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Effect of Chronic Cigarette Smoke Exposure on Lung Clearance of Tracer Particles Inhaled by Rats[1]

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Cigarette smoking can influence the pulmonary disposition of other inhaled materials in humans and laboratory animals. This study was undertaken to investigate the influence of cigarette smoke exposures of rats on the pulmonary clearance of inhaled, relatively insoluble radioactive tracer particles. Following 13 weeks of whole-body exposure to air or mainstream cigarette smoke for 6 hr/day, 5 days/week at concentrations of 0, 100, or 250 mg total particulate matter (TPM)/m³, rats were acutely exposed pernasally to ^{85}Sr-labeled fused aluminosilicate (^{85}Sr-FAP) tracer particles, then air or smoke exposures were resumed. A separate group of rats was exposed to the ^{85}Sr-FAP then serially euthanized through 6 months after exposure to confirm the relative insolubility of the tracer particles. We observed decreased tracer particle clearance from the lungs that was smoke concentration-dependent. By 180 days after exposure to the tracer aerosol, about 14, 20, and 40% of the initial activity of tracer was present in control, 100 mg TPM/m³, and 250 mg TPM/m³ groups, respectively. Body weight gains were less in smoke-exposed rats than in controls. Smoke exposure produced lung lesions which included increased numbers of pigmented alveolar macrophages distributed throughout the parenchyma and focal collections of enlarged alveolar macrophages with concomitant alveolar epithelial hyperplasia and neutrophilic alveolitis. The severity of the lesions increased with smoke exposure duration and concentration to include interstitial aggregates of pigmented macrophages and interstitial fibrosis. Our data confirm previous findings that exposure to cigarette smoke decreases the ability of the lungs to clear inhaled materials. We further demonstrate an exposure–concentration related magnitude of effect, suggesting that the cigarette smoke-exposed rat constitutes a useful model for studies of the effects of cigarette smoke on the disposition of inhaled particles.

Cigarette smoking induces a variety of carcinogenic and noncarcinogenic effects in humans and laboratory animals. One issue of concern is the extent to which smoking might influence pulmonary responses to other inhaled toxic materials. This influence could take the form of a direct alteration of the disposition of another inhaled agent; for example, it has been reported that cigarette smoking delays the pulmonary clearance of inhaled, insoluble particles in humans (Bohning *et al.*, 1982) and in laboratory animals (Mauderly *et al.*, 1989a). In cases in which the relatively insoluble particles contain radionuclides, retarded clearance would increase the radiation dose and could potentially modify the resulting biological effects.

Our laboratory is currently studying potential interactions between chronic cigarette smoke exposure and inhaled $^{239}PuO_2$ in producing lung cancer in rats. As a part of this study, we used relatively insoluble ^{85}Sr-labeled fused aluminosilicate tracer particles (^{85}Sr-FAP) to investigate how an initial subchronic (3 months) whole-body exposure to smoke might influence the ability of the lungs to clear deposited particles under conditions of continued smoke exposure. We performed the present study to determine if cigarette smoke-induced decreased particle clearance would be observed in the rats and, if so, the extent to which decreased clearance was (1) quantitatively similar to previously reported values for rats exposed pernasally to cigarette smoke, (2) dependent on the exposure concentration of smoke, and (3) correlated with histological changes in the lungs.

MATERIALS AND METHODS

Animals. We used 126 male and female F344 rats [CDF (F344)/CrlBR; Charles River Laboratories, Raleigh, NC] 28 ± 3 days of age at receipt. The rats were quarantined and conditioned to the whole-body exposure chambers (H2000; Lab Products, Inc., Maywood, NJ; 12 ± 2 air changes per hour) for 2 weeks after receipt. Food (Wayne Lab Blox, Allied Mills, Chicago, IL) and water were available *ad libitum*. Chamber temperatures were maintained at 24 ± 2°C, humidity at 40 to 70%, and lights on a 12-hr on/off cycle.

During the second week of conditioning, the rats were weighed and randomly assigned to groups by weight (Path-Tox System, Xybion, Cedar

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