Health Effects of Nanoparticles in Susceptible Persons

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Air-Blood Barrier

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

.... 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 Homeostasis

Immune response
Inflammation
Inhibition
Tolerance

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

Chronic obstructive pulmonary disease (COPD)

Heart disease
Cancer
Diabetes

0 5 10 15 20 25 30 35 40 45 50
Year of death

Rate per 100,000 individuals

0 50 100 150 200 250 300 350 400 450 500 550
Year of death

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

Genetics

Socio-economic status

1/4 of COPD patients are never-smokers

Aging Populations

Sahni and Barnes, Lancet 2009

Lung destruction in COPD

Normal

- Airways held open by chondro attachments

Chronic Obstructive Pulmonary Disease

- Mucous hypersecretion (mucosal obstruction)
- Disrupted alveolar attachments (alveolar destruction)
- Microvascular and peribronchial inflammation and fibrosis (obliterates bronchiolar)

Airflow limitation

Barnes P. NEJM 2000; 343:362-381

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

Airflow limitation in Asthma

Normal
- Bronchial mucosa
- Normal bronchial wall (muscle layer, connective tissue)

Asthma
- Oedema
- Mucus production
- Muscle contraction
Lung function measurement

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

- Consistent evidence: Adverse health effects of short-term exposure to PM$_{2.5}$: 10 $\mu$g/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

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)
"Oxford Street vs Hyde Park" in asthmatics – The LONDON Experience!

<table>
<thead>
<tr>
<th>Location</th>
<th>PM$_{2.5}$</th>
<th>Ultrafine Particles</th>
<th>Carbon</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxford St</td>
<td>28.3</td>
<td>63.7</td>
<td>7.5</td>
</tr>
<tr>
<td>Hyde Park</td>
<td>11.9</td>
<td>18.3</td>
<td>1.3</td>
</tr>
</tbody>
</table>

Significant differences (*p* < 0.01) with significance indicated.

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?

Children’s Health Study, Gauderman et al, NEJM 2004

More children with FEV1 < 80% in areas with poor air quality.
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

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

Swiss study on Air Pollution and Lung Disease in adults

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

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


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

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)