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DIFFERENTIAL SPATIAL DISTRIBUTION OF SYNTHETIC NANO- AND MICRO-PARTICLES EXPLAINS THE EFFECTS ON CARDIOVASCULAR FUNCTION – IMPLICATIONS FOR AIR POLLUTION HEALTH EFFECTS

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Particulate matter (PM) air pollution presents a major environmental and public health challenge because of its non-uniform size distribution and chemical composition. Air quality regulations generally categorize particulate matter (PM) size into PM_{10}, $PM_{2.5}$, and ultrafine particles (UFPs) with aerodynamic diameters smaller than 10, 2.5, and 0.1 µm, respectively. We examined the differential impact of particle size per se on selected organ systems using a custom whole-body mouse exposure system using synthetic PM (SPM). The micrometer-sized SPM accumulated in the lungs as the primary entry organ, while ultrafine SPM showed less accumulation, implying a transition into circulation. Micro SPM-exposed mice exhibited inflammation and NADPH oxidase-derived oxidative stress in the lungs. Ultrafine SPM-exposed mice did not show oxidative stress in the lungs but rather at the brain, heart, and vasculature levels. Endothelial dysfunction and blood pressure increase were more pronounced in ultrafine SPM exposed mice, supported by increased endothelin-1 and decreased endothelial nitric oxide synthase expression, enhancing constriction and reducing vasodilation. To derive a preliminary estimate of the cardiovascular disease burden of UFPs in humans, we used new high-resolution exposure data at a global scale, and applied hazard ratios from an epidemiological cohort study. We derived a UFP-associated incidence of 419 (95% CI 78–712) thousand cardiovascular disease cases per year in the European Union and 5.6 (95% CI 1.1–9.3) million globally. This work provides novel insights into the different toxicological profiles of inhaled ultrafine particles and public health consequences of exposure, guiding future studies.