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TITLE: SHORT-TERM INFLAMMATORY RESPONSES FOLLOWING INTRATRACHEAL INSTILLATION OF FINE AND ULTRAFINE CARBON BLACK IN RATS.

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ABSTRACT: Ultrafine carbon black (ufCB) 14 nm in diameter and fine carbon black (CB) 260 nm in diameter were instilled intratracheally in rats at mass of 125 microg, and the bronchoalveolar lavage (BAL) profile at 6 h was assessed. UfCB generated a 50% neutrophil alveolitis 6 h after intratracheal instillation compared to CB, which showed similar activity to the phosphate-buffered saline (PBS) vehicle control. UfCB instillation also produced a marked increase in lactate dehydrogenase (LDH) levels in BAL fluid, which was associated with increased epithelial permeability measured as total protein. In contrast, CB had much less of an effect in increasing BAL protein. Although both particle types caused a decrease in glutathione (GSH) in lung tissue compared to control, the greatest depletion was seen in ufCB-treated animals. To investigate time response, bronchoalveolar lavage was carried out at 6 h, 24 h, and 7 days after a single 125-microg instillation of ufCB. Neutrophil influx was relatively persistent and was still maintained 7 days later. Tumor necrosis factor (TNF) production by BAL leukocytes increased gradually postinstillation, whereas NO production became significantly higher at 24 h after instillation and remained at raised levels up to 7 days. Higher doses of CB caused more inflammation than the ufCB. Thus, in the instillation model, a localized dose of particle over a certain level causes the particle mass to dominate the response, rather than the surface area. In contrast to the effect of CB, which showed a dose-related increasing inflammatory response, ufCB at the highest dose caused less of a neutrophil influx than at the lower dose. Six hours after intratracheal instillation, the threshold dose for neutrophil influx occurred at 50 microg. Calculation of surface area of particles instilled suggested that this was likely to be an overload-inducing dose of particles, as gauged from recent experiments with inhaled particles. In summary, this study provides evidence in a rat instillation model that ufCB has greater ability than CB to produce lung inflammation and oxidant stress at a relatively low dose of 125 microg. At high doses, however, BAL is not a reliable indicator of pulmonary response, since the overall response seems to scale to mass or volume of instilled particulate without an influence of surface area.