Acute exposure to air pollution aggravates acute myocardial infarction and subsequent ischemic heart failure in mice

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Purpose: Clinical, but not experimental evidence has suggested that exposure to air pollution particulate matter (PM) aggravates myocardial infarction (MI) in humans. Here, we aimed to describe mechanisms and consequences of an acute PM exposure in an experimental mouse model of MI.

Methods and Results: C57BL/6J mice were exposed to an air pollution particulate matter (PM) surrogate (Residual Oil Fly Ash) by intranasal installation, prior to surgical permanent ligation of the left anterior descending coronary artery (LAD). Mice exposed to PM showed exaggerated ischemic heart failure with decreased fractional shortening and diastolic dilatation in echocardiography 6 month after MI. Histological analysis demonstrated an increase in the infarct area by 45 ± 12 % and enhanced inflammatory cell recruitment into the myocardium of PM-exposed mice 6 days after MI. Augmented cell recruitment was caused by increased activation of circulating myeloid and vascular endothelial cells. Consistently, PM exposure increased leukocyte recruitment a model of sterile peritonitis and in intravital microscopy. Mechanistically, PM exposure potentiated levels of circulating pro-inflammatory cytokines, such as of TNF-α by up to 327 ± 100 %. Increased activation of endothelial cells and leukocytes could be reversed by TNF-α antibody blockade. We identified alveolar macrophages as primary source of elevated cytokine production. Accordingly, *in vivo* depletion of lung macrophages by clodronate inhibited cytokine secretion, while lymphocyte-free $Rag1^{-/-}$ mice where susceptible to PM, indicating that macrophages, but not lymphocytes, are the cause of the inflammatory response following air pollution.

Conclusion: Our data demonstrate that an acute exposure to environmental PM worsens MI and its clinical outcome in mice. These findings provide a novel functional link between air pollution and inflammatory pathways, and emphasize the importance of environmental factors in cardiovascular disease.