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THE EFFECTS OF METALS ON INNATE LUNG DEFENSE MECHANISMS

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Epidemiological studies have demonstrated that inhalation of increased levels of metal-containing particulate air pollution may exacerbate preexisting health conditions and augment pulmonary infection. The objective of this paper is to review the animal studies which have examined the effect of metals that are associated with inhaled particulates on innate lung defense responses. Animal infectivity models have been developed as a means to determine the mechanisms by which inhaled toxicants may affect lung defenses against infection. Due to the prevalence of different metal-containing particulates in the environment and workplace, numerous animal studies have evaluated the effects of agents such as fly ash, concentrated ambient air particulates, and welding fumes on lung defense mechanisms. The alveolar macrophage is the primary lung cell responsible for non-specific innate pulmonary host defenses. Toxicological evidence indicates that metals associated with different occupational and environmental particulates may alter macrophage function and increase the susceptibility to lung infection. Changes in macrophage phagocytosis and the production of reactive oxygen and nitrogen species have been observed. In addition, the macrophage secretion of pulmonary cytokines, which are important in immune cell responses, has been shown to be affected by metal-containing particulates. Recent evidence suggests that the soluble metal fraction of specific environmental particulates is responsible for the alterations observed in lung immune responses. Studies are ongoing in an attempt to assess the role that individual metals (e. g. Cr, Fe, Ni, V, and Mn) may play in suppressing lung defense against infection. With the use of animal infectivity models, it is possible to determine the mechanisms by which metal-containing particulates may suppress lung defenses in order to develop a better understanding of how to prevent adverse health effects and protect susceptible populations at risk.

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PARTICULATE PHAGOCYTOSIS IN THE PATHOGENESIS OF HUMAN DISEASE

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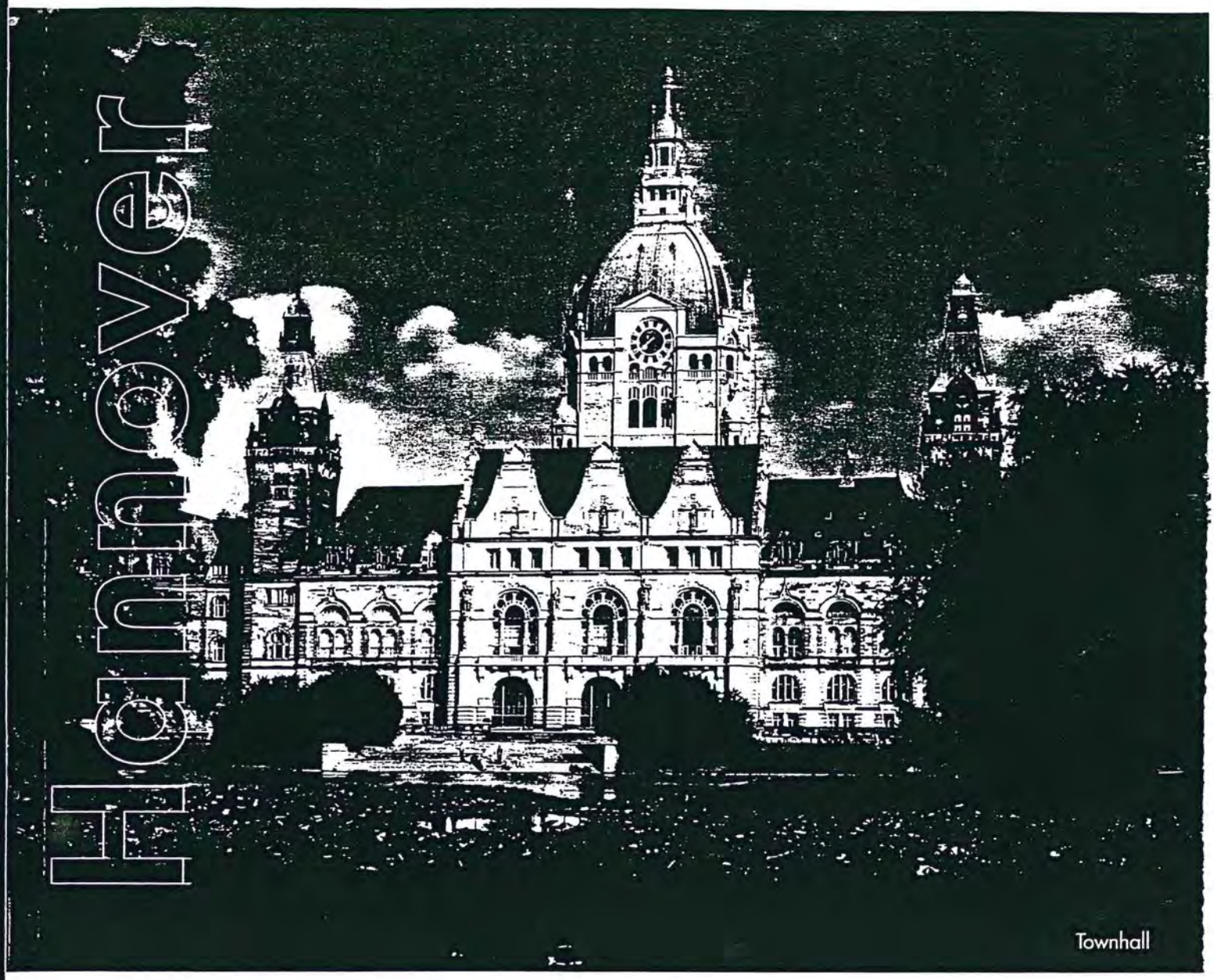
Exposure to ambient air pollution particles has been associated with increased cardiopulmonary morbidity and mortality. Alveolar macrophages (AM) and alveolar/bronchial epithelial cells are primary responsible to phagocytose and process inhaled particles. Alveolar macrophages release tumor necrosis factor ά (TNF-ά) in a dose dependent manner when exposed to ambient particles. They also produce a variety of other mediators including IL-1β, IL-6, IL-8, MIP-1ά and GM-CSF. Bronchial and alveolar epithelial cells also produce a variety of mediators when they phagocytose ambient particles that include IL-1, IL-8, GM-CSF, LIF, TNF and RANTES. Interaction of AM and epithelial cells amplified their mediator release. These mediators contribute to the local inflammatory response in the lung induced by exposure to particles. Some of these mediators (IL-1β, IL-6 and GM-CSF) also contribute to the systemic inflammatory response induced by exposure to particles. We conclude that phagocytosis of inhaled ambient particles by lung cells induces both a local as well as a systemic inflammatory response and we propose that these responses contribute to the adverse cardiopulmonary health effects associated with exposure to air pollution.



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