

AUTHORS: Lambert AL, Mangum JB, DeLorme MP, Everitt JI.

TITLE: ULTRAFINE CARBON BLACK PARTICLES ENHANCE RESPIRATORY SYNCYTIAL VIRUS-INDUCED AIRWAY REACTIVITY, PULMONARY INFLAMMATION, AND CHEMOKINE EXPRESSION.

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ABSTRACT: Exposure to particulate matter (PM) may exacerbate preexisting respiratory diseases such as asthma, chronic obstructive pulmonary disease (COPD), bronchitis, and pneumonia. However, few experimental studies have addressed the effects of PM on lower respiratory tract (LRT) viral infection. Respiratory syncytial virus (RSV) is a major etiological agent for LRT infections in infants, the elderly, and the immunocompromised and may lead to chronic wheezing and the development of asthma in children. In this study, we examined the effects of carbon black (CB) on RSV-induced pulmonary inflammation, chemokine and cytokine expression, and airway hyperresponsiveness in a mouse model of RSV. Female BALB/c mice were instilled via the trachea (i.t.) with 1×10^6 plaque forming units (pfu) RSV or with uninfected culture media. On day 3 of infection, mice were i.t. instilled with either 40 micro g ultrafine CB particles or with saline. End points were examined on days 4, 5, 7, and 14 of RSV infection. Viral titer and clearance in the lung were unaffected by CB exposure. Neutrophil numbers were elevated on days 4 and 7, and lymphocyte numbers were higher on days 4 and 14 of infection in CB-exposed, RSV-infected mice. CB exposure also enhanced RSV-induced airway hyperresponsiveness to methacholine, bronchoalveolar lavage (BAL) total protein, and virus-associated chemokines monocyte chemoattractant protein (MCP-1), macrophage inflammatory protein (MIP-1 alpha), and regulated upon activation, normal T cell expressed and secreted (RANTES). MIP-1 alpha mRNA expression was increased in the alveolar epithelium, where ultrafine particles deposit in the lung. These data demonstrate a synergistic effect of ultrafine CB particles on RSV infection, and suggest a potential mechanism for increased respiratory infections in human populations after PM exposure.