Dominance of Nitrogen Dioxide Toxicity in the Biological Effects of Inhaled Diesel Exhaust

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Automotive emission particles and gases such as nitrogen dioxide (NO_2) are implicated in adverse health impacts. To determine relative contributions of NO_2 and particles, the exhaust was treated through a diesel oxidation catalyst (DOC) to remove NO_2 and a HEPA filter to remove particles. Fisher rats were exposed by inhalation for 4h to clean air, untreated exhaust (particles, 0.25mg/m^3; particle count mode, 70nm; CO, 6ppm; NO, 44ppm; NO_2, 4ppm), DOC exhaust (particles, 2mg/m^3; particle count mode, 100 nm; CO, 0.5ppm; NO, 18ppm; NO_2, <0.1ppm), or DOC/HEPA exhaust (particles, <0.0001mg/m^3; CO, NO and NO_2 unchanged from DOC exhaust). Animals were euthanized 2h or 24h post-exposure. Exposure to the untreated exhaust resulted in acute lung injury characterized by increased lung lavage neutrophilia 24h post-exposure and elevated gene expression of interleukin-6, prostaglandin synthase and metallothionein 2h post-exposure. Exposure to DOC exhaust or to DOC/HEPA exhaust did not result in lung injury nor affected a wide panel of clinical (hematology, transaminases, creatine kinase, lactate dehydrogenase etc), biochemical (lung lavage and plasma cytokines, endothelins), and gene expression (inflammation, xenobiotic metabolism, oxidative stress and vasoregulation in lung and heart) endpoints. Delivery of particles in animals inhaling DOC exhaust was confirmed by dark lung macrophages, which was absent from animals exposed to DOC/HEPA exhaust or clean air. Inhalation of diesel emission particles (2mg/m^3, 4h) from the DOC exhaust (NO_2 <0.1ppm), almost two orders of magnitude higher than the Canada Wide Standard for $PM_{2.5}$ (30µg/m^3, 24h average) or the US National Ambient Air Quality Standard (35µg/m^3, 24h average) was not sufficient to cause frank biological effects in healthy rats. The data suggest that the toxic potency of inhaled diesel emissions, and the potency of fresh diesel emission particles may be dominated by effects of NO_2.

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