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Final Report. Toxicity Of Selected Particulates To Alveolar Macrophages

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16. Abstract (Limit: 200 words)

The effects of metals on alveolar macrophage function were studied in-vitro. Cadmium (7440439) (Cd), mercury (7439976) (Hg), nickel (7440020) (Ni), lead (7439921) (Pb), aluminum (7429905) (Al), iron (7439896) (Fe), and chromium (7440473) (Cr) were incubated with alveolar macrophages and effects on oxygen (7782447) consumption, glucose metabolism, lysosomal enzyme release, and release of antibacterial substances were determined. All metals inhibited the rate of oxygen consumption, the release of lysosome enzyme, and glucose metabolism by the macrophages. The metals substantially inhibited the release of antibacterial substances. Hg had the greatest inhibitory effect, followed by Ni, Cd, Pb, Al, Fe, and Cr, in that order. All metals reduced the rate of foreign body ingestion by the cells. The authors conclude that metals inhibit the release of antibacterial substances from alveolar macrophages and have adverse effects on other aspects of cellular function. One adverse effect of metal exposure may be an increased frequency of respiratory infection.

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FINAL REPORT

Title: Toxicity of selected particulates to alveolar macrophages

Alveolar macrophages are free cells found in the alveoli and smaller airways of the lungs. Their function is to ingest foreign particles and bacteria which have been inhaled into the lungs. Many metals found in workplaces, such as mines, smelters, refineries, and recovery operations, are present on airborne particles. Since these particles are extremely small, they may be inhaled into the alveoli of the lungs where alveolar macrophages are located. Therefore, metals may produce increased frequencies of infection and other respiratory diseases via toxic effects on alveolar macrophages. The objectives of this investigation were 1) to develop techniques with which to study the effects of metals on these phagocytic cells and 2) to use these techniques to study metal effects on alveolar macrophage function.

One primary response of alveolar macrophages to inhaled bacteria or particles is the release of antibacterial substances, such as superoxide anion. In order to measure superoxide release in vitro , cytochrone c, a heme protein, must be included in the incubation medium. However, metals bind to cytochrome c. Therefore, another technique must be used to assess the effects of metals on the release of antibacterial substances from alveolar macrophages. We demonstrated that chemiluminescence is a measure of the amount of antibacterial substances released from the cells. Thus, measurement of

chemiluminescence is an effective technique to use in the study of metal effects on alveolar macrophages.

The effects of seven metals, cadmium, mercury, nickel, lead, aluminum, iron, and chromium, on various aspects of alveolar macrophage function were studied. All metals produced an inhibition of oxygen consumption and glucose metabolism in the cells. The metals also produced inhibition of the rate at which particles were ingested by the cells and inhibition of lysosomal enzyme release. However, the metals were most effective at producing inhibition of particle-induced release of antibacterial substances from alveolar macrophages. The order of potency for the metals was mercury > nickel = cadmium > lead = aluminum = iron = chromium. The results of these experiments indicate that metals inhibit the release of antibacterial substances from alveolar macrophages and they are detrimental to other aspects of cellular function. Thus, one harmful effect of exposure to metals may be an increased frequency of respiratory infections.

The publications which appeared as a result of this work are shown below. In addition, ten abstracts were published.

Miles, P.R., P. Lee, M. Thrush, and K. Van Dyke. Chemiluminescence associated with phagocytosis of foreign particles in rabbit alveolar macrophages. Life Sciences. 20: 165-170, 1977.

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Castranova, V., L. Bowman, M.J. Reasor, and P.R. Miles. The effects of heavy metal ions on oxygen metabolism in rat alveolar macrophages. Toxicology and Applied Pharmacology. 53: 14-23, 1980.

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