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TITLE: SYSTEMIC EFFECTS OF INHALED ULTRAFINE PARTICLES IN TWO COMPROMISED, AGED RAT STRAINS.

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ABSTRACT: Epidemiological studies associate morbidity and mortality with exposure to particulate air pollution in elderly individuals with existing cardiopulmonary disease. These associations led to the hypothesis that inhaled particles can exert adverse effects outside of the lung, particularly on the cardiovascular system. We tested this hypothesis by examining the pulmonary and peripheral effects of inhaled ultrafine carbon particles in old rats that were injected with endotoxin (lipopolysaccharide, LPS) to model systemic gram-negative bacterial infection. Fischer 344 rats (23 mo) and spontaneously hypertensive (SH) rats (11-14 mo) were injected with LPS (2 mg/kg, i.p.) immediately before being exposed to inhaled ultrafine carbon particles for 6 h (150 microg/m³, CMD = 36 nm). Controls were injected with sterile saline or were sham exposed. Twenty-four hours after LPS injection, bronchoalveolar lavage (BAL) fluid, cells, and blood were obtained to assess endpoints of inflammation, oxidant stress, coagulability, and the acute-phase response. LPS did not cause an influx of neutrophils (PMNs) into the alveolar space, but did increase the number and percentage of circulating PMNs and the concentration of plasma fibrinogen in both rat strains. Inhaled ultrafine particles did not induce lung inflammation in either rat strain. In both strains, ultrafine particles (UFP) were found to decrease the number of blood PMNs, increase the intracellular oxidation of a fluorescent dye (DCF₂) in blood PMNs, and affect plasma thrombin-anti-thrombin (TAT) complex and fibrinogen levels. UFP were also found to interact with ip LPS with respect to plasma TAT complex levels and blood PMN DCF₂ oxidation. Differences between the two rat strains were also found for TAT complex levels, BAL cell reactive oxygen species release, and DCF₂ oxidation in both BAL macrophages and blood PMNs. These results suggest that inhaled ultrafine carbon particles inhaled at concentrations mimicking high episodic increases in urban air can exert extrapulmonary effects in old rats and that they can change the systemic response to an inflammatory stimulus.