EFFECTS OF SULFURIC ACID ON FERRET RESPIRATORY TRACT CLEARANCE

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This study was performed to assess the effects of sulfuric acid inhalation, and partly to examine the potential suitability of the laboratory ferret as a respiratory tract clearance model. Separate groups of ferrets were first exposed nose-only to purified air, 0.5 mg/m^3 of sulfuric acid aerosol, and 1.0 mg/m^3 of sulfuric acid aerosol for 4 h. Following the deposition of radiolabeled tracer microspheres, the clearance rates from the head and chest regions were monitored using collimated radiation detection equipment. The results indicate that (1) neither of the acid atmospheres produced a statistically significant effect on the clearance rate of the head region; (2) the high-acid atmosphere produced a significant acceleration in the clearance rate of the lung region; and (3) the long-term lung clearance rate of the purified air-exposed ferrets was very close to that observed with humans. Also, the ferrets were docile and easy to handle, and seemed to be well suited to this type of study.

INTRODUCTION

Many animal species have been successfully used as models by toxicologists in respiratory tract deposition and clearance studies. Among these are rabbits (Chen and Schlesinger, 1983; Schlesinger, 1990), dogs (Wolff et al., 1981), donkeys (Schlesinger et al., 1979), rats (Kenoyer et al., 1981; Mannix et al., 1983), sheep (Sackner et al., 1981), mice (Fairchild et al., 1975), guinea pigs (Wolff et al., 1986), and hamsters (Harbison and Brain, 1983). When selecting an animal model for a particular clearance study, the investigators must consider many practical factors, including the cost of purchasing and housing (feeding, etc.) the animals, the number of animals that would be required to observe a significant physiological effect, and the ease of performing the measurements. Most im-

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portantly, the anatomical and physiological similarity of the respiratory system of the animal to the human respiratory system, and the availability of healthy animals, are key features for many studies.

If several animal models exist for respiratory tract clearance studies, why should one consider another? Our long-term plans are for studies that include heavy exercise during inhalation exposure, prolonged exposure of young animals with developing lungs, and the study of animals that have infections produced by common human respiratory tract pathogens. Upon investigating the available species of animals bred for laboratory research, the ferret seemed very promising in relation to our long-term interests. The dog would also be very useful for our plans, but its expense and requirement for spacious kennels were serious drawbacks. The rabbit was considered, but concerns over its potential in exercise and developmental studies weighed against that choice.

Although we have traditionally used rats in radiolabeled particle clearance studies, the rat has some problems related to this application. First, it is too small to reliably obtain simultaneous head and chest radiation counts (without cross-interference) following an exposure to tracer particles of a size that deposit throughout the entire respiratory system. Second, the respiratory system of the rat, while not unlike that of the human in cellular makeup, lacks some anatomical structures, such as respiratory bronchioles, that are present in the human and some other mammalian species (Tyler, 1983; Phalen and Oldham, 1983).

The use of ferrets in medical research is not new. The animal has a history of service in studies of distemper, influenza (several strains of human influenza virus infect ferrets), poliomyelitis, and measles, and in endocrinology, cardiology, teratology, and gastroenterology research (Thornton et al., 1979). Recently, the ferret has been increasingly used in chemical toxicology studies (Oldham et al., 1990). Ferrets are considerably less expensive to purchase and house than are many other nonrodent species (dogs, primates, sheep, etc.). However, when compared with rats, ferrets are about four times more expensive to purchase and about five times more costly to house. The ferret is a large enough animal so that radiation emitted by tracer particles deposited in the head and chest regions can be separately measured. Domesticated ferrets are generally friendly, cooperative, and easy to handle (Moody et al., 1985). Healthy ferrets are available from reputable suppliers, and a sufficient number of them can be housed simultaneously without putting an undue burden on animal housing capacities. In preliminary tests in our laboratory, ferrets seemed to adapt well to a moderate level of exercise on a treadmill. Furthermore, their lung development time and lifespan are convenient for both developmental period studies and chronic studies. Most importantly, the ferret has a respiratory bronchiole anatomy and a physiology that are closer to the human than are

those of many other species (Phalen, 1984; Vinegar et al., 1985). The ferret has more submucosal glands in the bronchial wall than the dog (Moody et al., 1985), and a number of respiratory bronchiole generations (three to four orders) that is very similar to the number of generations in humans (three to five orders). Most other species have far fewer generations (rat, essentially no respiratory bronchioles; guinea pig, one order; rabbit, one to two orders; hamster, one order) (Phalen and Oldham, 1983).

In order to gather information on the usefulness of the ferret as a clearance model, a study involving the exposure of groups of ferrets to purified air and to two concentrations of sulfuric acid (H_2SO_4) was performed. The remainder of this paper deals with this study.

MATERIALS AND METHODS

The animals used in this study were ordered from a supplier of high quality laboratory ferrets (Marshall Farms; North Rose, N.Y.). Thirty female ferrets (3 mo of age—all born on the same day; body mass range 450–600 g) were delivered to the laboratory 1 wk before the start of the experiment. The ferrets had been raised by the supplier in sanitary (but not barrier) conditions, and each ferret was examined by a veterinarian at Marshall Farms prior to shipment. Although the animals were certified to be "clinically free of any contagious, infectious, or communicable diseases," they were not designated as "specific pathogen free." At our laboratory the ferrets were housed in a facility (accredited by the American Association for Accreditation of Laboratory Animal Care) supplied with purified air, and they were kept two ferrets per cage ($2 \times 2 \times 2.5$ ft) on a wood chip litter. They were given food (Wayne dry cat food) and water ad libitum, and were kept on a 24-h light cycle (light 7 a.m.–7 p.m.). During our study the ferrets were under the care of a certified animal technician who examined the animals grossly several times a week. No signs of disease were noted. In order to prevent infections, personnel handling ferrets wore clean lab coats, masks, and gloves. It was not feasible to keep the ferrets on our laminar air barrier isolators due to the large size of the cages. We plan to do so in the future to further reduce the risk of infection. Infections are a problem because they may artifactually change (most likely slow) particle clearance rates (Pavia et al., 1980).

The methods used in performing the study were similar to those used in our concurrent rat studies (Mannix et al., 1983; Prasad et al., 1988). Three groups of 10 ferrets each were exposed nose-only to the following atmospheres for 4 h: purified air; 0.5 mg/m^3 H_2SO_4; 1.0 mg/m^3 H_2SO_4. The groups were well matched with respect to body mass. At the start of the study the group mean masses ($\pm$ SE) were as follows: purified air, 563 $\pm$ 23 g; 0.5 mg/m^3 H_2SO_4, 572 $\pm$ 16 g; 1.0 mg/m^3 H_2SO_4,

563 ± 18 g. The relative humidity in each exposure was regulated at about 85%. Nose-only exposure tubes were used in order to provide for the comfort of the ferrets, and to prevent the neutralization of H_2SO_4 by ammonia generated from the ferrets' excreta. The chambers were supplied with air that had passed through coarse particulate filters, gas scrubbers, a humidifier, and a high-efficiency particle filter. When appropriate, H_2SO_4 was injected into the airstream just prior to the exposure chamber. The H_2SO_4 aerosol [about 0.3 μm mass median aerodynamic diameter, geometric standard deviation (GSD) of about 2] was generated by nebulizing an aqueous H_2SO_4 solution using a Collison nebulizer. This particle size was selected for the study because the main mass of sulfate present in the ambient aerosol in many urban and rural areas is in the 0.2–0.6 μm (MMD) size range (Altshuller, 1976). The aerosol was brought to Boltzmann charge equilibrium by passage through a ^{85}Kr aerosol neutralizer. Filter samples collected from an unused exposure port using mass samplers and multistage impactors were analyzed by ion chromatography in order to characterize the H_2SO_4 aerosol.

At the end of the 4-h exposures the ferrets were removed from the exposure chambers and the nose-only tubes were plugged into the wall of the radiotracer deposition system. For 30 min the ferrets inhaled ^{51}Cr-labeled microspheres (activity median aerodynamic diameter = 1.9 μm; GSD < 1.3). A particle size of 1.9 μm was used because particles of this size have been determined to have acceptable deposition fractions (in order to obtain reliable counting data) in the upper respiratory tract and alveolar region of similar-sized species (Schlesinger, 1985a). These tracer particles, which were labeled at this laboratory (Hinrichs et al., 1978), were produced from commercial monodisperse polystyrene latex microspheres, and were generated using a Lovelace-type nebulizer. Immediately following the deposition the ferrets were removed from the deposition system and their muzzles were washed to reduce the quantity of externally deposited particles. The ferrets were then placed into cylindrical plastic counting tubes and were taken to the counting laboratory, where they were positioned into a two-detector ferret counting system that was designed to separately detect radiation emitted by particles deposited in the head (between the tip of the nose and the middle of the trachea) and chest (the lower half of the trachea through the deep lung) regions (Fig. 1).

Each of the 30 ferrets received its first head (nasal and tracheal regions) and chest (lung region) counts within 15 min of the end of the deposition. The ferrets were subsequently counted at each of the following time points postdeposition: 1, 2, 3, 4, 5, 9, 24, 48, 95, 165, 332, 500, and 668 h. The data obtained during the first 24 h were primarily useful in characterizing the head (or nasal) clearance; the data obtained between 48 and 668 h were used to monitor lung clearance. The counting times ranged from 100 s per ferret for the early counts (0–24 h), to

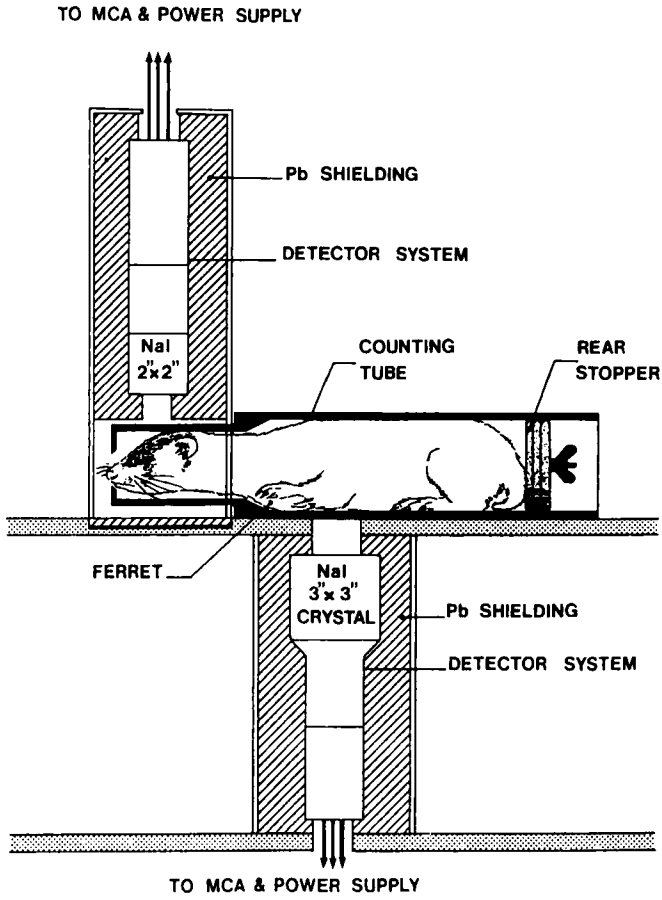

FIGURE 1. Head and chest counters for measuring uncleared tracer particles in laboratory ferrets. An approximate size reference is provided by the NaI crystal dimensions (diameter × thickness).

200 s for the later counts (after 24 h). Since both the head and chest counts were obtained simultaneously, the counting protocol went very smoothly and efficiently.

In addition, six ferrets were selected from the group that was exposed to purified air in order to determine the clearance kinetics of the ferret over a 6-mo period (6.5 times the half-life of the tracer radioisotope, ^{51}Cr). In order to accomplish this, ferrets with relatively large quantities of deposited radioactivity were used, and the radiation detector collimation was modified in order to increase the counting efficiency, and also to accommodate the growth of the ferrets. This modification involved removing some of the lead shielding from the section of the collimator posterior to the center of the animals. The ferrets were subsequently counted at each of the following time points (in days)

postdeposition: 45, 52, 57, 64, 72, 79, 87, 92, 99, 114, 128, 141, 156, 170, 181. The counting times ranged from 300 s per ferret at the start, up to 600 s toward the end of the study.

RESULTS

This study was novel for us in that (1) it was our first particle clearance study in which ferrets were used, and (2) it was the first study at our laboratory in which radiation counts of the upper respiratory tract were used to characterize early clearance. Therefore, we analyzed the data in several ways. The upper respiratory tract and lung results are described separately below.

Upper Respiratory Tract (Head Region) Clearance

Figure 2 is a graph of the data obtained by counting the head (and upper trachea) region of the ferrets between 0 and 24 h postdeposition. It appears from this figure that the group exposed to 1.0 mg/m^3 H_2SO_4 cleared the radiolabeled particles at a somewhat slower rate than did the purified-air-exposed group. In addition, the group exposed to 0.5 mg/m^3 H_2SO_4 appears to have cleared the particles at an accelerated

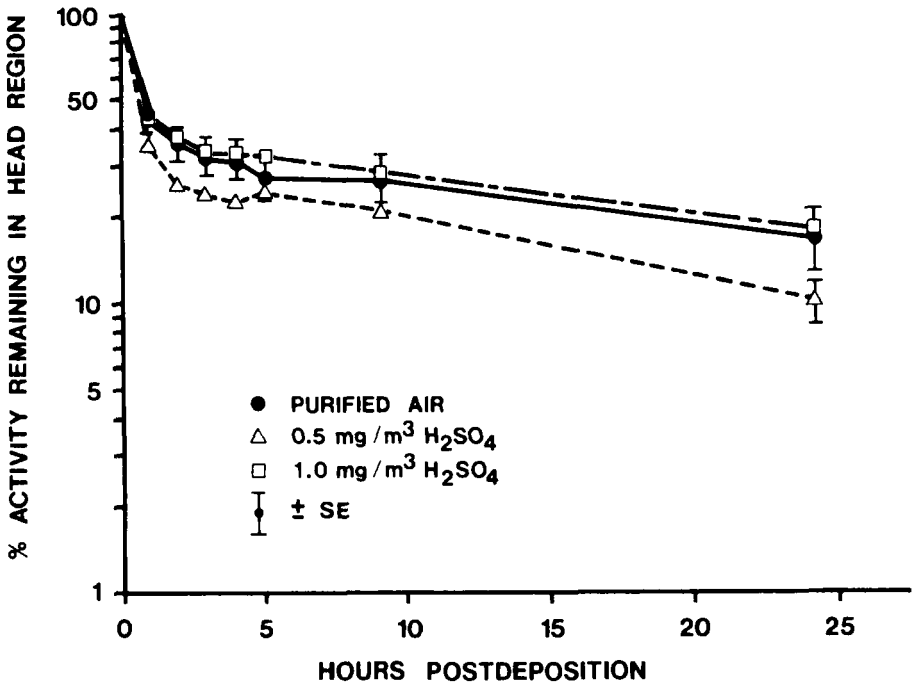

FIGURE 2. Clearance of ^{51}Cr-labeled tracer particles from the head region of the ferrets. Error bars represent ±1 standard error of the mean for the purified-air-exposed group.

TABLE 1. Double Exponential Fit of Upper Respiratory Tract Clearance Data

Atmosphere	Number	Exponential fit	RMS
Purified air	9[a]	$88 \exp(-1.96t) + 35 \exp(-0.028t)$	0.03
0.5 mg/m^3 H_2SO_4	10	$104 \exp(-2.38t) + 27 \exp(-0.034t)$	0.02
1.0 mg/m^3 H_2SO_4	10	$104 \exp(-2.59t) + 37 \exp(-0.027t)$	0.05

Note. Data obtained up to 165 h postdeposition; t, time postdeposition; RMS, residual mean square.

[a]One ferret turned around in its tube and asphyxiated during the study.

rate. However, the results of analyses performed using these data indicate that these effects were not statistically significant. Among the analyses performed were (1) a cumulative analysis of the counting data for each ferret in which the net counts were summed between 0 and 24 h postdeposition and the time at which 50% of the net counts were obtained was calculated; (2) analyses of the mean radioactivity remaining in the head region of the groups of ferrets at both 24 and 48 h postdeposition; and (3) an analysis in which the data from each group were fit to a double exponential function, the function then being integrated between 0 and 24 h, and the time at which 50% of the total integrated counts remained was calculated. The data were fit to a double exponential (see Table 1) since it appears from Figure 2 that there are both early (less than 5 h postdeposition) and late (greater than 5 h postdeposition) clearance phases. The trend in the results of each of these analyses was toward an acceleration in the rate of clearance for the group of ferrets exposed to 0.5 mg/m^3 H_2SO_4, and a deceleration in the rate of clearance for the group exposed to 1.0 mg/m^3 H_2SO_4. This biphasic response was expected (see Discussion). Therefore, our conclusion is that these effects were real. They were not, however, statistically significant (two-tailed t-test, $p > .1$).

Lung (Chest Region) Clearance

The results of the chest counting data (48–668 h postdeposition) are displayed in Figure 3. The regression line drawn through the data for the 0.5 mg/m^3 H_2SO_4 group follows the line for the purified air group very closely, with very little apparent difference in slope or intercept. However, the line for the group exposed to 1.0 mg/m^3 H_2SO_4 has a greater slope and a lower intercept value. The statistical analysis of the data involved fitting the curve for each ferret to a single exponential function, and from the function calculating a biological half-time (T_B), corrected for decay of the radioisotope. Means and standard deviations were calculated for the three groups of ferrets and the biological half-times were compared statistically. The results of these analyses indicate that the 1.0 mg/m^3 H_2SO_4 atmosphere did produce a statistically signifi-

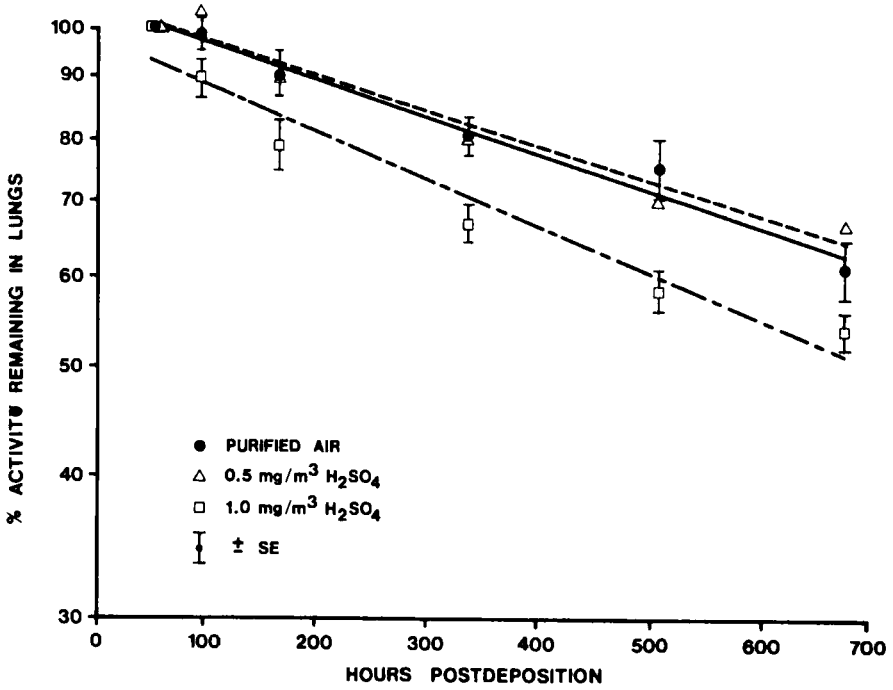

FIGURE 3. Clearance of ^{51}Cr-labeled tracer particles from the lung region of the ferrets. Error bars (±1 standard error of the mean) have been added to the figure for the purified-air-exposed group (solid line) and the 1.0 mg/m^3 H_2SO_4-exposed group.

cant acceleration in lung clearance (Table 2). The 0.5 mg/m^3 H_2SO_4 atmosphere did not produce a significant effect. The difference in the intercepts of the lines is perhaps due to the fact that the tracer particle deposition occurred after the pollutant exposure. It is possible that the exposure to 1.0 mg/m^3 H_2SO_4 led to a different respiratory system deposition pattern in that group of ferrets as compared to the deposition patterns of the ferrets exposed to purified air or 0.5 mg/m^3 H_2SO_4. This could occur if the prior higher level H_2SO_4 exposure altered the breathing pattern of the ferrets.

TABLE 2. Effect of H_2SO_4 Atmospheres on Lung Clearance of Tracer Particles

Atmosphere	Number	$\bar{T}_B$[a] ± SD (h)	ΔT_B ± SE (h)	p[b]
Purified air	9[c]	1126 ± 701	—	—
0.5 mg/m^3 H_2SO_4	10	773 ± 293	−353 ± 252	0.19
1.0 mg/m^3 H_2SO_4	10	630 ± 147	−496 ± 239	0.05

[a] T_B, Lung clearance biological half-time.
[b] Two-tailed t-test. Critical p = .1.
[c] One ferret turned around in its tube and asphyxiated during the study.

Long-Term Particle Clearance

A linear regression analysis was performed using the long-term (6 mo) counting results, and from the slope of the line it was determined that the long-term biological half-time (T_L) for clearance of the radiolabeled particles was 191 ± 30 (SE) days. The fit of the data to the single exponential function was acceptable (correlation coefficient = .97); however, the physical decay of the radioisotope led to a greater degree of uncertainty in the data (as evidenced by the standard errors) toward the end of the study.

The data were normalized using the day 45 counting data (as opposed to the 48-h data) because (1) the problem of ferret growth was most severe prior to that day, and (2) the collimator was modified just before that day, making it difficult to compare the pre day-45 and post day-45 data. Had the collimator not been modified, it would have been impossible to obtain reliable counting data past about 120 d postdeposition due to the low residual radioactivity remaining in the ferrets lungs. Opening up the collimator greatly improved the counting efficiency.

DISCUSSION

It is a difficult matter to compare the results of our ferret clearance study with the clearance results obtained by investigators who exposed other species to H_2SO_4. Aside from the species used, experimental protocols can vary greatly with respect to the following: (1) the size distribution of the H_2SO_4; (2) the duration of exposure to H_2SO_4; (3) the exposure concentration of H_2SO_4; (4) the size of the radioactive tracer particles (if they are used); (5) the experimental protocol (tracer deposition before or after H_2SO_4 exposure, counting schedules, etc.); (6) the method of particle deposition (inhalation, instillation); (7) the region of the respiratory system being monitored (total lung, nasal region, trachea, bronchial region); (8) the methods used to analyze the clearance data (biological half-life, mean residence time, log-normal fit of data, etc.). Our results for clearance in the region between the tip of the nose and the middle of the trachea are consistent with the findings described in other published studies performed by investigators who studied tracheobronchial clearance using a variety of species (Schlesinger, 1985b; Wolff, 1986). In general, an exposure to H_2SO_4 seems to stimulate mucociliary (upper respiratory tract) clearance at low exposure concentrations, and slow it at higher levels. The results of our analysis indicate that exposure to 0.5 mg/m^3 H_2SO_4 slightly speeded the clearance of tracer particles in the head region, while exposure to 1.0 mg/m^3 H_2SO_4 slowed the rate of clearance from this region. These results are not unlike those reported by Schlesinger et al. (1984), in

which marginal bronchial clearance effects were noted following exposures of humans and rabbits to H_2SO_4 at levels close to the ones studied here, even though significant effects were observed following exposures to both lower and higher H_2SO_4 concentrations. In fact, if we use our upper respiratory tract (0–24 h postdeposition) clearance data to estimate mean residence times (a parameter commonly used by Schlesinger and his colleagues), we find that the 0.5 mg/m^3 H_2SO_4 group exhibited about a 40-min reduction in mean residence time when compared to the control group, while the group exposed to 1.0 mg/m^3 H_2SO_4 exhibited a mean residence time about 10 min longer than that of the control group. These changes in clearance rates are quite similar to those observed by Schlesinger et al. in rabbit studies and are in the same direction as the changes observed by their group at New York University in their human studies (Amdur, 1989). Wolff (1986) also described studies in which comparable effects were observed following exposures of donkeys and dogs to H_2SO_4. He noted in this review paper that rabbits, humans, donkeys, and dogs all exhibit a speeding of tracheal clearance at low H_2SO_4 levels (0.1–0.5 mg/m^3), and a depression in the clearance rate at higher levels. Our ferret upper respiratory tract clearance data indicate that the group of ferrets exposed to 0.5 mg/m^3 H_2SO_4 had cleared about 14% more particles (on the average) by 5 h postdeposition than did the purified air group. The group exposed to 1.0 mg/m^3 H_2SO_4 had cleared about 15% fewer particles than the purified air ferrets by 5 h postdeposition. It again appears that the ferret results are similar to the results obtained by investigators using other species of animals. Although the clearance rate from the nasal and upper tracheal region may be somewhat different from that of the tracheobronchial region, the regions are histologically similar (ciliated epithelium, etc.) and should respond in a like manner to the insult of an air pollutant exposure.

Our data also indicate the existence of two separate, if not independent, components of head region clearance. Approximately 70% of the deposited material was cleared with a short half-life by 5 h postdeposition. The remaining material was cleared with a relatively long half-life. In fact, about one-third of this material was present at 48 h postdeposition; approximately one-fifth remained at 95 h. Our data imply that we are measuring two anatomically different compartments in the upper respiratory tract (ciliated versus nonciliated airways, nose versus sinuses, etc.), which have very different clearance rates associated with them. By carefully shaving the snouts of the ferrets and counting the fur, we established that the slow-clearing region was not an anomaly caused by fur contamination.

Very few, if any, acid toxicology studies have been performed in which the clearance of tracer particles from the lung region was followed for up to a month postdeposition. Our data suggest effects of the

1.0 mg/m^3 H_2SO_4 atmosphere on the clearance of the tracer particles. This finding warrants a followup study.

The experiment was a success in many ways. The ferrets proved to be easy to handle and it was not difficult to get them to repeatedly go into the counting tubes. The counting lab was ergonomically designed so that the study could be performed with a minimum of stress on the investigators during the long and repetitious data collection periods. The ferret counting system functioned well in isolating the head and chest regions of the ferrets. Also, the observed effects of sulfuric acid on clearance further support the potential usefulness of the ferret clearance model.

One problem that was encountered was that radioactive material cleared by the upper airways and moving through the gastrointestinal tract necessarily moved into the region collimated for chest (lung) counting. We did determine (via longitudinal scans) that most of this material was gone by about 6 h postdeposition, so that none of the subsequent counts were affected. (Lung clearance normally occurs over a sufficiently long period of time that interferences in the data during the first 6 h postexposure are not important.) Another problem that arose was that the ferrets grew in size (length and mass) during the period in which the lung clearance data were accumulated (48–668 h). Although the ferrets were ordered to arrive at an age at which the literature from Marshall Farms indicated that they would be nearly "full-grown," they did continue to grow throughout the study. Since the nasal clearance analysis only considered data collected over a 48-h period, it was not affected. However, some of the decrement in counts observed during the lung counting phase (>48 h) was due to the ferrets partially growing out of the region of the detection system that was collimated to receive radiation. In other words, during the chest counting period (48–668 h) the majority of the reduction in counts observed was due to the clearance of the radiolabeled particles—but some of the reduction was due to the growth of the ferret lungs out of the most sensitive region of the collimated detection system. Since the groups of ferrets were well matched with respect to weight, the data obtained for the three groups can still be compared and the effects on lung clearance that we observed are valid. (Between the start of the study and 668 h postdeposition, the purified air group increased in mass (on the average) by 29%, the 0.5 mg/m^3 H_2SO_4 group by 27%, and the 1.0 mg/m^3 H_2SO_4 group by 26%.) But the actual rates of clearance from the lung region are probably slower than were indicated by the biological half-times calculated here (actual biological half-times > measured biological half-times). This problem can be eliminated in the future by using older (and, unfortunately, more expensive) animals.

The overwhelming majority of clearance experiments performed by other investigators have been concerned primarily with the effects of

pollutants on early (mucociliary) clearance. Very few studies have been reported in which long-half-life tracers were used and the biological removal of insoluble particles was monitored for periods approaching 6 mo. One rather comprehensive study performed by Bailey et al. (1989) involved an interspecies comparison of lung clearance rates of "moderately soluble" monodisperse cobalt oxide particles labeled with ^{57}Co. The particles employed in this study were 1.7 μm in diameter. (The ^{51}Cr-labeled particles used in our study were 1.9 μm.) Lung clearance of the particles was followed for at least 6 mo after inhalation by humans, baboons, dogs, guinea pigs, rats (including Sprague-Dawley), and hamsters. The results were plotted in Figure 5 of their publication. From their data (fraction of radioactivity in the lung region vs. days postdeposition), we were able to calculate long-term biological half-times (T_L) for the various species with which they worked. Several of the species (including guinea pigs and HMT-strain rats) had clearance curves that were not fitted well by a single exponential function; biological half-times were not calculated for these animals. The results of our analysis were as follows: humans, T_L = 219 days; baboons, T_L = 150 days; Sprague-Dawley rats, T_L = 64 days; hamsters, T_L = 63 days; beagle dogs, T_L = 52 days.

Although these values are not exact, they are reasonable estimates based on their data. Since we calculated the T_L of the ferret to be 191 days, we feel that the clearance pattern of this animal may more closely resemble that of humans than of any of the species enrolled in the Bailey et al. study. The striking similarity of the human and the ferret long-term biological half-times may be a result of the similar subgross airway structure, specifically the several orders of respiratory bronchioles, in these two species.

Bohning et al. (1982) studied the clearance rate of 3.6-μm polystyrene latex microspheres from the lungs of nonsmoking adults. They found the long-term phase of particle clearance occurred with a half-time of 296 days. Since the particles used in this study were nearly twice the size of the 1.9-μm particles utilized in our study, it is somewhat difficult to compare the results of their study with our results. Larger particles may be expected to clear with a different half-time than do smaller particles.

In order to compare the ferret and the human with respect to inhaled particle deposition, we performed deposition calculations for the tracheobronchial tree for a wide range of particle sizes. Our particle deposition calculations are based on the equations published by Yeh and Schum (1980). We used tracheobronchial anatomical values based on our own original measurements of lung casts (Phalen et al., 1985; Oldham et al., 1990). The ventilation parameters were "resting" for the human, and our measured values (from pulmonary function studies) for the ferrets. The results (Fig. 4) predict that the ferret is more similar to

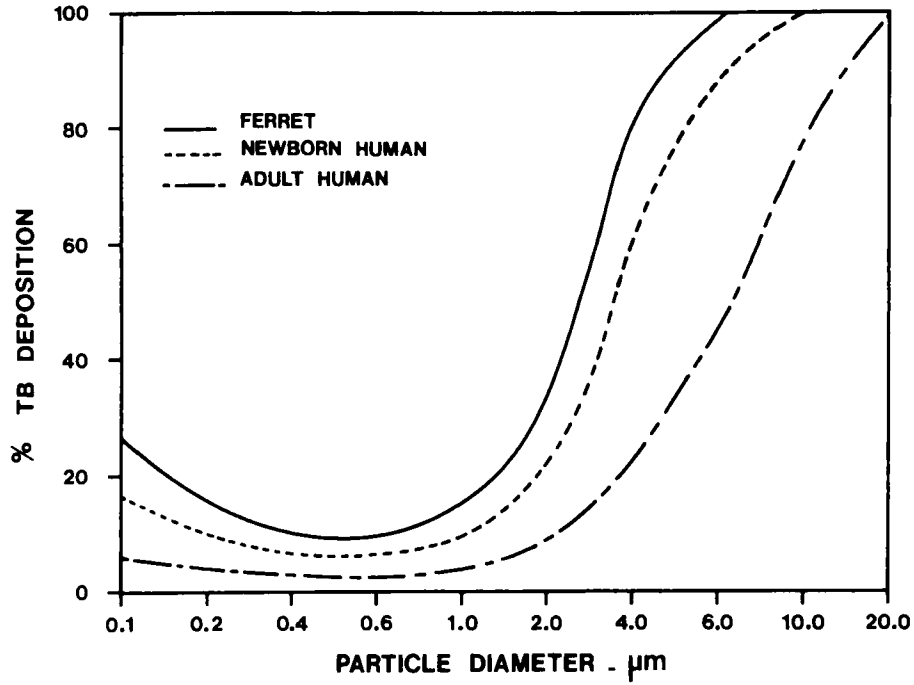

FIGURE 4. Calculated particle deposition efficiency (as percentage of particles entering the trachea) in the tracheobronchial (TB) airways for ferrets and humans at resting ventilation. The calculations are for unit density (1 g/cm^3) spheres.

the newborn than the adult human with respect to tracheobronchial deposition efficiencies.

In conclusion, with respect to respiratory tract anatomical and handling considerations, the ferret is potentially an attractive animal model. In addition, from the results obtained in our study, we believe that ferrets could be a useful model for investigators performing particle clearance studies. The authors do not believe, however, that other commonly used species are inappropriate.

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