ALTERATION OF PULMONARY IMMUNE/INFLAMMATORY RESPONSES BY DIESEL EXHAUST PARTICLES (DEP)

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This research was carried out to characterize the alteration of pulmonary responses to bacterial infection by DEP and the effect of DEP on alveolar macrophage (AM) function using a rat model. In vitro studies showed that DEP activated AM to release reactive oxygen species, but had little or no effect on AM secretion of IL-1 and TNF-α. However, when AM were challenged with 0.1 μg/ml lipopolysaccharide (LPS), DEP markedly inhibited the LPS-stimulated cytokine production. This inhibitory effect was attributed to the organic component of DEP. The in vitro results were confirmed in animal studies at several exposure doses (intratracheal, 5 and 35 mg/kg body weight) and exposure times (1, 3, and 7 days). Using *Listeria monocytogenes* as a bacterial model for cell-mediated immune studies, rats were exposed to DEP (5 mg/kg) or saline for 3 days and then intratracheally infected with 5000 *L. monocytogenes*. The results showed that pulmonary bacteria killing at 7 days post-*Listeria* exposure was significantly compromised in DEP-exposed rats but not in rats exposed to saline. Cellular measurements showed that DEP-exposure alone resulted in increased cell counts of AM and neutrophils at 3 and 5 days post-exposure. *Listeria* had no effect on cell counts, but the combined DEP and *Listeria* exposure resulted in a decrease in these phagocytes compared to the sum of their individual effects. In addition, AM showed increased production of nitric oxide in response to *Listeria* infection. In DEP-exposed rats, however, the *Listeria*-stimulated NO production by AM was abrogated at all time points. These results suggest that AM secretion of NO may play an important role in the host defense mechanism. By inhibiting AM function, DEP may increase the susceptibility of the lung to bacterial infection. Our preliminary studies also showed that DEP lowered IFN-γ mRNA levels from cells isolated from pulmonary lymph nodes. The potential that DEP suppress cellular but enhance humoral immune responses through alteration of macrophage function is currently under investigation. (NIH 1RO1 HL6263001A1)

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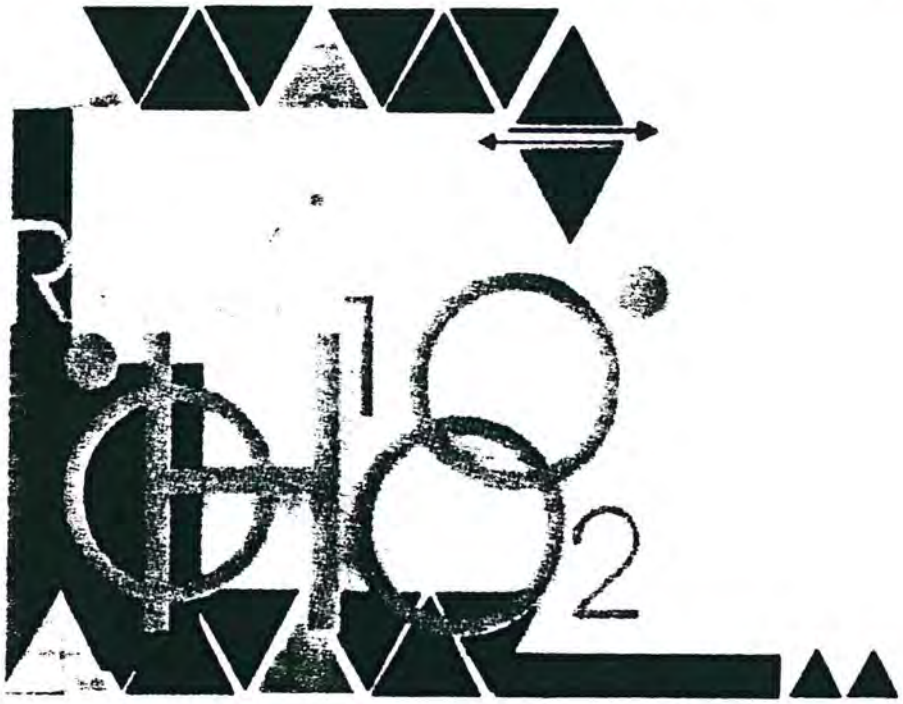

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