Human Clinical Studies of Ultrafine Particles

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## TABLE 3. Pooled Results of Poisson Regressions of the Association of Hospital Readmissions and Same-Day Air Pollution Concentrations

<table>
<thead>
<tr>
<th>Pollutant</th>
<th>Unit</th>
<th>Hospital Readmissions, RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Myocardial Infarction Angina Pectoris Cardiac*</td>
</tr>
<tr>
<td>PNC</td>
<td>10 000/cm³</td>
<td>1.039 (0.998–1.082)†   1.020 (0.992–1.048) 1.026 (1.005–1.048)</td>
</tr>
<tr>
<td>PM₁₀</td>
<td>10 μg/m³</td>
<td>1.026 (0.996–1.058)   1.008 (0.986–1.032) 1.021 (1.004–1.039)</td>
</tr>
<tr>
<td>CO</td>
<td>0.2 mg/m³ (0.172 ppm)</td>
<td>1.022 (0.998–1.047)   1.009 (0.992–1.026) 1.014 (1.001–1.026)</td>
</tr>
<tr>
<td>NO₂</td>
<td>8 μg/m³ (4.16 ppb)</td>
<td>1.028 (0.997–1.060)   1.032 (1.006–1.058) 1.032 (1.014–1.051)</td>
</tr>
<tr>
<td>O₃†</td>
<td>15 μg/m³ (7.5 ppb)</td>
<td>1.000 (0.954–1.048)   1.044 (1.012–1.077) 1.026 (1.001–1.051)</td>
</tr>
</tbody>
</table>

*Hospital admissions for acute myocardial infarction, angina pectoris, dysrhythmia, or heart failure.

†Random-effects model.

‡Daily maximum 8-hour average.
Do UFP Contribute to PM-Related Cardiovascular Disease?

- Why might UFP be important in CV disease?
- UFP deposition in the respiratory tract
- Human clinical studies of carbon UFP
Ultrafine Particles

- UFP: <100 nm
- High surface area
- Evade macrophage phagocytosis
- Predicted high pulmonary deposition
- May enter lung interstitium and blood
Fractional Deposition of Inhaled Particles in the Human Respiratory Tract
(ICRP Model, 1994; Nose-breathing)

Figure courtesy of J. Harkema
Pulmonary Capillaries
UFP Beyond the Airways
Geiser et al., EHP 2005
Ambient Ultrafine Particles Have Oxidant Activity

Li et al., Environ Health Perspect 2003
Question: Does UFP exposure affect the circulation?

- Pulmonary vs Systemic
- Implications for cardiac outcomes
Experimental Protocol

UFP or Air

Symptoms
Phlebotomy
Exhaled NO
DLCO
Spirometry
Oximetry

Resting HRV
Flow-mediated dilatation
Exposure to Carbon UFP

- Count median diameter ~26 nm, GSD ~1.6
- 2 hrs by mouthpiece
- Intermittent exercise
Effects of Ultrafine Particles
10 to 50 µg/m³ for 2 hr

No effects on:
- Symptoms
- Lung function
- Airway inflammation
- Soluble markers of inflammation
- Cardiac rhythm, ST segment of ECG
A noninvasive marker of pulmonary vascular effects:

blood leukocyte expression of adhesion molecules
Leukocyte Recruitment in Inflammation
Blood Leukocytes: Markers of Vascular Events

Interactions of Blood and the Pulmonary Circulation, 2002
Change in Monocyte ICAM-1 Expression 3.5 h after Exposure

Frampton et al., Environ Health Persp 2006

ANOVA exposure effect
p = 0.012
Pulmonary Diffusing Capacity for CO (D\textsubscript{L}CO):
Sensitive to changes in pulmonary capillary blood volume
Hypothesis: Pulmonary vascular effects of PM—a function of particle size and surface area?

<table>
<thead>
<tr>
<th></th>
<th>Mass (µg/m³)</th>
<th>Number (particles/cm³)</th>
<th>Count Median Diameter (nm)</th>
<th>GSD</th>
<th>Surface Area m²/g</th>
</tr>
</thead>
<tbody>
<tr>
<td>UFP</td>
<td>55 ± 2.8</td>
<td>9.8x10⁶ ± 1.3</td>
<td>32 ± 1.2</td>
<td>1.63 ± 0.02</td>
<td>750</td>
</tr>
<tr>
<td>FP</td>
<td>114 ± 20.9</td>
<td>867 ± 155</td>
<td>292 ± 23.7</td>
<td>1.71 ± 0.05</td>
<td>7</td>
</tr>
</tbody>
</table>
Conclusion: Carbon UFP exposure may alter pulmonary vascular endothelial function in healthy subjects.

Does exposure to UFP alter systemic endothelial function?
Systemic Endothelial Function:
Forearm Flow-Mediated Dilatation
Proposed UFP Vascular Effects

Before Exposure

PM
AM
NO
OONO-

Monocyte
CD11a/CD18
TF
TF

O2-

Fibrin & platelet deposition

After Exposure

Platelets

Proposed UFP Vascular Effects
Summary & Speculation

- UFP fractional deposition high, increases with exercise and asthma
- UFP may impair pulmonary & systemic endothelial function
- Effects on endothelial function may underlie diverse cardiovascular effects
- Likely role for reactive oxygen species & NO
- Relative absence of airway effects
- Vascular effects of ambient UFP may be greater
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