, tidal volume and minute ventilation were lower than in
our study (391 vs. ~590 ml, 5.83 vs. ~10 L/minute, respectively), and the
particle size dispersion was greater (GSD 1.7 vs. 1.6 for our study). Never-
thless, total respiratory deposition was comparable. Brown et al. found a
DF (based on differences in technetium-99m specific activity) of 0.54 ±
0.09, and our study found number DFs of 0.66 ± 0.11 nm (Series 1, Table
3) and 0.63 ± 0.03 (Series 2, Table 4). The higher DF in our studies is con-
sistent with the smaller particle size and narrower size distribution.

Data from the current study showed no significant gender differences,
with a slight trend toward lower DF in women (0.68 ± 0.13 for men, 0.65 ±
0.12 for women, $p = .70$). $V_T/TLC$ was similar for men and women. Our
data suggest that, in healthy subjects breathing spontaneously by mouth at

![Figure 4](https://example.com/figure4.png)

**FIGURE 4.** Particle number deposition fraction and total particle deposition at rest and exercise. Left panel shows the DF from all 19 subjects (Series 1 and 2) breathing at rest, and 7 subjects during exer-
cise (Series 2). Right panel shows the calculated total particle deposition over 1 h for 7 subjects in Series
2 completing both rest and exercise exposures to 25 µg/m$^3$ UFP.
rest, there are no clinically important gender-related differences in deposition of UFP. However, the limited statistical power of this study does not exclude the possibility of small gender-related differences.

In the present study during exercise, subjects increased $V_T$ and flow rates spontaneously in response to the demands of exercise. These changes would be expected to have opposing effects on deposition. We found that total respiratory number DF increased during exercise about 32% over resting measurements (Table 4). With exercise, measured values exceeded predicted values by about 22% for 26 nm particles (Figure 3). One possible explanation for the divergence of these experimental data from model predictions is turbulence. The increased flow demands during exercise will move the turbulence-to-laminar flow transition point distally, to smaller generation airways, enhancing deposition in those airways where laminar flow becomes turbulent. Prediction models do not account for the effects of increased turbulence in the airways during exercise. Further studies are needed to determine the effects of exercise on regional deposition of UFP, and the effects of varying exercise intensity.

To estimate UFP dose, total particle deposition was calculated using the deposition fraction, minute ventilation, and exposure time. For the 7 subjects studied at both rest and exercise, minute ventilation during exercise increased 3.3-fold. When combined with the increase in DF, total particle deposition increased more than 4.5-fold (Figure 4). These findings indicate that lung deposition of particles in the ultrafine size range during exercise is greater than expected from changes in minute ventilation, and exceeds estimations using model predictions of deposition. Exercise enhancement of deposition was greatest for the smallest particles in the size distribution.

Predictive models indicate that the regional deposition of UFP in the size range used in this study is predominantly alveolar. For example, the recently released version of the multiple path particle deposition model (MPPD Version 1.0, October 2002, Chemical Industry Institute of Toxicology) predicts that for a monodisperse 26-nm particle inhaled by mouth at rest, the greatest fractional deposition would occur in airway generations 18 to 21, with 49.3% of retained particles depositing in airway generations 18 and above. Under the same conditions with exercise, the highest fractional deposition is predicted to be in airway generations 19 to 22, with 67.7% of retained particles depositing in airway generations 18 and above. Thus, exercise would be expected to substantially increase UFP dose in the alveolar region of the lung, through increased intake of particles, increased total deposition fraction, and shifting of deposition toward the alveolar region. Exercise may therefore increase the likelihood of alveolar epithelial effects or translocation of particles to the lung interstitium or capillary blood (Nemmar et al., 2001).

The prediction models for lung deposition were able to reasonably estimate the measured overall DF for UFP at rest (Figures 1 and 2). However, experimental data deviated from model predictions in the 3 largest particle
size bins (Figures 2 and 3), in which the DF reached a plateau or increased slightly. This may result in part from the increased experimental variability associated with the small number of particles in the tail of the size distribution. The data from Jaques and Kim (2000), using aerosols with varying particle size and narrower size distributions than in the current study, indicate that deposition at these particle sizes does not deviate significantly from predicted values.

It must be kept in mind that this study utilized inhalation by mouthpiece. Thus particle deposition in the nose was bypassed. However, fractional deposition in the nasopharyngeal region is predicted to be low for 20–40 nm particles (ICRP, 1994), suggesting that nasal breathing will not differ greatly from oral breathing in terms of total or alveolar deposition. This was confirmed experimentally by Schiller et al. (1988), who compared deposition of 20-nm particles during breathing by mouthpiece and nasal mask, and found no significant difference. Mouthpiece breathing tends to alter respiratory patterns, with larger $V_T$ and minute ventilation than during unencumbered breathing (Paek & McCool, 1992). Increased $V_T$ increases particle deposition. Therefore, our findings may not reflect conditions of spontaneous oro-nasal breathing. For example, Bennett et al. (1996) found that, for subjects breathing by mouthpiece, the deposition of 2000-nm monodisperse carnauba wax particles was greater and more variable during spontaneous mouthpiece breathing than when subjects reproduced their “normal” breathing pattern which had been determined off the mouthpiece. The increased $V_T$ associated with mouthpiece breathing would be expected to increase DF relative to unencumbered breathing. Only relatively young, healthy, nonsmoking subjects were studied; the findings may differ with age or in people with significant airways disease or congestive heart failure.

In summary, these studies confirm that the DF of UFP is high in healthy subjects, and increases with decreasing particle size. Deposition increases further with exercise, to a greater degree than predicted by modeling estimates. The combination of increased particle intake, increased deposition, and the high deposition of UFP in the alveolar region indicates that UFP burden to the alveolar epithelium is significantly greater during exercise. This may have implications for the health of children and others exercising outdoors near highways or other sources of UFP.

REFERENCES


