

Schulz H. / GSF-Forschungszentrum für Umwelt und Gesundheit

### **Cardiovascular effects of nanoparticles**

---

Over the past decades epidemiological and toxicological studies have provided a body of evidence that elevated levels of ambient particulate air pollution are associated with increased cardiovascular morbidity and mortality. Various cardiovascular risk factors, i.e. elevated heart rate, decreased heart-rate variability, arterial vasoconstriction, augmented systolic blood pressure, and increased plasma viscosity were associated with ambient particle exposure. These changes may result in detrimental consequences for cardiac function, especially in patients with ischemic heart disease, cardiac arrhythmias, and congestive heart failure. Related to those findings, recent toxicological studies have put special emphasis on adverse effects mediated by nanoparticles, the environmental source of which are primarily traffic related combustion processes. With increasing commercial interest in nanoparticles or nanotubes, the risks associated with occupational exposure will become a matter of concern. Recent investigations provide evidence that nanoparticles can be quickly translocated from the lungs into the circulation and to secondary target organs, such as liver, heart, spleen, and brain. Therefore, the following mechanisms mediating cardiovascular effects of inhaled nanoparticles are postulated: (A) pulmonary and/or systemic inflammatory responses leading to endothelial dysfunction and a pro-coagulatory state, (B) direct interactions of translocated nanoparticles with endothelium and/or blood constituents promoting thrombogenesis, (C) dysfunction of the autonomic nervous system mediated by direct reflexes from intrapulmonary receptors and/or by local or systemic inflammatory stimuli, (D) cardiac malfunction due to ischemic responses in the myocardium and/or altered ion-channel functions in myocardial cells. Available data from experimental particle instillations and in-vitro studies are supportive of hypothesis (A) and give evidence for inflammation-mediated enhanced thrombus formation and aggravation of atherosclerotic lesions. In a study designed to specifically address hypothesis (B), we were recently able to demonstrate that intra-arterial application of nanoparticles significantly enhances platelet accumulation on the venular endothelium of healthy mice. Particle-induced platelet adhesion was strongly associated with deposition of fibrin and increased expression of von-Willebrand factor on the endothelial surface. Inflammatory parameters were not elevated, indicating that nanoparticles may have the potential to exert a pro-thrombotic effect in the vascular system without triggering inflammatory processes. To examine the hypothetical pathway (C) – dysfunction of the autonomic nervous system in response to nanoparticle inhalation – heart rate and heart-rate variability were studied in rats during a 24h exposure to carbonaceous nanoparticles. A mild but consistent increase in heart rate with a significant associated decrease in heart-rate variability was observed. These results point to a particle-induced alteration of cardiac autonomic balance, which is mediated by a sympathetic stress response. In summary, the current toxicological evidence is clearly supportive of adverse cardiovascular effects arising from nanoparticle exposure, but the available data are as yet too scarce to provide a comprehensive understanding of the different pathophysiological pathways involved.

[back to index](#)