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Project Summary

Effects of Sulfur Oxide Pollutants on Respiratory Function, Particle Deposition and Bronchial Clearance

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The effects of sulfur oxide pollutants on respiratory function, particle deposition, and bronchial clearance were explored in a series of three studies, two on donkeys and one on humans. In the first study, the effects of one-hour inhalation exposures to 0.3 - 0.6 μm H_2SO_4 and $(NH_4)_2SO_4$ aerosols in the donkey were studied in terms of alterations in pulmonary flow resistance and dynamic compliance, and changes in the regional deposition and tracheobronchial mucociliary clearance of an inert test aerosol. In the second study, the effect of chronic inhalation exposures to sulfuric acid mist upon mucociliary clearance from the lungs was studied, using the donkey as an analogue for man. Four animals were exposed one hour per day, five days per week, for six months; two to a concentration of 102 μg/m³, the others to 106 μg/m³. In the final study, the mucociliary particle clearance and respiratory mechanics of twelve healthy nonsmokers exposed to ½ μm H_2SO_4 at 0 (control), 100, 300, and 1,000 μg/m³ for one hour per day for four days were examined.

Introduction

This report summarizes the work performed under Contract 68-02-1726 through its termination at the end of January 1979. It includes descriptions of experimental studies on animals which ended on April 15, 1978 and also studies on human volunteers which ended at the end of January 1979

Discussion

The work under this contract was divided into three studies: (1) effects of short-term exposures to sulfuric acid and ammonium sulfate aerosols upon bronchial airway function in the donkey; (2) effect of chronic inhalation of sulfuric acid mist upon mucociliary clearance from the lungs of donkeys; and (3) effects of sulfuric acid aerosols upon mucociliary particle clearance and respiratory mechanics in healthy nonsmoking humans. Each of these studies is described in the following pages

Short-Term Exposures in Donkeys

A series of tests were conducted to study the physiological response of the lungs of four donkeys to H_2SO_4 and $(NH_4)_2SO_4$. The response was characterized in terms of changes in pulmonary flow resistance (R_L), pulmonary compliance (C_L), regional deposition, and mucociliary tracheobronchial clearance. The sulfate

aerosols were in the 0.3-0.6 μm size range.

Measurements of R_L and C_L were performed, using the esophageal ballon technique, following one-hour exposures to $(NH_4)_2SO_4$ at mass concentrations up to 3.0 mg/m^3. No significant change in R_L or C_L was observed; however, normal intra-animal variability was found to be quite large and, depending upon the specific donkey, a 25-40% change in R_L and 10-20% for C_L would have to occur before any change could be considered significant.

Mondisperse, insoluble ferric oxide aerosols tagged with a γ-emitting isotope, were used to monitor any changes in regional deposition and clearance induced by exposure to the sulfur oxides.

The relative tracheobronchial tree vs. alveolar distribution of ferric oxide was not altered by prior, one-hour inhalations of up to 3.1 mg/m^3 $(NH_4)_2SO_4$ or up to 1.4 mg/m^3 H_2SO_4. The lack of measurable effect upon deposition supports the lack of measurable effect upon R_L, since both indices would be affected by alterations in bronchial calibre.

Mucociliary clearance of ferric oxide was not affected by one-hour exposures to $(NH_4)_2SO_4$ at concentrations up to 1.6 mg/m^3. However, significant effects were observed following one-hour exposures to H_2SO_4. The responses differed in the different donkeys. Two of the four animals exhibited a progressive change in the control rate of clearance during the course of the year-long series of ~12 one-hour exposures to H_2SO_4 exposures.

The other two animals exhibited a definite, short-term slowing of clearance following single exposures to submicron H_2SO_4, but had no changes in clearance in control tests There was however, considerable inter-individual variability in response at comparable exposure levels, with one donkey responding at concentrations $\geq$~700 μg/m^3 and the other responding as low as 194 μg/m^3. The short-term effect of H_2SO_4 upon clearance does not become apparent until ~30 minutes following initiation of acid exposure.

Chronic Inhalation in Donkeys

The chronic exposure study involved the inhalation exposure of four donkeys via nasal catheters to 100 μg/m^3 of submicrometer H_2SO_4 for one-hour per day, five days per week for six months.

The animals were studied in pairs, with the initial series of chronic exposure tests being done on Donkeys Ethel and Gus. They had both exhibited transient, but no persistent effects following single one-hour exposures. The second series was done on Donkeys Kevin and Leon, who had not previously been exposed to any inhaled irritants. Each individual animal had a characteristic clearance rate which was quite reproducible on repeated test runs in the pre-exposure control series.

In all four animals, clearance times became erratic within the first week of exposure to the sulfuric acid mist, with the rate becoming significantly different from control on many test days. However, the degree and the direction of change in rate differed to some extent in the different animals.

Among the four animals, the most dramatic response was shown by Donkeys Leon and Kevin; of these two, Donkey Leon demonstrated the most severe effect from the acid exposure.

Donkey Leon exhibited transient slowing and speeding of clearance during the first two months of acid exposure. However, these transient slowdowns became more severe, and beginning in the fifth month and continuing until the end of the exposure series, a sustained impairment of clearance occurred, and clearance remained abnormal throughout four months of follow-up measurements.

Donkey Kevin initially showed some transient slowing, but appeared to have returned to within normal limits during the first month of exposure. However, beginning within the fourth month, clearance became erratic and exhibited a progressive sustained slowing until the end of the exposure series, with abnormal clearance persisting throughout the four month follow-up after the termination of exposure.

Donkey Gus exhibited transient clearance slowdowns during the first three months of acid exposure, but returned generally to within normal limits after this period. The magnitude of clearance slowdowns in the last three months was much less than during the initial three months. Occasional excursions were observed during the follow-up period, with most tests tending towards the lower limit of normal clearance time.

Donkey Ethel also exhibited some transient slowdowns; however, the general trend was towards an accelerated rate of clearance beginning at about the third month of acid exposure. Subsequently, she exhibited clearance which was faster than that of her pre-exposure average in all but one test performance during the follow-up period

The sustained, progressive slowing of clearance observed in Donkeys Kevin and Leon, two initially healthy and previously unexposed animals, is a very significant observation, since any persistent alteration of normal mucociliary clearance can have important pathological implications.

Aerosol Effects in Humans

Twelve healthy nonsmokers inhaled ½μm (σ_g = 1.9) H_2SO_4 at 0 (control), 100, 300 and 1,000 μg/m^3 for one hour via nasal mask in random sequence on four separate days. Respiratory mechanical function was assessed by body plethysmography, partial forced expiratory maneuver and nitrogen washout before and ½, 2 and 4 hours after the H_2SO_4 exposure. A *99m*Tc tagged Fe_2O_3 aerosol (7.5 μm AMAD, σ_g = 1.1) was inhaled ~10 min. before each H_2SO_4 exposure, with flow rate = 1.0 lps, tidal volume = 1 liter and breathing rate = 15/min. Lung retention of the deposited radioactivity was monitored by two 12.5 x 5 cm D.NaI scintillation detectors located within cylindrical collimators and placed externally over the right mid-lung field. A tracheal probe containing six rectangular (1 x 4 x 2.75 cm) collimated scintillation detectors was used to determine the tracheal mucus transport rates (TMTR's) of boli of activity

No consistent changes in respiratory mechanics were observed following H_2SO_4 exposure at any level, but mucociliary clearance was markedly altered. In individuals whose control run tracheobronchial clearance half-times ($TB_{1/2}$) were greater than the mean, there was an increased rate of bronchial clearance ($\Delta TB_{1/2}$ = -56 min., $p \leq 0.01$) following exposure to 100 μg/m^3. Following exposure to 1,000 μg/m^3, clearance was slowed ($\Delta TB_{1/2}$ = +60 min., $p \leq 0.05$). At 300 μg/m^3 there was a wide range of response with increases in some and decreases in others. The TMTR's for this group increased significantly ($p \leq 0.09$) with increasing concentration. On the other hand, for the individuals with faster than average control run clearance rates, their $TB_{1/2}$'s were unchanged following exposure at all three concentrations, while their

TMTR's decreased with increasing concentration ($p \leq 0.10$). Thus, brief exposures to submicron sulfuric acid at concentrations that may be encountered in both the ambient and occupational environments can affect mucociliary clearance, an important pulmonary defense mechanism.

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The complete report, entitled "Effects of Sulfur Oxide Pollutants on Respiratory Function, Particle Deposition and Bronchial Clearance," (Order No. PB 81-168 288; Cost: $8.00, subject to change) will be available only from:
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