Health Effects of Ambient Ultrafine Particles – Do we know enough?

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Ambient Air Pollution – Worldwide Problem

London, middle of XX century

Beijing, beginning of the XXI century
Health Effects of Ambient Ultrafine Particles

- Health Effects of Fine Particles
- Modes of Action of Particles Depend on their Size
- Health Effects of Ultrafine Particles
- Research Needs
Review of evidence on health aspects of air pollution for guidance of EU policy

OBJECTIVE:
To provide the European Commission and its stakeholders with scientific evidence-based advice on health aspects of air pollution in support of the comprehensive review of air quality legislation due in 2013.

Full WHO technical report was published in June 2013
Health Effects of Particulate Air Pollution – REVIHAAP Conclusions (A1)

1. Short-term exposure to PM$_{2.5}$ on both mortality and morbidity
2. Long-term exposures to PM$_{2.5}$ on mortality and morbidity
3. Long-term exposure to PM$_{2.5}$ is a cause of both cardiovascular mortality and morbidity

ESCAPE: European Study of Cohorts for Air Pollution Effects

- Existing cohort studies
- Spatial variability of air pollution based on Geographic Information Systems
- Outcomes
  - Children’s health
  - Respiratory health
  - Cardiovascular Health
  - Mortality

PM2.5 results

Eeftens, Atm Env 2012
ESCAPE:
Fine Particles (5 µg/m³) and Total Mortality

<table>
<thead>
<tr>
<th>Threshold</th>
<th>N of cohorts</th>
<th>PM2.5</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 µg/m³</td>
<td>9</td>
<td>1.02 (0.87-1.19)</td>
</tr>
<tr>
<td>15 µg/m³</td>
<td>11</td>
<td>1.04 (0.98-1.11)</td>
</tr>
<tr>
<td>20 µg/m³</td>
<td>17</td>
<td>1.07 (1.01-1.13)</td>
</tr>
<tr>
<td>25 µg/m³</td>
<td>17</td>
<td>1.06 (1.00-1.12)</td>
</tr>
<tr>
<td></td>
<td>19</td>
<td>1.07 (1.02-1.13)</td>
</tr>
</tbody>
</table>

The ACS study found a Relative Risk of 1.030 / 5 µg/m³

Beelen et al. Lancet 2013
Risk for Incident Coronary Artery Disease for 5 μg/m³ PM$_{2.5}$

Adjusted for: Age (time variable), year of enrolment, sex, marital status, education, occupation, smoking status, smoking duration and smoking intensity, socioeconomic area-level variables

Cesaroni et al. BMJ 2014
Health effects of fine particles are consistently shown.

The evidence today is substantially strengthened compared to the 2005 WHO guidelines.
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Epidemiological and toxicological studies have shown PM$_{2.5}$ and PM$_{10}$ comprises fractions suggesting a role for both the chemical composition (such as transition metals and combustion-derived primary and secondary organic particles) and physical properties (size, particle number and surface area).
PM Composition related to Health Effects

- PM Composition
  - Black carbonaceous particles
  - Secondary organic aerosols
  - Secondary inorganic aerosols
  - Coarse particles
  - Ultrafine particles
Biokinetics provides the dose estimate for both the primary and secondary organs and tissues and therefore it is the rationale for subsequent toxicological studies assessing potential health risks.

Kreyling et al., Nat Biotech, 2010
Particles Impact the Lung and their Effects Go Beyond
Cardiovascular disease due to traffic exposures and fine particles

Blood

1. Systemic Oxidative stress and Inflammation

3. PM or constituents in the circulation

Bronchioles/Alveoli

PM and/or constituents transmitted into blood

Pulmonary oxidative stress & inflammation

Activation of lung ANS reflex arcs

2. ANS imbalance

ANS

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Brook et al. 2010
Organs of the human body affected by particulate air pollution

- Respiratory mortality
- Respiratory symptoms
- Rhinitis/Pneumonia
- Airway inflammation
- Decreased lung function
- Decreased lung growth
- Lung cancer

- Insuline Resistance
- Diabetes

- Changes in blood pressure
- Endothelial function
- Increased blood coagulation
- Systemic inflammation

- Stroke
- Diseases of the central nervous system

- Cardiovascular mortality
- Cardiovascular hospital admission
- Changes in heart rate variability
- ST-segment depression

- Premature birth
- Decreased birth weight
- Decreased foetal growth
- Intrauterine growth retardation
- Decreased sperm quality

Modified after Peters et al. JOEM 2011
Health Effects of Ambient Ultrafine Particles

Particle sizes determine their location of deposition and their fate within the body

Particle chemistry determines their mode of action
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Research gaps for ultrafine particles

Understanding the Health Effects of Ambient Ultrafine Particles

HEI Review Panel on Ultrafine Particles

http://www.healtheffects.org/Workshops/Brussels2013/Presentations/Shaikh.pdf
Key Findings: Observational Epidemiologic Studies

- Short-term studies only
  - Time-series, panel studies
  - Variable study designs
  - Single studies

- No studies of long term exposures
Key Findings: Observational Epidemiologic Studies

- Some studies have found clear, independent associations of ultrafines with adverse effects on health.
- For Example: Studies in Erfurt (’95 – ’01)
  - Increased mortality
  - Total number concentration
  - Adjusted for co-pollutants
  - Generally, only for lag 4 days post-exposure

Figure 3. Relative risk estimates for UFP NC, adjusted for gaseous pollutants in two-pollutant models. Erfurt, Germany, September 1995 to August 2001.

Stölzel et al. (2007)
Key Findings:
Observational Epidemiologic Studies

• Other studies have not...
  – Associations observed with NOx, NO2, PM10, PM2.5, but not as strongly with total UFP
  – Weaker in two-pollutant models

 Associations with pediatric asthma hospitalizations in Copenhagen
( Iskandar et al., 2012)
Overall Conclusions

- Motor vehicles, especially diesel, have been important sources of emissions and exposures to ambient UFPs but emissions set to change substantially in the years ahead.

- UFPs differ from larger particles in their deposition, clearance and potential for translocation.

- Experimental and epidemiologic studies provide suggestive, but not consistent, evidence of adverse effects of short-term exposures to ambient UFP.

- The lack of support for a substantial, independent effect “does not mean that such effects, as one part of the broader effects attributable to PM$_{2.5}$ can be entirely ruled out.”

And, therefore,

- “The current evidence does not support a conclusion that “exposure to UFPs alone can account in substantial ways for the adverse effects … of PM$_{2.5}$.”
Novel Evidence: The 2008 Beijing Olympics

- Monitoring of PM$_{10}$ and NO$_2$ at 8 official monitoring sites
- Monitoring of PM$_{2.5}$ and particle size distribution at Peking University
- Cardiovascular disease mortality for the Beijing urban area

![Graph showing PM and NO$_2$ levels before, during, and after the Olympics.]

Su et al. to be submitted
Novel Evidence: The 2008 Beijing Olympics

Sizes of PNC

- 3-10nm
- 10-30nm
- 30-50nm
- 50-100nm
- 3-100nm

PNC [cm$^{-3}$]

- Before Olympics
- During Olympics
- After Olympics

Su et al. to be submitted
Novel Evidence: The 2008 Beijing Olympics Cardiovascular Disease Mortality

Su et al. to be submitted

% Change per IQR

PM2.5  PM10  NO2  3-10  10-30  30-50  50-100  3-100nm

-4  -2  0  2  4  6  8  10  12  14  16  18
Health Effects of Ambient Ultrafine Particles

Health effects of ultrafine particles are shown for short-term exposures.

Capture important properties of ambient aerosols in addition to fine particles.

Need to be controlled at the source to reduce health effects in urban areas.
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Critical data Gaps for Ultrafine Particles to Promote an Ambient Standard

- Studies on long-term health effect studies based on prospective cohort studies
- Studies on short-term health effects based on multicenter time-series studies including meta-analyses
- Studies on personal short-term exposures and health effects in panel studies
- Studies assessing all criteria pollutants and black carbon jointly with ultrafine particles
ULTRA III: Closing Gaps in Research on Ambient Ultrafine Particles

- Measurements of ultrafine particles
- Chemical composition of ultrafine particles
- Microclimate data
- Modeling of residential exposures
- Links to ongoing epidemiological re-examinations in KORA including preclinical phenotypes determined by imaging

NO$_2$
Thank you very much for your attention!