Health Effects of Nanoparticles in Susceptible Persons

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Air-Blood Barrier

Air-blood barrier = 0.2 μm
1/100 hair thickness

Courtesy Institute of Anatomy, Bern University
The lung in numbers...

at rest, we breathe:

- 12 times per minute 0.5 litres of air
- 360 litres per hour
- 10'000 litres per day (\(10^{12}\) particles)
- 3 000 000 litres per year

\(\text{x40 with exercise}\)
Immune Homeostasis

- Immune response
- Inflammation
- Inhibition
- Tolerance

Excessive and/or inappropriate inflammation
Functional impairment of lung (gas exchange etc.)
- e.g. allergic asthma, autoimmune disease

Immune suppression with susceptibility to infections
- e.g. AIDS, immune-suppressive drugs

Chronic obstructive pulmonary disease (COPD)

- Heart disease
- Cancer
- Stroke
- Accidents
- COPD
- Diabetes

Global Alliance Against Chronic Respiratory Diseases (GARD). 2007
COPD: tip of the iceberg

**Diagnosed COPD**
2.4 – 7 Mill.

**Estimated COPD**
15.3 – 17.1 Mill.

Not diagnosed or wrong diagnosis


Risk Factors for COPD

- Cigarette smoke
- Occupational dust and chemicals
- Environmental tobacco smoke (ETS)
- Indoor and outdoor
- Socio-economic status
- Aging Populations

Genes
Infections
Socio-economic status

Aging Populations
Sahi and Barnes, Lancet 2009

Lung destruction in COPD

Normal
- Airway held open by chondral attachments

Chronic Obstructive Pulmonary Disease
- Airway held open by chondral attachments
- Macrophages and peribronchial inflammation and fibrosis (abnormal bronchial tissue)

Airflow limitation

Barnes P, NEJM 2000; 343:269-280

Lung destruction in COPD

Normal lung

Smoker's lung (Emphysema)
Asthma

235 million persons suffer from asthma, most common chronic disease in children

- dyspnea (difficulty breathing)
  - acute or chronic
  - at rest or with physical exercise
  - possibly trigger identifiable
  - reversible
- cough
- sometimes sputum production
- possibly related to allergies

Asthma triggers...quite a few around

Allergens
Viruses
Inhalative air pollution

Genes
Environment

Allergens
Inhalative air pollution

Inflammation
Bronchial Hyperreactivity
Remodeling of airways
Symptoms

Airflow limitation in Asthma

Normal
Asthma

Bronchial mucosa
Bronchial wall (muscle layer, connective tissue)
Oedema
Mucus production
Muscle contraction
**PM$_{2.5}$ - related Respiratory Mortality & Morbidity**

- Consistent evidence: Adverse health effects of short-term exposure to PM$_{2.5}$: 10 μg/m$^3$ increment associated with 1.04% (95% CI 0.52% to 1.56%) increase in the risk of death.
- Associations for respiratory causes of death larger than for cardiovascular causes, 1.51% (1.01% to 2.01%) vs 0.84% (0.41% to 1.26%).
- Caveats: Small study bias for single-city mortality studies and multicity studies of cardiovascular disease; heterogeneity for effect estimates in different regions of the world.
- Data supports policy measures to control PM$_{2.5}$ concentrations.

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**Acute exposure in a street tunnel: The Stockholm Tunnel Study**

- 16 healthy individuals exposed during 2 hours in street tunnel with intense traffic.
- Examination (including bronchoscopy) before and after exposure.
- **RESULTS**
  - Transiently increased respiratory symptoms.
  - Increases inflammatory cells in broncho-alveolar lavage fluid.
  - Expression of transcription factors in bronchial mucosa (c-jun).
  - BUT: no changes in lung function (FEV1).

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**Lung function measurement**

- Volume (Vol) over time (Time).
- Normal, COPD, Asthma.

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**PM$_{2.5}$ - related Respiratory Mortality & Morbidity**

- Graph showing mortality and morbidity by cause.
"Oxford Street vs Hyde Park" in asthmatics – The LONDON Experience!

<table>
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<tr>
<th></th>
<th>Oxford Str</th>
<th>Hyde Park</th>
<th>Sign.</th>
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<tbody>
<tr>
<td>PM$_{2.5}$</td>
<td>28.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ultrafine part.</td>
<td>63.7</td>
<td>18.3</td>
<td>p&lt;0.01</td>
</tr>
<tr>
<td>Carbon</td>
<td>7.5</td>
<td>1.3</td>
<td>p&lt;0.01</td>
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McCreanor J et al, NEJM 2007

Effects on lung function

→ increased inflammatory markers in airways after air pollution exposure
→ decreased lung function in mild / moderate asthmatics

Development of lung function from cradle to coffin...

Reduced age-dependent lung function increase in children due to air pollution?

areas with poor air quality
↓
more children with FEV1 < 80%

Children's Health Study, Gauderman et al, NEJM 2004
Is age-dependent lung function increase in children improved by better air quality?

Children's Health Study

- **Improved** age-dependent lung function increase after migration to areas with **less air pollution**
- **Reduced** age-dependent lung function increase after migration to areas with **more air pollution**


Effect of air pollution on adult lung function

SAPALDIA

Swiss study on Air Pollution and Lung Disease in adults

Downs SH et al. NEJM 2007

Reduced lung function decline with improved air quality?
PM10-related effect on lung function

Improved air quality reduced physiological decline in lung function
→ +3 ml FEV1 per 10 μg/m³ decrease PM10

[NOTE: Effect of smoking cessation greater!
→ +12 ml FEV1 per 1 pack/year]

Downs SH et al, NEJM 2007

Childhood asthma & traffic-related air pollution?

Asthma events associated with proximity to primary roads with odds ratio of 0.97 (95% CI: 0.94,0.99) for a 1 km increase in distance
→ asthma events are less likely as the distance between the residence and a primary road increases

Li S et al. Environmental Health 2011, 10:34

Traffic-related PM10 & adult onset asthma?

Asthma incidence associated with change in TPM10

Independent of education, workplace exposure, passive smoking, parental asthma or allergies, random area effects, lung function or co-pollutants


Conclusions

- Susceptible individuals to adverse effects of ambient particles: Children, COPD, Asthma
- Acute exposure to ambient particles:
  - trigger acute, inflammatory effect on respiratory tract
  - worsen lung function in asthmatics
- Chronic air pollution:
  - slows age-related lung function increase (children)
  - accelerates lung function decline (adults)
- Risk for asthma and exacerbation increased by air pollution (children & adults)