Health effects of (particulate) air pollution

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Pneumology, Lung Toxicology
Air pollution and Health

- Introduction
  - Current situation - general observations
- General mechanisms involved
- Overview of a few key studies
  - Near Road...
  - Cardiovascular
- Final remarks
Air pollution and Health

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Air pollution

Volatile matter \((\text{NO}_x, \text{SO}_2, \text{CO}, \text{O}_3)\)

Particulate matter (PM)

Introduction

Current situation

Annual average PM$_{2.5}$ (µg/m$^3$)
Risk estimates provided by several short term studies per increment of 10 μg/m$^3$ in PM$_{2.5}$ or PM$_{10}$ (1-5 days)

<table>
<thead>
<tr>
<th>Primary Source</th>
<th>Exposure Increment</th>
<th>All-Cause</th>
<th>Cardiovascular</th>
<th>Respiratory</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meta-estimate with and without adjustment for publication bias</td>
<td>20 μg/m$^3$ PM$_{10}$</td>
<td>1.0 (0.8–1.2)</td>
<td>1.2 (1.0–1.4)</td>
<td>...</td>
</tr>
<tr>
<td>Meta-estimates from COMEAP report to the UK Department of Health on CVD and air pollution</td>
<td>20 μg/m$^3$ PM$_{10}$</td>
<td>...</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>NMMAPS, 20 to 100 US cities</td>
<td>20 μg/m$^3$ PM$_{2.5}$</td>
<td>0.4 (0.2–0.8)</td>
<td>0.6 (0.3–1.0)*</td>
<td>1.2 (0.4–1.9)</td>
</tr>
<tr>
<td>APHEA-2, 15 to 29 European cities</td>
<td>20 μg/m$^3$ PM$_{10}$</td>
<td>1.2 (0.8–1.4)</td>
<td>1.5 (0.9–2.1)</td>
<td>...</td>
</tr>
<tr>
<td>US, 6 cities</td>
<td>10 μg/m$^3$ PM$_{2.5}$</td>
<td>1.2 (0.8–1.6)</td>
<td>1.3 (0.3–2.4)</td>
<td>0.6 (–2.9, 4.2)</td>
</tr>
<tr>
<td>US, 27 cities, case-crossover</td>
<td>10 μg/m$^3$ PM$_{2.5}$</td>
<td>1.2 (0.3–2.1)</td>
<td>0.9 (–1.2, 2.0)</td>
<td>1.8 (0.2, 3.4)</td>
</tr>
<tr>
<td>California, 9 cities</td>
<td>10 μg/m$^3$ PM$_{2.5}$</td>
<td>0.6 (0.2–1.0)</td>
<td>0.6 (0.0, 1.1)</td>
<td>2.2 (0.6, 3.9)</td>
</tr>
<tr>
<td>France, 9 cities</td>
<td>20 μg/m$^3$ BS</td>
<td>1.2 (0.5–1.8)$\S$</td>
<td>1.2 (0.2–2.2)$\S$</td>
<td>1.1 (–1.4, 3.2)$\S$</td>
</tr>
<tr>
<td>Japan, 13 cities, age &gt;65 y</td>
<td>20 μg/m$^3$ SPM</td>
<td>1.0 (0.8–1.3)</td>
<td>1.1 (0.7–1.5)</td>
<td>1.4 (0.9–2.1)</td>
</tr>
<tr>
<td>Asia, 4 cities</td>
<td>10 μg/m$^3$ PM$_{10}$</td>
<td>0.55 (0.26–0.85)</td>
<td>0.59 (0.22–0.93)</td>
<td>0.62 (0.16–1.04)</td>
</tr>
<tr>
<td>US, 112 cities</td>
<td>10 μg/m$^3$ PM$_{2.5}$</td>
<td>0.98 (0.75–1.22)</td>
<td>0.85 (0.46–1.24)</td>
<td>1.68 (1.04–2.33)</td>
</tr>
<tr>
<td></td>
<td>10 μg/m$^3$ PM$_{10}$</td>
<td>0.46 (0.21–0.71)</td>
<td>0.32 (0.00–0.64)</td>
<td>1.16 (0.43–1.89)</td>
</tr>
<tr>
<td></td>
<td>10 μg/m$^3$ PM$_{2.5}$</td>
<td>0.77 (0.43–1.12)</td>
<td>0.61 (0.05–1.17)</td>
<td>1.63 (0.69–2.59)</td>
</tr>
<tr>
<td></td>
<td>10 μg/m$^3$ PM$_{10}$</td>
<td>0.47 (0.21–0.73)</td>
<td>0.29 (–0.04, 0.61)</td>
<td>1.14 (0.043–1.85)</td>
</tr>
</tbody>
</table>

0.5-1.2 % increase in daily mortality
0.4-1% increase in daily (CV) mortality
0.6-1.6 % increase in daily pulmonary mortality

(Brook et al. Circulation 2010)
Risk estimates provided by several long term cohort studies per increment of 10 \( \mu g/m^3 \) in PM\(_{2.5}\) or PM\(_{10}\).
Risk estimates per increment of 10 µg/m³ in PM$_{2.5}$ or 20 µg/m³ in PM$_{10}$ for different time scales
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inhaled ultrafine particles (Ø < 0.1 µm)

- pass into the circulation
- “direct” effects on cardiovascular endpoints
General mechanisms
Deposition/fate of (ultra)fine particles

Inhaled particles (all sizes)

↑ pulmonary inflammation
↑ systemic release of mediators (systemic spill over)

Inflammation receptors (cellular - vascular)

Leuven 20060419
Arbeidsgeneeskunde
General mechanisms
Schematic overview

UFP

PM$_{2.5}$ coarse fraction PM$_{10}$

direct translocation

stimulation irritant receptors

inflammation + oxidative stress

cardio-electro physiological effects

Systemic Spill over

direct effects on vessel wall + blood cells

systemic inflammation + oxidative stress

direct translocation

stimulation irritant receptors

inflammation + oxidative stress

cardio-electro physiological effects

Systemic Spill over

direct effects on vessel wall + blood cells

systemic inflammation + oxidative stress

size

lung

circulation

time

acute

chronic
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Figure 1
Ultafine particle size distribution (top panel) and normalized particle number concentration for different size ranges (bottom panel) as a function of distance from a highway in Los Angeles. From Zhu et al. (8). Reprinted with permission from Elsevier.

Table 2: Summary of near-highway health effects studies

<table>
<thead>
<tr>
<th>Citation</th>
<th>Location</th>
<th>Highway traffic intensity</th>
<th>Pollutants measured*</th>
<th>Distance from highway</th>
<th>Health Outcomes</th>
<th>Statistical association</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schwartz et al. 2005 (22)</td>
<td>Boston</td>
<td>NA</td>
<td>PM$_{2.5}$, BC, CO</td>
<td>NA</td>
<td>Heart rate variability</td>
<td>Decreases in measures of heart rate variability</td>
</tr>
<tr>
<td>Adar et al. 2007 (23)</td>
<td>St. Louis, Missouri</td>
<td>NA</td>
<td>PM$_{10}$, BC, UFP</td>
<td>On highway in busses</td>
<td>Heart rate variability</td>
<td>Decreases in measures of heart rate variability</td>
</tr>
<tr>
<td>Hoek et al. 2002 (24)</td>
<td>Netherlands</td>
<td>NA</td>
<td>BC, NO$_2$</td>
<td>Continuous*</td>
<td>Cardio-pulmonary mortality, lung cancer, asthma</td>
<td>1.41 OR for living near road</td>
</tr>
<tr>
<td>Torne et al. 2007 (41)</td>
<td>Worcester, Mass.</td>
<td>NA</td>
<td>PM$_{2.5}$</td>
<td>Continuous*</td>
<td>Acute myocardial infarction (AMI), asthma</td>
<td>5% Increase in odds of AMI</td>
</tr>
<tr>
<td>Venn et al. 2001 (49)</td>
<td>Nottingham, UK</td>
<td>NA</td>
<td>NA</td>
<td>Continuous*</td>
<td>Wheezing in children</td>
<td>1.08 OR for living w/ in 150 m of road</td>
</tr>
<tr>
<td>Nicolaï et al. 2003 (58)</td>
<td>Munich, Germany</td>
<td>&gt;30,000 veh/d</td>
<td>Soot, benzene, NO$_2$</td>
<td>Traffic counts within 50 m of house</td>
<td>Asthma, respiratory symptoms, allergy, asthma</td>
<td>1.79 OR for asthma and high traffic volume</td>
</tr>
<tr>
<td>Gauderman et al. 2003 (59)</td>
<td>Southern California</td>
<td>NO$_2$</td>
<td>Continuous*</td>
<td>NA</td>
<td>Asthma, respiratory symptoms</td>
<td>Increased asthma closer to freeways</td>
</tr>
<tr>
<td>McCormick et al. 2006 (60)</td>
<td>Southern California</td>
<td>NA</td>
<td>NA</td>
<td>Continuous*</td>
<td>Asthma</td>
<td>Large risk for children living with 75 m of road</td>
</tr>
<tr>
<td>Ryan et al. 2007 (61)</td>
<td>Cincinnati, Ohio</td>
<td>&gt;1,000 trucks/d</td>
<td>PM$_{2.5}$</td>
<td>400 m</td>
<td>Wheezing in children</td>
<td>NA</td>
</tr>
<tr>
<td>Kim et al. 2004 (62)</td>
<td>San Francisco</td>
<td>90,000–210,000 veh/d</td>
<td>PM$_{2.5}$, BC, NO$_x$</td>
<td>School sites</td>
<td>Childhood asthma</td>
<td>1.07 OR for high levels of NO$_x$</td>
</tr>
<tr>
<td>Wyp et al. 1993 (63)</td>
<td>Munich, Germany</td>
<td>7,000–125,000 veh/d</td>
<td>NO$_x$, CO</td>
<td>School sites</td>
<td>Asthma, bronchitis</td>
<td>Several statistical associations found</td>
</tr>
<tr>
<td>Bruneckreff et al. 1997 (64)</td>
<td>Netherlands</td>
<td>80,000–152,000 veh/d</td>
<td>PM$_{10}$, NO$_2$</td>
<td>Continuous*</td>
<td>Lung function</td>
<td>Decreased FEV with proximity to heavy truck traffic</td>
</tr>
<tr>
<td>Janssen et al. 2003 (65)</td>
<td>Netherlands</td>
<td>30,000–155,000 veh/d</td>
<td>PM$_{2.5}$, NO$_x$, benzene</td>
<td>&lt; 400 m</td>
<td>Lung function, respiratory symptoms</td>
<td>No association with lung function</td>
</tr>
<tr>
<td>Peters et al. 1999 (66)</td>
<td>Southern California</td>
<td>NA</td>
<td>PM$_{10}$, NO$_x$</td>
<td>NA</td>
<td>Asthma, bronchitis, cough, wheeze</td>
<td>1.54 OR of wheeze for boys w/ exposure to NO$_x$</td>
</tr>
<tr>
<td>Brauer et al. 2007 (67)</td>
<td>Nethantlands</td>
<td>Highways and streets</td>
<td>PM$_{2.5}$, NO$_2$, soot</td>
<td>Modeled exposure</td>
<td>Asthma, allergic, bronchitis, respiratory symptoms</td>
<td>Strongest association was with food allergies</td>
</tr>
<tr>
<td>Vissor et al. 2004 (68)</td>
<td>Amsterdam</td>
<td>&gt;10,000 veh/d</td>
<td>NA</td>
<td>NA</td>
<td>Cancer</td>
<td>Multiple associations</td>
</tr>
<tr>
<td>Vina et al. 2006 (69)</td>
<td>10 European countries</td>
<td>NA</td>
<td>PM$_{10}$, NO$_x$, SO$_2$</td>
<td>NA</td>
<td>Cancer</td>
<td>1.46 OR near heavy traffic, 1.30 OR for high exposure to NO$_x$</td>
</tr>
<tr>
<td>Gauderman et al. 2007 (70)</td>
<td>Southern California</td>
<td>NO$_2$</td>
<td>Continuous*</td>
<td>NA</td>
<td>Lung Function</td>
<td>Decreased FEV for those living near freeway</td>
</tr>
</tbody>
</table>

*As defined in article cited (veh/d = vehicles per day; veh/h = vehicles per hour).
*UFP = ultrafine particles; FP = fine particles; PM$_{2.5}$ = particles with aerodynamic diameter ≤ 2.5 μm; PM$_{10}$ = particles with aerodynamic diameter ≤ 10 μm; BC = black carbon; PAH = polycyclic aromatic hydrocarbons; VOCs = volatile organic compounds
*P pollutant measurements were made along a transect away from the highway
*Proximity to each participant to a major road was calculated using GIS software
*Statistical association between proximity to highway or exposure to traffic-generated pollutants and measured health outcomes
NA = not applicable; measurements were not made.

Conclusions

Growing evidence that freshly-emitted air pollutants (downwind) from major highways, motorways, and freeways include elevated levels of ultrafine particulates (UFP), black carbon (BC), oxides of nitrogen (NOx), and carbon monoxide (CO).

People living (or spending substantial time) within about 200 m of highways are exposed … Evidence of the health hazards …

- Development of asthma and reduced lung function in children.
- Particulate matter (PM) that show associations with cardiac and pulmonary mortality
- Less work has tested the association between lung cancer and highways …
Tsai et al. Comparisons of commuter's exposure to particulate matters while using different transportation modes, Science of the total environ, 405, 71-11, 2008.

### Table 2 – Trip-averaged concentrations and whole-trip exposure (mean ± SD) of PM by four commuting modes in Taipei, Taiwan 2005

<table>
<thead>
<tr>
<th>Pollutants</th>
<th>Commuting mode</th>
<th>Trip-averaged concentrations a</th>
<th>N (trip)</th>
<th>Trip duration (minutes)</th>
<th>Whole-trip exposures b</th>
</tr>
</thead>
<tbody>
<tr>
<td>PM_{10}</td>
<td>Motorcycle</td>
<td>112.8 ± 38.3</td>
<td>16</td>
<td>28.4 ± 4.2</td>
<td>3247 ± 1241</td>
</tr>
<tr>
<td></td>
<td>Car</td>
<td>41.9 ± 14.4</td>
<td>16</td>
<td>30.0 ± 4.9</td>
<td>1268 ± 522</td>
</tr>
<tr>
<td></td>
<td>Bus</td>
<td>70.0 ± 22.5</td>
<td>16</td>
<td>43.1 ± 5.1</td>
<td>3039 ± 1133</td>
</tr>
<tr>
<td></td>
<td>MRT</td>
<td>64.9 ± 29.3</td>
<td>16</td>
<td>33.9 ± 8.3</td>
<td>2138 ± 826</td>
</tr>
<tr>
<td>PM_{2.5}</td>
<td>Motorcycle</td>
<td>67.5 ± 31.3</td>
<td>16</td>
<td>28.4 ± 4.2</td>
<td>1942 ± 977</td>
</tr>
<tr>
<td></td>
<td>Car</td>
<td>22.1 ± 9.6</td>
<td>16</td>
<td>30.0 ± 4.9</td>
<td>671 ± 335</td>
</tr>
<tr>
<td></td>
<td>Bus</td>
<td>38.5 ± 15.6</td>
<td>16</td>
<td>43.1 ± 5.1</td>
<td>1687 ± 833</td>
</tr>
<tr>
<td></td>
<td>MRT</td>
<td>35.0 ± 17.4</td>
<td>16</td>
<td>33.9 ± 8.3</td>
<td>1149 ± 501</td>
</tr>
<tr>
<td>PM_{1.0}</td>
<td>Motorcycle</td>
<td>48.4 ± 24.7</td>
<td>16</td>
<td>28.4 ± 4.2</td>
<td>1388 ± 742</td>
</tr>
<tr>
<td></td>
<td>Car</td>
<td>16.2 ± 6.2</td>
<td>16</td>
<td>30.0 ± 4.9</td>
<td>489 ± 219</td>
</tr>
<tr>
<td></td>
<td>Bus</td>
<td>31.3 ± 14.0</td>
<td>16</td>
<td>43.1 ± 5.1</td>
<td>1373 ± 752</td>
</tr>
<tr>
<td></td>
<td>MRT</td>
<td>26.5 ± 12.6</td>
<td>16</td>
<td>33.9 ± 8.3</td>
<td>870 ± 364</td>
</tr>
</tbody>
</table>

### Table 4 – Comparisons of PM concentrations while commuting between special events and normal operation for motorcycle and bus commuters in Taipei, Taiwan 2005

<table>
<thead>
<tr>
<th>Pollutants a</th>
<th>Motorcycle (N=336 events)</th>
<th>Bus (N=345 events)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Idling Mean ± SD</td>
<td>Driving Mean ± SD</td>
</tr>
<tr>
<td>PM_{10}</td>
<td>103.9 ± 45.6</td>
<td>98.8 ± 38.3</td>
</tr>
<tr>
<td>PM_{2.5}</td>
<td>56.7 ± 40.1</td>
<td>53.3 ± 31.7</td>
</tr>
<tr>
<td>PM_{1.0}</td>
<td>39.0 ± 30.1</td>
<td>36.6 ± 23.9</td>
</tr>
</tbody>
</table>

a Unit: PM concentration in µg/m³.

*p-value < 0.05 by using paired t-test.
Tsai et al. Comparisons of commuter's exposure to particulate matters while using different transportation modes, Science of the total environ, 405, 71-11, 2008.

Fig. 1—Regression of commuter's whole-trip PM exposures by fixed-site air monitoring data for four commuting modes in Taipei, Taiwan, 2005.
Particle number counts (PNCs), PM2.5, PM10, and soot on 47 weekdays (08:00 – 10:00) June 2007-2008 on two routes in diesel and electric buses, gasoline- and diesel-fueled cars & on bicycle.

- **PNC** exposures were highest in diesel buses (38,500 particles/cm³) & cyclists along the high-traffic intensity route (46,600 particles/cm³); lowest in electric buses (29,200 particles/cm³).
- **PM10** exposure was highest from diesel buses (47 μg/m³) and lowest along the high- and low-traffic bicycle routes (39 and 37 μg/m³). **Soot** exposure was highest in gasoline-fueled cars, diesel cars, and diesel buses and lowest along the low-traffic bicycle route.

- Minute ventilation (volume of air per minute) of cyclists = 2x car and bus passengers ➔ inhaled air pollution doses were highest for cyclists.

- Conclusions: **Commuters’** rush hour exposures were significantly influenced by mode of transport, route, and fuel type.
60 asthmatic adults randomized, crossover study.  
2 h walk: Oxford Street of Hyde Park 
Real-time exposure, physiological, and immunologic measurements.

Result: Oxford street = higher exposures fine, ultra-fine, elemental carbon, and nitrogen dioxide & asymptomatic reductions lung function: FEV1 - 6.1% and FVC - 5.4% & neutrophilic inflammation and airway acidification

Effects were greater in subjects with moderate asthma than in those with mild asthma.

The changes were associated most consistently with exposures to ultrafine particles and elemental carbon.
Associations residential traffic &
asthma - COPD in adults in S Sweden.
(n = 9319, 18–77 years)
Geographical Information System (GIS) - residential addresses to
road database & emission database (NOx.)

**Exposure:** cars/minute within 100 m (none to >10 cars/minute)

**Result:**
- Asthma: 1.40 (95% CI = 1.04–1.89)
- COPD 1.64 (95%CI = 1.11–2.4)

**Conclusion**
Living close to traffic is associated with prevalence of asthma & COPD


### Table 5: COPD diagnosis and chronic bronchitis symptoms in relation to traffic.

<table>
<thead>
<tr>
<th></th>
<th>COPD Diagnosis</th>
<th>Chronic bronchitis symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>n (%)</td>
</tr>
<tr>
<td><strong>Heavy traffic</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>6041</td>
<td>243(4.0%)</td>
</tr>
<tr>
<td>Yes</td>
<td>3275</td>
<td>172(5.3%)</td>
</tr>
<tr>
<td><strong>Heaviest road within &lt;100 m</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>no heavy road</td>
<td>3755</td>
<td>153(4.1%)</td>
</tr>
<tr>
<td>&lt;2 cars/min</td>
<td>2235</td>
<td>95(4.3%)</td>
</tr>
<tr>
<td>2–5 cars/min</td>
<td>1820</td>
<td>71(3.9%)</td>
</tr>
<tr>
<td>6–10 cars/min</td>
<td>886</td>
<td>60(6.8%)</td>
</tr>
<tr>
<td>&gt;10 cars/min</td>
<td>578</td>
<td>34(5.9%)</td>
</tr>
<tr>
<td><strong>NOx (µg/m³)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0–8</td>
<td>1855</td>
<td>74(4.0%)</td>
</tr>
<tr>
<td>8–11</td>
<td>1855</td>
<td>68(3.7%)</td>
</tr>
<tr>
<td>11–14</td>
<td>1855</td>
<td>87(4.7%)</td>
</tr>
<tr>
<td>14–19</td>
<td>1858</td>
<td>83(4.5%)</td>
</tr>
<tr>
<td>&gt;19</td>
<td>1851</td>
<td>101(5.5%)</td>
</tr>
</tbody>
</table>

* a Adjusted for age, sex, and smoking. [OR(95%CI)].

The table shows the prevalence of COPD diagnosis and chronic bronchitis symptoms associated with different levels of traffic and air pollution, including heavy traffic, heaviest road within 100 m, and NOx concentrations. The odds ratios (OR) and confidence intervals (CI) are provided for each category. The p-trend values indicate the statistical significance of the trend across different categories.
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    - Cardiovascular

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- Double-blind placebo-controlled study
- 20 men (mean 60 y) with prior MI (35±4 months before)
- Exposure do dilute diesel-exhaust or filtered air:
  - 300 µg/m³, 1,260,000 particles (20-120 nm)/cm³
  - 1 h with 2 x 15 min exercise (110-150 W)
- ECG during exercise
- Vascular study 6-8 h after exercise
The normal ST segment has a slight upward concavity.

Flat, downsloping (= depressed ST segments) may be associated with coronary ischemia.
Cardiovascular morbidity

Figure 1. Myocardial Ischemia during 15-Minute Intervals of Exercise-Induced Stress and Exposure to Diesel Exhaust or Filtered Air in the 20 Subjects.

Panel A shows the average change in the heart rate and in the ST segment in lead II. Panel B shows the maximum ST-segment depression during inhalation of diesel exhaust as compared with filtered air (P=0.003), and Panel C shows the total ischemic burden during inhalation of diesel exhaust as compared with filtered air (P<0.001); the values in Panels B and C are averages of the values in leads II, V2, and V5. In all three panels, red indicates exposure to diesel exhaust, and blue exposure to filtered air. T bars denote standard errors, and mVsec millivolt seconds.

- Prospective cohort study, Germany:
  - 2000 - : 4494 persons, 45-74 y
  - Coronary artery calcification (CAC) by electron-beam CT
- Exposure: distance of residence to major roads
- OR for high CAC (> 75th percentile):
  - > 200 m from major road : 1 (ref)
  - 101-200 m : 1.08
  - 51-100 m : 1.34
  - < 50 m : 1.63
Cardiovascular morbidity


- **Experimental study**
  - compared the *pro-atherogenic* effects of ambient particles of <0.18 microm (ultrafine particles UFP) with particles of <2.5 microm (fine FP) in genetically susceptible (apolipoprotein E-deficient) mice (particles from air of LA)

- **outcome**
  - **UFP significantly** larger early atherosclerotic lesions ⇔ PM(2.5) or filtered air.
  - UFP inhibition of the anti-inflammatory capacity of plasma high-density lipoprotein and greater systemic oxidative stress (increase in hepatic malondialdehyde levels and upregulation of Nrf2-regulated antioxidant genes)
Cardiovascular morbidity

PM <0.18 µm
n/cm³

<table>
<thead>
<tr>
<th></th>
<th>FA</th>
<th>FP</th>
<th>UFP</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 mg/m³</td>
<td>~5,000</td>
<td>3.88x10⁵</td>
<td>5.59x10⁵</td>
</tr>
<tr>
<td>0.4 mg/m³</td>
<td></td>
<td></td>
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<tr>
<td>0.1 mg/m³</td>
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5h/d 3d/wk x3 (75 h)

DOI: 10.1161/CIRCRESAHA.107.164970
Cardiovascular morbidity


Case-crossover study, 691 nonfatal MI (Augsburg; 1999-2001) activity before onset of MI (standardized interview-based diary)?

1h before MI vs control (24-71 h before MI)

- any means of transportation → O.R.=2.92
  - car → O.R.=2.60
  - bicycle → O.R.=3.94
  - public transport → O.R.=3.04

Proportion of subjects with exposure to traffic (%)

Control period

<table>
<thead>
<tr>
<th>Hours before MI</th>
<th>Proportion (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>-72</td>
<td>4</td>
</tr>
<tr>
<td>-48</td>
<td>6</td>
</tr>
<tr>
<td>-24</td>
<td>6</td>
</tr>
<tr>
<td>0</td>
<td>12</td>
</tr>
</tbody>
</table>

O.R.
- 2.92
- 2.01
- 1.50
Cardiovascular morbidity

Acute

- Previous 2h and 24h PM$_{2.5}$ concentration is associated with MI \((Peters \ et \ al. \ Circulation \ 2001)\)
- Participation in traffic is associated with MI (OR 2.9 95%CI 2.2-3.8) \((Peters \ et \ al. \ NEJM \ 2004)\)
- Same-day PM$_{10}$ is associated with hospitalization for CVD \((Dominici \ et \ al. \ JAMA \ 2006)\)
- Risk of PM$_{2.5}$-related fatal CHD women (RR 1.4) > men (RR 0.9 per 10µg/m$^3$) \((Chen \ et \ al. \ Environ \ Health \ Perspect \ 2005)\)
- RR of PM$_{2.5}$-related fatal CHD in post-menopausal women (n>65000): 1.76 (95%CI 1.25-247) \((Miller \ et \ al. \ N \ Engl \ J \ Med \ 2007)\)

![Acute exposure diagram](attachment:diagram.png)

- Atherosclerotic plaque rupture
- Blood platelet activation
Air pollution and Health

- Introduction
  - Current situation - general observations
- General mechanisms involved
- Overview of a few key studies
  - Near Road...
  - Cardiovascular
- Final remarks
General mechanisms
Schematic overview

Direct translocation

Stimulation of irritant receptors

Inflammation + oxidative stress

Cardio-electro physiological effects

Direct effects on vessel wall + blood cells

Systemic inflammation + oxidative stress

Direct effects on vessel wall + blood cells

Systemic Spill over

Acute

Chronic
Particulate air pollution and health?

- Complex interaction
  - Multiple possible health effects
    - Lung: Asthma - COPD
    - Systemic – Cardiovascular effects: clotting – arthrosclerosis – BP – HRate
    - Dependent on timing of exposure (children – adults ..)
  - Multiple particle
    - Size (UFP – FP – Coarse)
    - Composition
    - Fresh vs old
  - Multiple confounders
    - Pollutant gasses
    - Smoking
    - Indoor PM
Particulate air pollution and health?

- Complex interaction
  - Multiple possible health effects
    - Lung: Asthma - COPD
    - Systemic – Cardiovascular effects: clotting – artherosclerosis – BP – Heart rate
    - Dependent on timing of exposure (children – adults ..)
  - Multiple particle
    - Size (UFP – FP – Coarse)
      - Soot (or Black Carbon) strongly associated with respiratory diseases such as Asthma & COPD
      - Near Road - Traffic related studies - show strong association with :
        - Pulmonary effects in children
        - CV-effects
    - Composition
    - Fresh vs old
  - Multiple confounders
    - Pollutant gasses
    - Smoking
    - Indoor PM
How do ambient particles compare to smoking?

Pope et al. Circulation 2009, 120, 941-8

The diagram illustrates the relative risk of mortality adjusted for cardiopulmonary, cardiovascular, and IHD events. The estimated daily dose of PM$_{2.5}$ (mg) is plotted against the relative risk of mortality. The data points show a significant increase in risk with increasing estimated daily dose of PM$_{2.5}$.

SHS: Secondhand smoke

Air pollution

Cardiopulmonary events

Cardiovascular events

IHD: Ischemic Heart Disease

estimated daily **dose** of PM$_{2.5}$ (mg)
How do ambient particles compare to smoking? Pope et al. Circulation 2009, 120, 941-8

Graph showing adjusted relative risk of mortality due to exposure from second-hand cigarette smoke (SHS) and air pollution compared to cardiovascular and cardiopulmonary risks. The graph includes data from different exposure levels of SHS and PM2.5, with estimated daily dose (mg) on the x-axis and adjusted relative risk of mortality on the y-axis.
Thank you for your attention
Acute?
Chronic

Blood

PM or constituents in the circulation
UFP, soluble metals, Organic compounds

Vasculature
Vasoconstriction
Endothelial dysfunction
PM-mediated ROS
↑ BP
? Atherosclerosis

Blood
? ↑ Platelet aggregation

PM and/or constituents transmitted into blood

Pulmonary oxidative stress & inflammation
“Systemic spill-over”

ANs

Sub-acute & Chronic

ANS imbalance
↑ SNS / ↓ PSNS

Vasculature
Vasoconstriction
Endothelial dysfunction
Neural-mediated ROS
↑ BP

Blood
↑ Platelet aggregation

Heart
↓ HRV
↑ Heart rate
↑ Arrhythmia potential

Cellular inflammatory response (↑ activated WBCs, platelets, MPO)
↑ Cytokine expression/levels (↑ IL-1β, IL-6, TNF-α)
? ↑ ET, histamine, cell microparticles, oxidized lipids; ↓ anti-oxidants

Activated or Inflamed fat

Direct actions

Activated or Inflamed liver

Acute phase response
↑ Clotting factors
Fibrinogen, CRP

Adipokines
(PAI-1, Resistin)

Vasculature
Endothelial cell dysfunction/vasoconstriction, ↑ ROS
Atherosclerosis progression/plaque vulnerability
↑ Thrombogenicity (e.g. tissue factor)

Metabolism
Insulin resistance, dyslipidemia, impaired HDL function

Blood
↑ Coagulation, thrombosis; ↓ fibrinolysis (e.g. PAI-1)

Brooks et al. Circulation 2010, 121, 2331-78