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TITLE: ACUTE PULMONARY EFFECTS OF COMBINED EXPOSURE TO CARBON NANOTUBES AND OZONE IN MICE

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ABSTRACT: Ozone (O₃) is a well-investigated gaseous air pollutant known to produce acute and chronic toxicity in the respiratory system. Whether prior exposure to nanoparticles influences the toxicity of O₃ has not been well investigated. To determine if there are toxicological interactions between particulate and gas exposures, we examined acute pulmonary effects of a 3-h ozone exposure (0.5 ppm) in female C57Bl mice that had been preexposed to a single dose of 20 μg multiwall carbon nanotubes (CNT) by pharyngeal aspiration 12 h earlier. A total of four groups were compared: (1) PBS/air-control, (2) PBS/O₃, (3) CNT/air, and (4) CNT/O₃. Analyses of the bronchoalveolar lavage fluid (BALF) and lung tissue samples collected at 5 and 24 h post O₃ exposure were performed for various markers of cytotoxicity and inflammation using standard enzyme-linked immunosorbent assay (ELISA) and immunoblot procedures. The results showed a pronounced cellular response and increase in various cytotoxicity/inflammatory markers in the lungs of CNT-exposed mice. Ozone by itself produced minimal effects, but in CNT-exposed animals there was a significant increase in total bronchoalveolar lavage (BAL) cells and polymorphonuclear leukocytes. Additionally, protein, lactate dehydrogenase (LDH), tumor necrosis factor (TNF)-α, interleukin (IL)-1β, and mucin levels in BALF at 5 and 24 h were higher in CNT-exposed animals than in corresponding air-exposed controls or animals exposed to O₃ alone. A comparable increase over the controls was also observed in the CNT/O₃ group, but neither an additive nor a synergistic interaction was observed in mice that received sequential exposure to CNT and ozone. In fact, some CNT-induced cytotoxic/inflammatory responses were attenuated in mice following exposure to both CNT and low levels of ozone. These results are contrary to enhanced responses that were anticipated and may represent the development of "cross-tolerance" reported by others for some sequentially administered pollutants.