Nanoparticles: health hazards and risks

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Conclusions
• There is no evidence on the significant health and environmental risks concerning nanotechnology
• Previous knowledge on aerosols predicts risks that needs to be considered

• Importance of the particle size: surface area, penetration to human body
• Importance of the composition: solubility, surface composition
• Importance of the shape: Characteristics of fibres

• Challenges on occupational hygiene: novel experimental techniques and expertise on new properties
• Protection needs particle characterisation

Six messages
1. Nanoparticles are not new
2. Occupational nanoparticles are present in many environments
Background aerosol in a cast iron foundry

Emissions from arch welding processes

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3. Health risks of aerosols are real
**Quartz**

- Micrometer sized
- Inflammation, cell damage, fibrosis, tumors
- Surface area (strongly reactive), formation of free radicals
- Other mineral particles may cause lung damage in high concentrations (overloading), probably due to surface area.

**Asbestos**

- Fibres with length at least 3 x thickness
- Small diameter: penetration to deep lungs
- Length more than 15 µm: Not transported by macrophages
- Asbestosis, lung cancer, mesothelioma, tumors
- Main properties solubility and surface activity

**Ambient air**

Soot and SO$_2$ annual concentrations 1984-1996

Clancy et al., Lancet 2002;360:1210-14
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Cardiovascular and respiratory mortality 1984-1996

Clancy et al., Lancet 2002;360:1210-14

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Ambient air

- Most particles ultrafine (nanoparticles)
- Epidemiologic research indicate links between fine particles and respiratory and cardiovascular diseases
- 10 µg/m³ increase in concentration causes ca. 1% increase in cardiovascular diseases
- Note! Particles mostly non-toxic such as ammonium salts or carbon
- Explanation: transition metals in surfaces producing radicals or just large surface area causing oxidizing stress

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What causes harmful effects?

- **Inflammation reactions**: in respiratory system, hearth and/or blood circulation
- **Micro-coagulation of blood**:
- **Autonomic reflex**: respiratory symptoms, lower exhale efficiency, changes in hearth electrical functioning
- **Cell damages in respiratory system**: increased risk for cancer

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4. Why would size matter?
5. Exposure to synthetic nanoparticles

Now significant production of:
- Titanium dioxide
- Black carbon
- Zinc oxide
- Iron oxide

Near future
- Nanotubes: research institutes and industry
Nanoparticles and -tubes

• Important, as estimated to exist in first consumer products
• Toxicity:
  – Surface area
  – Surface chemical activity
  – Physical size: -penetration to tissues and organs
  – Solubility
• CNT:
  – Fibre structure and small size
  – Persistency in lungs
  – Surface iron or other metals: catalytic effect

6. Health risks of synthetic nanoparticles

Main open questions:

• Are engineered nanoparticles harmful and how harmful?
• Main sources and emissions?
• Health relevant properties and measurables?
  – What type of detectors and instruments should be used in determining exposure?
• Chain: emission-concentration-exposure-dose-effect
Airway exposure to silica coated TiO2 nanoparticles induces pulmonary neutrophilia in mice.


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Pulmonary inflammation in mouse lungs after TiO2 exposure

• None of the nanoTiO2 preparation tested, other than SiO2 coated rutile, elicited pulmonary inflammation in mice !!!
• Exposure to nanoSiO2 did not induce any inflammatory effects !!!

Hypothesis

Inhalation exposure to silica coated nanoTiO2

Accumulation into the alveolar macrophages
Escape from the membrane bound lysosomes into the cytosol
Interfering proper cell signalling ??
Expression and secretion of proinflammatory cytokines and chemokines
Recruitment of neutrophils and formation of pulmonary inflammation

• Nanoparticle induced lung inflammation could not be explained by the surface area of the particles, their primary or agglomerate particle size or radical formation capacity, but is rather explained by the surface coating.

• Our findings emphasize that it is vitally important to take into account in the risk assessment that alterations of nanoparticles, e.g. by surface coating, may drastically change their toxicological potential.

Carbon nanotubes introduced into the abdominal cavity of mice show asbestos-like pathogenicity in a pilot study


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LETTERS
Female C57Bl/6 mice were intraperitoneally instilled with 50 µg of vehicle control, nanoparticulate carbon black (NPCB), short-fibre amosite (SFA), long-fibre amosite (LFA), two curled/tangled MWNT samples of different lengths (NTtang1, NTtang2) and two samples containing long MWNTs (NTlong1, NTlong2).

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- Different type of nanoparticles may elicit drastic differences in the inflammatory response
- Surface coating may have critical effect to the toxicity of the nanoparticles
- Underlying disease influence significantly to the health effects of nanoparticles. We can not study only healthy people

✓ Be careful with the risk assessment at the moment. We have gained a lot information during the recent few years but our knowledge is still scanty.

✓ However, we have got enough information to be sure that we have to continue research in this area

**Assessment of hazards of CNT**

- There is convincing evidence that CNT induce pulmonary inflammation and associated toxicity
- CNT may have the potential to induce mesotheliomas, but this needs to be confirmed using appropriate exposure route (reaching of MWCNT of pleura has been shown by Hubbs et al. 2009)
- There are data to provide evidence on CNT genotoxicity in vitro and in vivo also requiring confirmation from other studies
- All studies suffer from high doses or in adequate exposure route for risk assessment