Early Inflammatory Changes in Lung Following PuO2 or Pu Nitrate Contamination in the Rat

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Increases in cancer incidence and mortality among workers overexposed to alpha-emitting radionuclides, such as plutonium (Pu), have been described with lung tumors of epithelial origin being the most common. However, the question of mechanisms leading to tumor formation following inhalation of radionuclides remains. The main factor controlling tumor incidence seems to be associated with radiation dose distribution, the more homogenous the distribution, the higher the incidence of cancer. In addition, some evidence exists regarding the role of the inflammatory response as a cofactor of tumorigenesis. The present study aims to determine the early inflammatory changes following pulmonary Pu contamination with the insoluble compound, PuO2 or the moderately soluble compound, Pu nitrate. Adult male Sprague-Dawley rats were exposed to PuO2 aerosols using a nose-only inhalation procedure (Initial lung deposit 4.7-43.4 kBq), or received intratracheal administration of Pu nitrate (25 kBq). Fourteen days post contamination, rats were euthanized and bronchoalveolar lavages (BAL) carried out. Activity was measured by liquid scintillation in lungs, femurs and liver. Distribution of activity within lung compartments was also studied. Activation of alveolar macrophages was evaluated by measurement of inflammatory mediators in supernatants collected 24h after plating and intracellular acid phosphatase activity determination, as well as by CD68 immunolabelling on lungs. The higher solubility of Pu nitrate as compared to PuO2 is illustrated by higher activity deposits in skeleton and liver, and lower retention in lungs. However, at this time point, lung distribution does not vary between the 2 compounds, the majority of activity being retained in the cellular fraction of BAL, mainly macrophages. Activation of macrophages is observed in the two groups of contaminated animals, with an enhanced production of TNF-alpha, MCP-1, CINC-1 and MIP-2, and an increased acid phosphatase activity, as compared to sham-contaminated rats. The level of activation was found to be dependant on the initial lung deposit following PuO2 contamination. Our results provide evidence for an early inflammatory response following Pu lung contamination and the role of macrophages whatever the solubility of the Pu compound.

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