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TITLE: PULMONARY INFLAMMATORY RESPONSE TO INHALED ULTRAFINE PARTICLES IS MODIFIED BY AGE, OZONE EXPOSURE, AND BACTERIAL TOXIN.

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ABSTRACT: Epidemiological studies demonstrate associations between increasing levels of ambient particles and morbidity in the elderly with cardiopulmonary disease. Such findings have been challenged partly because particles may not act alone to cause these effects. We hypothesized that carbonaceous ambient ultrafine particles and ozone can act together to induce greater oxidative stress and inflammation in the lung than when administered alone and that these effects would be amplified in the compromised, aging lung. Two models of a compromised lung were used: endotoxin priming and old-age emphysema (TSK mice). Young (10 wk) and old (22 mo) male F344 rats and male TSK mice (14-17 mo) were exposed to ultrafine carbon particles (count median diameter 25 nm, 110 micrograms/m³) and to ozone (1 ppm) alone and in combination for 6 h. Inhalation of low-dose endotoxin (70 and 7.5 units estimated alveolar deposited dose in rats and mice, respectively) was used to model respiratory-tract infection. Cellular and biochemical lavage parameters and oxidant release from lung lavage cells were assessed 24 h after exposure. Inflammatory cell influx into the alveolar space was observed for both species and age groups: The combination of inhaled ultrafine carbon and ozone after endotoxin priming resulted in the greatest increase in lavage-fluid neutrophils. In general, the unstimulated and stimulated release of reactive oxygen species (ROS) from lavage inflammatory cells correlated well with the neutrophil response. There were significant effects of carbon particles as well as a consistent interaction between carbon and ozone as determined by analysis of variance (ANOVA). However, this interaction was in the opposite direction in young rats versus old rats and old TSK mice: Carbon and ozone interacted such that ROS activity was depressed in young rats, whereas it was enhanced in old rats and old TSK mice, indicating age-dependent functional differences in elicited pulmonary inflammatory cells. These results demonstrate that ultrafine carbonaceous particles inhaled for short periods of time can induce significant pulmonary inflammation and oxidative stress that are modified by age, copollutants, and a compromised respiratory tract.