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# Potential mechanisms for acute health effects and lung retention of inhaled particles of different origin

**AKADEMISK AVHANDLING**

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# ABSTRACT

**Background:** Environmental particle exposure is known to have negative health effects. There is limited knowledge about how size and origin of particles influence these effects. There is also little known regarding the fate of ultrafine particles (particles in nanosize; < 100 nanometers in diameter) after being inhaled.

**Aim:** The main objective of this thesis was to study acute health effects in humans and their potential underlying mechanisms, resulting from exposure to particles of different origins. Another aim was to develop a method for measuring human lung retention (clearance) of ultrafine carbon particles.

**Methods:** In this human exposure study, twenty healthy volunteers and sixteen individuals with sensitive airways diagnosed with mild asthma were exposed to a subway environment and a control environment for two hours each. Acute health effects in the airways and blood were measured using different markers indicating inflammation, effects on coagulation and lung function. A new exposure method was developed for the study of lung retention of inhaled ultrafine particles. Carbon particles were labeled with radioactive indium-111. The labeling allowed one week of follow up of particulate retention in ten healthy volunteers. One volunteer was followed for totally 29 days.

**Results:** After exposure to a subway environment, healthy individuals had significant increase in fibrinogen (coagulation factor) and regulatory T-cells expressing CD4/CD25/FOXP3 in peripheral blood. In asthmatics we found a statistically significant increased frequency of CD4 cells expressing T-cell activation marker CD25 in bronchoalveolar (lung) lavage fluid but no significant increase of regulatory T-cells in blood.

We developed a method for labeling and generating ultrafine carbon particles with a radioactive isotope indium-111 for use in human studies. A follow-up of healthy volunteers who inhaled the particle aerosol found a limited deposition of particles in the central airways. Seven days after exposure, measured lung retention was 91% at the group level. After correction for free radioactivity leaching from urine and blood samples, respectively mucociliary clearance from the central airways, the cumulative lung-particle retention was approximated to 96%. There was little translocation of particles from the lungs to the blood circulation (0.3%). The volunteer who was followed up for a total of 29 days demonstrated 10% further clearance of particles from the lungs.

**Conclusion:** Healthy individuals and asthma patients display different inflammatory responses following exposure to a subway environment. The health effects were not as pronounced in comparison to our previous studies performed in a road-tunnel environment with similar mass levels of particles with diameters <2.5  $\mu\text{m}$  and <10  $\mu\text{m}$  (PM<sub>2.5</sub> and PM<sub>10</sub>), but with a higher number concentration of ultrafine particles, nitrogen monoxide and dioxide than in the subway. The different results show that health-risk assessment cannot be based solely on mass concentration information such as PM<sub>2.5</sub> and PM<sub>10</sub>. More complex measurements of particles are needed, and should include the number concentration levels of ultrafine particles as well as knowledge about the source of the particles. Results from deposition and retention studies indicate limited translocation to circulating blood in healthy lungs during the first week, with faster clearance from central lung regions compared to the peripheral regions. This is probably due to mucociliary clearance from the larger airways.

**Keywords:** Particulate air pollution, human exposure, inflammation, retention, translocation

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