OXIDANTS, ANTI-OXIDANTS AND MONOKINES IN THE PATHOGENESIS OF COAL WORKERS PNEUMOCONIOSIS (CWP).

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Many studies on mechanisms of fibrogenic lung injury are now focused on oxidant mediated damage. During the inhalation of mineral dusts oxidants ($O_2^{\cdot -}$, H_2O_2 and HOCl) are generated in the lower respiratory tract, primarily due to the activation of inflammatory cells by particles present, in turn regulated by the release of cytokines as interleukin 1 (IL-1) from (mononuclear) phagocytes. After performing a case-control study among silicosis patients and healthy elderly controls (1), we now studied the anti-oxidant system in red blood cells of a group active coal miners with and without CWP. In addition, we compared the release of monokines from peripheral blood monocytes between the healthy and the diseased miners. In summarison, our data suggest:

- that monitoring the anti-oxidant system in red blood cells (or preferably the target-organ) provides an entrance for (early) health effect screening in developing fibrotic lung disease. The most sensitive parameters proved to be GSH, GSSG and the combination of the enzymes glutathione peroxidase and Superoxide dismutase;
- that measuring the endotoxin or mine dust induced release of monokines by blood monocytes is a tool worth studying in prospective studies to evaluate its possible application to identify those individuals susceptible to the fibrogenic effect of coal mine dust.

(1) Borm,PJA, Bast,A, Wouters,EFM et al (1987) Free Radical Res.Comms.3: 117-127.

POTENTIAL ROLE OF SILICON-OXYGEN RADICALS IN ACUTE LUNG INJURY. V. Vallyathan,* X. Shi and N.S. Dalal. *Division of Respiratory Disease Studies, National Institute for Occupational Safety and Health, and Chemistry Department, West Virginia University, Morgantown, WV 26505.

Occupational exposure to silica is associated with the development of acute and chronic silicosis. Chronic silicosis usually becomes manifest 20-40 years after first exposure and is characterized by the development of typical nodular lesions over a period of several decades. Acute silicosis, on the other hand, occurs much less commonly. It is manifested by a rapid onset following exposure and is characterized by a lipoproteinaceous exudate within air spaces. All the reported studies on the pathogenesis of silicosis have been focused on the elucidation of cellular mechanism leading to cell injury and the development of chronic silicosis. Since pulmonary responses to silica differ in the presentation of acute and chronic silicosis, we hypothesized the acute response is associated with some unique properties of dust generated by shearing or grinding as in sandblasting, drilling, tunnelling or mill operations. To test this hypothesis, we mechanically ground silica and measured Si-O$^{\cdot}$ radicals concentration using electron spin spectroscopy. We also studied the generation of $^{\cdot}$OH from Si-O$^{\cdot}$ radicals in biologic buffers and showed the biologic reactivity of freshly ground silica is enhanced substantially compared to aged silica by a greater respiratory burst, increased secretions of superoxide anion, hydrogen peroxide and nitro blue tetrazolium reduction. In addition, the freshly ground silica also induced a greater cytotoxicity by an enhanced ability for lipid peroxidation, greater release of lactate dehydrogenase from alveolar macrophages, and increased lysis of sheep erythrocytes. The results of these studies suggest that freshly fractured silica containing Si-O$^{\cdot}$ radicals leads to the generation of $^{\cdot}$OH radicals which may play a central role in cell membrane damage by the initiation of lipid peroxidation leading to acute silicosis.

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