Particulate Matter in Northern Climate of Helsinki Metropolitan Area, Finland

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ABSTRACT

Resuspension of particles from surfaces of paved roads has a major impact on ambient PM_{10} concentrations in the Helsinki Metropolitan Area. Annual average PM_{10} concentrations are relatively low, but there are quite frequent, high-level episodes in spring and fall. The highest 24-hour average values rise up to 150 $\mu g/m^3$ in urban traffic environments. Present measures to combat the air quality problems caused by resuspended particles have reduced annual TSP concentrations but they have had little effect on short-term PM_{10} levels.

INTRODUCTION

Helsinki is situated by the Baltic sea at latitude 60°N. The population in the Helsinki Metropolitan Area is 850,000 and the area is 743 km^2. In general, the ambient air quality is relatively good in the Helsinki area (1). There is some evidence, however, that even these low pollutant levels may cause adverse health effects especially during the cold wintertime (2). Emissions from energy production have decreased in recent years and emissions from industrial sources are low. Traffic is nowadays a major source of ambient air pollutants at breathing level because of the low emission height. Catalytic converters and reformulated fuels have lowered these emissions slightly, and only unleaded gasoline is used.

PM pollution and occasional high NO_2 concentrations during temperature inversions in winter make exceptions of the relatively good ambient air quality situation. The behavior of TSP and the contribution of resuspension to TSP concentrations have been studied in the Helsinki area (3). However, the impact of fugitive dust on PM_{10} concentration has been recognized only recently through analysis of seasonal variations in PM_{10} and gaseous pollutant concentrations.

METHODS

Air quality has been monitored periodically in the Helsinki area since the late 1950s. An automatic SO_2 monitoring network was established in 1975. Since 1983, the automatic monitoring has included several pollutants and it has been

extended to cover the whole Metropolitan Area. Currently five automatic multicomponent stations form the basis of the air quality monitoring network.

High volume TSP measurements were started in 1978. In 1987, high volume PM_{10} measurements were started with sample collection every fourth to sixth day, and in 1991 continuous PM_{10} measurements were added to the regime. Measurements have been conducted at several different sites in order to understand the variations in PM concentrations. All the results are calculated as arithmetic averages ($\mu g/m^3$) at 0 °C.

RESULTS AND DISCUSSION

Particulate Matter Emissions

Primary particles in the Helsinki area originate mainly from large power plants and traffic. PM emissions from power plants have decreased since 1980s due to the introduction of effective desulphurization processes removing also PM from the emissions. In addition, the number of area and small point sources and the total emissions from these sources have decreased in recent years. There has been also a slight decrease in direct particle emissions from traffic, which is due to introduction of new emission control measures.

Street sanding and salting and the use of studded tires during wintertime are regarded as the main reason why resuspension from paved roads is the main source of ambient PM in the Helsinki area. However, there are currently no quantitative estimates available on these indirect PM emissions.

Particulate Concentrations in Ambient Air

During recent years there has been a downward trend in annual average TSP concentrations in the Helsinki Metropolitan Area (4). Despite this favourable trend, both long-term and short-term TSP concentrations in the center of Helsinki were still relatively high in 1994 - 1995 (Table 1). The corresponding national guidelines were exceeded in urban traffic environments, and at other sites the concentrations were just below the guidelines.

Annual average PM_{10} concentrations have been low in recent years and there has not been any clear downward trend as with TSP (4). However, short-term PM_{10} concentrations have been relatively high, and in urban traffic environments they have exceeded the proposed new national air quality guideline (Table 1).

Resuspension of road dust dominates ambient TSP concentrations in the Helsinki area and primary emissions from stationary and mobile sources have only small effects. It was estimated in 1987 (3) by calculation of PM/SO_2 ratios in emissions and concentrations, that the average contribution of energy production to the TSP

concentrations was less than 5 %. Similarly, the contribution of direct traffic emissions was estimated to be less than 10 % by using PM/Pb ratios (3).

Seasonal and Diurnal Patterns in Concentrations

TSP, and to smaller extent PM_{10} concentrations, showed clear seasonal patterns. The highest monthly average concentrations were measured in spring, which was due to the relatively frequent occurrence of high-level TSP and PM_{10} episodes. In fall, the corresponding episodes were not as frequent and as high as in spring, and therefore the monthly average TSP and PM_{10} concentrations were elevated less than in spring (Fig. 1). The spring peaks coincided with melting of snow and drying of streets, while the fall peaks were probably due to the start of street sanding and the beginning of the use of studded tires.

The relative differences in monthly average PM_{10} concentrations were not as large as those in TSP, which reflected a higher portion of resuspension in TSP. The annual average PM_{10}/TSP ratio was approximately 0.30 at busy traffic sites and about 0.50 at other sites. The seasonal pattern in PM_{10} concentration supported the general view that photochemical formation of particles had only a minor contribution to the PM_{10} mass concentrations in the Helsinki area.

Analysis of diurnal variations in continuously measured PM_{10}, CO and SO_2 concentrations (Fig. 2) showed that the hourly PM_{10}/CO ratio was very different in April and September 1994. The average CO and SO_2 concentrations were approximately the same in April and September, while the PM_{10} concentrations were almost twice as high in April. Only in spring, PM_{10} concentrations followed closely CO concentrations. This finding suggested that the high PM_{10} concentrations in spring were mainly caused by resuspension of road dust by traffic, because there were no reasons to assume that the PM_{10}/CO ratio in primary traffic emissions would vary much between April and September. Furthermore, the SO_2 patterns supported the view that emissions from energy production had only a minor contribution to the PM_{10} concentrations.

Episodes of high PM_{10} concentrations

In 1994, the maximum 24-hour average PM_{10} concentration was 150 $\mu g/m^3$, which was measured at urban traffic environment in April. In 1995, the corresponding value was 174 $\mu g/m^3$, and it was measured in May. During this episode, the maximum 1-hour PM_{10} concentration was 488 $\mu g/m^3$, which was probably influenced to some extent by road construction work. The second highest 24-hour PM_{10} concentration, 100 $\mu g/m^3$, in 1995 was measured during another episode in March, when the maximum 1-hour PM_{10} concentration was 375 $\mu g/m^3$ (Fig. 3).

When the PM_{10} data were compared to the PM_{10} levels used in the newest WHO health effect assessment (5), the three-day-average PM_{10} concentration of 50 $\mu g/m^3$ was exceeded on six separate occasions and 100 $\mu g/m^3$ was exceeded once in 1994. The corresponding numbers in 1995 were 16 and one exceedances, respectively (Fig. 4). The PM_{10} concentrations of 50 and 100 $\mu g/m^3$ are regarded as PM pollution levels, which cause a 5 - 10 % increase in daily mortality, a 10 - 20 % increase in hospital admissions for respiratory conditions, and a 25 - 50 % increase in symptom exacerbations and a 35 - 70 % increase in bronchodilator use among asthmatic subjects. However, recent results of a Finnish epidemiological study (6) suggested that the higher-level PM_{10} pollution in spring might not affect the lung functions of primary school children with chronic respiratory symptoms similarly to the lower-level PM_{10} pollution in winter. It has been hypothesized that this difference might have been due to a lower toxicity of resuspended particles in comparison to combustion-related particles, which needs to be tested in future epidemiological studies.

CONCLUSIONS

PM pollution is considered as a major air pollution problem in the Helsinki Metropolitan Area. Present indirect evidence suggests that high-level PM_{10} episodes are caused mainly by resuspended particles from surfaces of paved roads. Direct, combustion-related particle emissions from energy production and traffic, and photochemical formation of particles from gaseous pollutants contribute much less to the PM_{10} mass concentrations. In spring, the three-day average PM_{10} concentrations exceed frequently levels, which according to the newest WHO assessment produce excessive mortality and morbidity among susceptible population groups such as respiratory and cardiovascular patients.

A comprehensive research program has been started in the Helsinki area in spring 1996 in order to study the chemical composition and size distribution of PM_{10}, and to estimate the contribution of different sources to ambient PM_{10} concentrations. The most important question in future epidemiological studies is, whether the high-level PM_{10} episodes caused mainly by resuspended particles are as harmful to human health as currently estimated for the PM_{10} pollution in general.

RECOMMENDATIONS

Several measures have been taken in the Helsinki Metropolitan Area in order to solve the air quality problems caused by large indirect PM emissions from the surfaces of paved roads. These measures include:

- faster cleaning of streets after melting of snow
- improved cleaning methods (e.g. vacuum street sweepers)
- increased use of gravel instead of sand as antiskid material
- use of washed sand and gravel
- reduction in total amount of antiskid material used in winter.

Nationally, the mass of studs in tires has been reduced and the period for permitted use of studded tires has become shorter. Campaigns have also been launched to inform about the necessity of effective street cleaning. These control measures probably explain the recent downward trend in annual TSP concentrations, but they do not seem to have had a similar effect on annual PM_{10} concentrations or on PM_{10} episodes in spring. Therefore, additional measures are needed to combat the air quality problems caused by resuspended particles.

The recently started studies on chemical composition and size distribution of ambient PM_{10} in the Helsinki area, and the associated epidemiological studies are expected to produce new information on the relative harmfulness of PM_{10} originating from different sources. This kind of information should help decision-makers in directing the PM emission cuts at different sources in a cost-effective way. If resuspended PM_{10} proved to be less harmful than combustion-related PM_{10}, this might have influences on national and international PM_{10} guidelines and standards.

ACKNOWLEDGEMENTS

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Table I. Annual mean and maximum 24-hour average TSP and PM_{10} concentrations in 1994-95 and comparisons with current and proposed new air quality guidelines in Finland.

		TSP $\mu g/m^3$						PM_{10} $\mu g/m^3$					
		Annual mean		Max		98-percentile [A]		Annual mean		Max		97-percentile[B]	
Guideline		60		-		150		-		-		-	
Proposed guideline		50		-		120		-		-		70	
Station	Siting /height (m)	1994	1995	1994	1995	1994	1995	1994	1995	1994	1995	1994	1995
Töölö	urban traffic/5	83	92	328	940[C]	301	381	28	31	150	173[C]	130	95
Kaisaniemi	urban/14	46	49	181	190	123	115	-	22	-	64	-	-
Tikkurila 1	suburban/2	33	36	112	261	84	143	20	20	55	49	-	-
Leppävaara	suburban traffic/5	54	45	273	307	209	140	22	19	142	48	-	-

(A = applies to 24-hour averages in a year
(B = 2. highest 24-hour average in a month, requires daily measuring method
(C = the maximum is probably influenced to some extent by road construction work

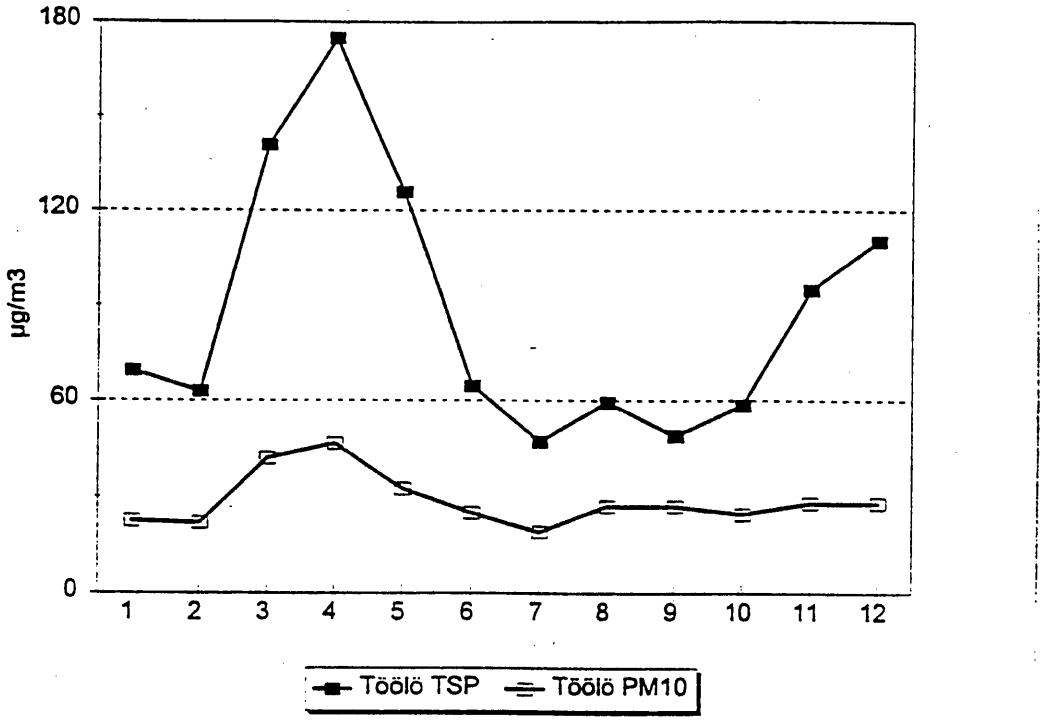

Figure 1. Seasonal variations in monthly average TSP and PM_{10} concentrations at urban traffic environment in 1994 -1995.

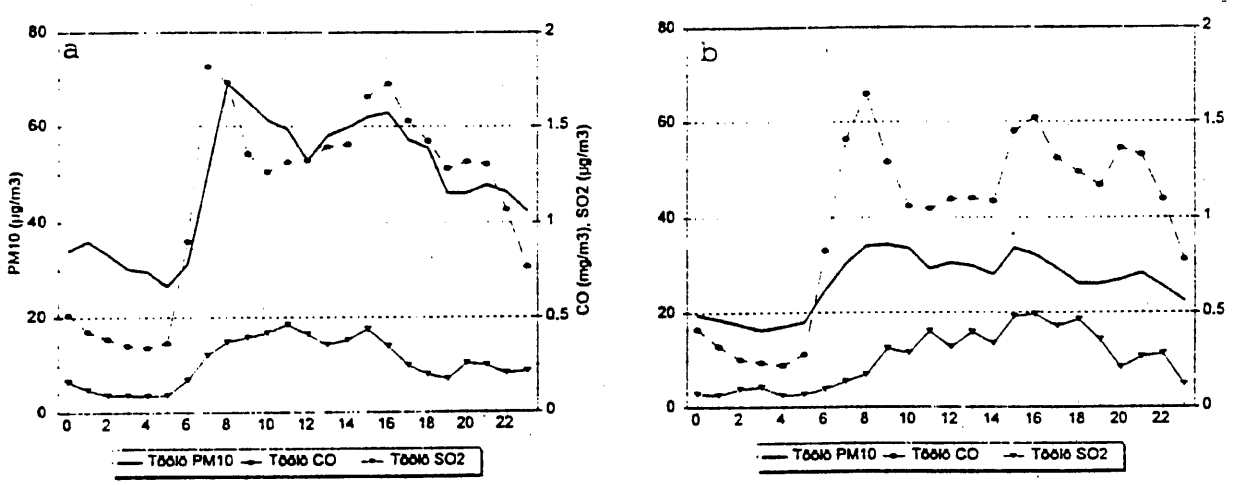

Figure 2. Diurnal variations in 1-hour average PM_{10}, CO and SO_2 concentrations at urban traffic environment in April (a) and September (b) 1994.

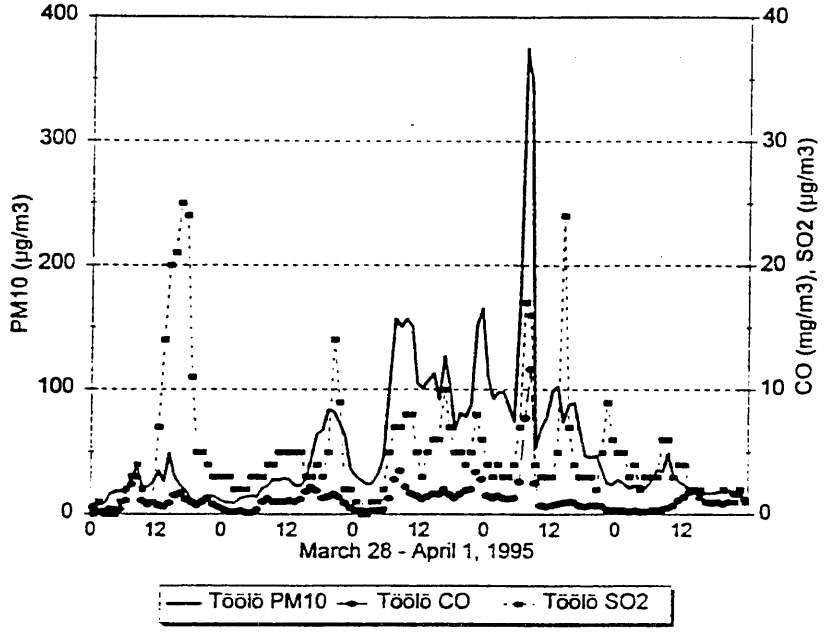

Figure 3. One-hour average pollutant concentrations during a PM pollution episode in March 1995.

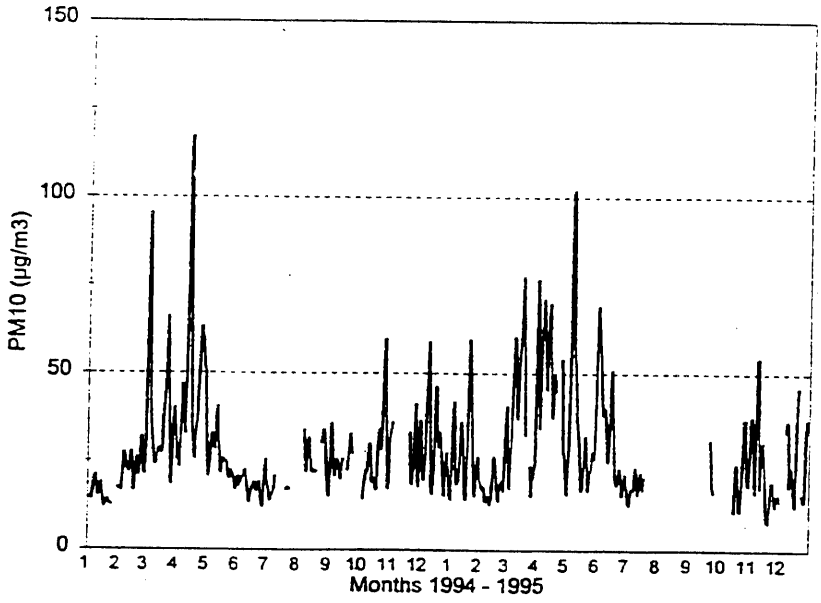

Figure 4. Three-day average PM_{10} concentrations and exceedances of 50 and 100 $\mu g/m^3$ in 1994 - 1995.

Degradation of Synthetic Vitreous Fibers in the Lung and In Vitro

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Abstract

In recent rat chronic inhalation studies, some synthetic vitreous fibers (SVFs) induced irreversible lung toxicity (refractory ceramic fibers induced fibrosis and mesotheliomas; rock wool induced fibrosis) while others did not (two fiber glasses and slag wool). Lung fiber burdens, dimensions and rates of clearance did not appear to be the only determinants of toxicity. In order to study possible relationships between fiber toxicity and fiber biopersistence in the lung, a study was conducted as follows: rats were exposed to high levels of one of four SVFs or to crocidolite asbestos for five days and then held for one year of recovery; during recovery, animals were periodically sacrificed for lung fiber analysis. Compared to crocidolite, the SVFs had low biopersistence. Longer SVFs disappeared from the lung more rapidly than short SVFs, suggesting breakage of long fibers. In contrast, long crocidolite disappeared more slowly than short, suggesting little or no breakage of long fibers. Over time in the lung, mean dimensions of SVFs decreased; in contrast, the mean length of crocidolite increased, probably due to macrophage clearance of short fibers. Incongruent dissolution (leaching) and morphological changes were observed in the three nontoxic SVFs but not in crocidolite or rock wool (or in refractory ceramic fiber in a separate study). Degradation of SVFs were also studied in vitro using simulated extracellular fluid. Some of the SVFs also dissolved incongruently in vitro, leaving a leached silica matrix that fragmented spontaneously. The rate of leaching correlated with the rate of breakage. In vitro simple (congruent) dissolution rates (k_{dis}) did not correlate with lung fiber disappearance. However, the ability of a fiber to be leached and broken in vitro was strongly associated with its rate of

disappearance from the lung. Leaching may also alter the bioreactivity of the fiber surface, thereby affecting toxicity.

Introduction

That dose, dimension and durability play important roles in determining fiber toxicity to the lung is generally agreed. However, findings from a recent series of rat chronic inhalation studies that these are not the only characteristics that affect fiber toxicity (Hesterberg et al., 1995). In these studies, five different synthetic vitreous fiber (SVF) compositions induced a range of toxicity in the rat lung even though the exposure aerosols and resultant lung burdens of the five SVFs were similar in fiber number and dimensions. Lung clearance rates of the SVFs during a post-exposure recovery period were also similar. Refractory ceramic fiber (RCF1) and crocidolite asbestos (which was used to validate the rat inhalation model) induced lung tumors, mesotheliomas, and fibrosis; rock wool (MMVF21) induced minimal fibrosis late in the study but no tumors; and slag wool (MMVF22) and two fiber glass insulation wools (MMVF10, MMVF11) induced neither tumors nor fibrosis (Table 1). Thus, dose, dimension and durability are not the only determinants of fiber toxicity.

In order to develop a more complete model of fiber toxicity that can incorporate these new findings, the issues of fiber biopersistence and transformation were further examined in two studies: (i) an in vivo fiber biopersistence study using the rat inhalation model; and (ii) an in vitro fiber degradation study using simulated extracellular fluid (SEF) in either a

flow-through system or a high volume dilution system. These studies are discussed in greater detail in Hesterberg et al., 1996a and b.

Of primary interest in these studies were the rate as well as the pattern of fiber dissolution. Among the various SVFs examined, two different patterns of fiber dissolution were observed (Figure 1): simple, congruent dissolution, in which all components dissolve from the surface of the fiber at near-equal rates, resulting in a gradual and usually steady reduction in dimensions down to zero and complete disappearance; and incongruent dissolution (leaching), in which some components dissolve much more rapidly than others, leaving a fiber consisting of a depleted matrix (primarily silica and alumina) but with fairly persistent dimensions. The traditional fiber dissolution rate constant, k_{dis} (mass loss per unit surface area over time), assumes a model of simple dissolution at constant velocity. K_{dis} is determined in vitro and is often used as an indicator of fiber biopersistence and potential in vivo toxicity. However, the present observations demonstrate that the correct model of fiber biotransformation for many SVFs, including three of the five compositions used in the chronic animal studies discussed above, is that of incongruent dissolution.

Biopersistence Study: Rat Inhalation Model

Methods

To study fiber biopersistence in the lung, rats were exposed by nose-only inhalation to a high level of one of four SVFs (MMVF10, MMVF11, MMVF21, or MMVF22 at 30 mg/m^3, approximately 250-350 fibers/cc) or to crocidolite asbestos (10 mg/m^3, approximately 2600 fibers/cc) for five days, six hours per day, and then held without further exposure for one year (Hesterberg et al., 1996a). Each of the SVF test fibers was size-selected to have approximate average dimensions of 1 µm X 20 µm. Crocidolite average dimensions were 7.7 µm x 0.3 µm. During the one year post-exposure recovery period, small groups of rats were periodically killed to analyze lung fiber numbers, dimensions, morphology and chemical composition. Refractory ceramic fiber (RCF1) was not included in this biopersistence study; however, data on RCF1 lung fibers were obtained from the rat chronic inhalation study, in which rats were exposed to 30 mg/m^3 SVF for various time points up to two years and maintained for various recovery periods (Hesterberg et al., 1995; McConnell et al., 1994).

Results

In the biopersistence study, as in the chronic study, the patterns of lung fiber deposition and clearance were similar for the four SVFs (Hesterberg et al., 1996a). However, the clearance pattern of crocidolite asbestos differed from those of the SVFs. Twenty-four hours after the termination of exposure, the lungs of animals in each fiber-exposure group contained

high levels of fiber: numbers of fibers >5μm in length per lung were 2-6 million for SVFs and nearly 30 million for crocidolite. During the post-exposure recovery phase, two different patterns of lung fiber clearance became apparent. In the SVF-exposed animals, the number of *long* fibers per lung decreased more rapidly than the number of short fibers (Table 2). In contrast, the reverse was true for crocidolite asbestos--the *short* fibers disappeared more rapidly than the long fibers. After one year of recovery, ~ 4% of long (>20μm) SVFs were retained in the lung compared to 83% of long crocidolite fibers (Table 3). SVF mean dimensions, especially length, decreased with time, but the crocidolite mean diameter remained unchanged and its mean length showed an apparent increase (Figure 2). This suggests that the SVFs were dissolving, leaching, and breaking while crocidolite was doing neither.

During the one year residence time in the lung, the two fibrous glasses and the slag wool (MMVF10, 11, and 22) exhibited incongruent dissolution, with losses in oxides of magnesium, calcium, and/or sodium (Hesterberg et al., 1996a and b). The leaching was apparent in these fibers by 91 days post-exposure or earlier. The more durable components forming the non-leachable matrix of these fibers were silica, alumina and iron. In contrast, the compositions of rock wool and crocidolite did not change significantly during this time. Data from the previous, chronic inhalation study also demonstrate that the chemical composition of RCF1 lung fibers did not change during 90 days of recovery (Hesterberg et al., 1995). The three SVF fibers that underwent incongruent dissolution also developed morphological changes, including pitting and furrowing of surfaces (Figure

3). In contrast, the morphologies of crocidolite, RCF1 and MMVF21 remained visibly unchanged.

Discussion: Biopersistence Study

The biopersistence study data suggest that incongruent dissolution and breakage of fibers could explain the lack of toxic effects of some fiber compositions. Longer SVFs disappeared from the lung more rapidly than short SVFs, suggesting that long fibers were either preferentially dissolving, or they were breaking, or both. The apparent lag in SVF short fiber clearance favors a breakage mechanism, in which long SVFs broke and thereby increased the population of short fibers more rapidly than macrophage-mediated clearance could reduce it. Crocidolite fibers, on the other hand, apparently did not break (or dissolve) while in the lung. Thus, macrophage-mediated clearance of short fibers was not competing with fiber breakage, and the number of short fibers initially declined more rapidly than the numbers of short SVFs.

The incongruent dissolution and morphological changes observed in the lung fibers of the three non-toxic SVFs (MMVF10, 11 and 22) during the recovery time also agree with a mechanism of breakage. As the more soluble constituents of the lung fibers leave the silica matrix, the weakened fibers may fragment, and the short pieces could then be eliminated by macrophage-mediated clearance.

The changes in SVF number, chemistry and/or morphology during lung residency demonstrate that biopersistence of fibers in the lung is not only

a matter of simple dissolution rates; leaching and fragmentation apparently play at least as great a role in lung fiber biotransformation and clearance. Furthermore, with these fibers, the degree of leaching correlates with chronic toxicity to the lung. Such a correlation could be based on leaching-induced fragmentation into short segments that can be cleared by macrophages and/or by changes in surface bioreactivity. Thus, biopersistence in the broad sense (which includes chemical and morphological transformation) may partially explain the range of lung toxicities induced by these five SVFs.

Fiber Transformation Studies: In Vitro Models

Methods

Glass fibers were subjected to degradation in simulated extracellular fluid (SEF, based on Gamble, 1967) buffered at pH 7.4 and maintained at 37°C in either (a) a high-volume dilution bioreactor system or (b) a flow through system. Fiber leaching and breakage were analyzed over time. Very brief summaries of these studies are presented below and described in detail in Bauer and Law, 1996.

High Volume Dilution System

For the high-volume dilution system, a test fiber was synthesized in the laboratory to have a formulation similar to that of Schuller 901 glass (from which the animal test fiber MMVF10 was derived from 901 glass) and to

have average dimensions of 3 μm X 5 mm. Because this laboratory fiber was prepared by a different process (continuous filament) than the commercial fiber (rotary process), it is not, strictly speaking, a true 901 glass. A number of replicate samples were prepared by sandwiching a thin web of fibers between a pair of triton-free Millipore® filters. Samples were placed in a bioreactor containing 100 L of SEF that re-circulates internally (not a flow-through system). The re-circulation rate was set at the maximum permeability rate of the filters holding the samples (3,050 cm/hr.). Samples were removed from the bioreactor at nine timepoints up to 744 hours (31 days) and analyzed for diameter distributions, mass loss, residual composition, and breakage. The dissolution rate, k_{dis}, was calculated from the mass loss data, based on a model of constant velocity dissolution. Fiber breakage was quantified by counting the number of fiber ends visible in 50 fields using optical microscopy.

The predicted time required for complete dissolution of the "901" glass fibers in the bioreactor was calculated to be approximately 800 hours (approximately 33 days), based on the observed k_{dis} and the initial fiber diameters and assuming dissolution at constant velocity. If the test fibers dissolved without breaking, the number of ends per 50 fields would not increase, as illustrated by the hypothetical 'Predicted' curve in Figure 4. However, the observed average number of ends per initial fiber increased from two to 40 after 430 hours in the bioreactor and then gradually declined to near-zero at 744 hours ('Observed' curve, Figure 4). This means that each fiber fragmented into an average of 20 segments by 430 hours. The upward-slope of the 'Observed' curve in Figure 4 could only result from fiber breakage, and the downward-slope of the 'Observed'

curve from 430 to 744 hours is apparently a result of loss of fibers by fragmentation into non-fibrous particles or by complete dissolution with the thinner fibers disappearing first. By the last time point (744 hours, 31 days), few fibrous particles (aspect ratio >3:1) were visible in the samples. Considering that the initial length of the fibers was 5 mm, it is also noteworthy that fiber segments less than 20 μm in length were found in samples leached for only 264 hr (11 days).

Flow-Through System

The flow-through system was used to investigate the degradation behaviors of most of the known commercial as well as several experimental glass fiber compositions (18 compositions in all) in SEF. Test fibers were synthesized in the laboratory as continuous filaments (air-attenuated) to be 8 μm X 5 mm. Thin fiber webs were deposited between 2 Nuclepore® filters and placed in SEF at a flow rate/sample surface area of 0.25 cm/hr, which was found to reproduce the morphologies and chemical compositions of the glass fibers recovered from laboratory animals following inhalation (Figure 5; also Hesterberg et al., 1996a). At intervals up to 5 months, effluent from the system was analyzed for dissolved fiber components. At 5 months, samples were carefully removed intact from the system and analyzed for *in situ* breakage. For each time point, the residual fiber composition was calculated from the effluent analysis data. The simple dissolution rate, k_{dis}, was also calculated from the data set. The magnitude of compositional change per unit time was determined for each test fiber and termed the leaching index, I(t), defined as the absolute value of the sum of the changes in mole fraction of each

component (thus, the greater the I(t), the more incongruent the leaching; explained further in Bauer and Law, 1996). A sample was considered to have undergone fragmentation if at least 10% of the fibers had visible break-points when examined by electron microscopy (Figure 6).

The in vitro flow-through system, effluent analysis data demonstrated that "901" glass underwent incongruent dissolution (leaching) similar to that observed in the high-volume dilution system and in the rat lung following inhalation; as in the lung, in vitro leaching removed components such as sodium, calcium and potassium more rapidly than matrix components, such as silica and alumina (Figure 5).

Incongruency of dissolution of the 18 glass test fibers correlated with fragmentation rates; at 5 months, all compositions that had an I(t) of ≥0.25 (i.e., the sum of the changes in the mole fraction of each component was greater than 0.25) also had at least ≥10% fragmentation. The time required for complete dissolution (based on a congruent dissolution model) of each test fiber in SEF was calculated from its k_{dis} and diameter range. Time required for 10% fiber breakage was calculated from each test fiber's rate of change of residual composition with time (dIt/dt). For each of the 18 glass compositions, the calculated time required for breakage was less than 60% of the calculated time required for complete dissolution (Figure 7). For example, the calculated times for the most durable fiber compositions were approximately 900 days for complete dissolution but only 500 days for breakage.

The degradation behavior of each of the five test fibers used in the animal studies (MMVF10, 11, 21, 22, and RCF1) was also investigated in the in vitro flow-through system. Fibers samples were leached in the flow-through system for 500 hours, then removed from the flow-through system, cut in cross section, and examined using electron microscopy. The degree of leaching was demonstrated not only by mass loss of constituents into the effluent, but also by the visible outer leached layer of the fiber in cross-section (Figure 8). After 500 hours in the flow-through system, the animal study test fibers exhibited a broad range of incongruent dissolution, including rapid leaching (MMVF10a, Figure 8a), moderate leaching (MMVF22, Figure 8b; and MMVF11, not illustrated), and no leaching (MMVF21, Figure 8c; and RCF1, not illustrated).

Discussion: In Vitro Models

In the high-volume dilution bioreactor study, 3 μm diameter "901" glass fibers (similar in composition to MMVF10) fragmented into shorter fibers and possibly non-fibrous particulates long before they disappeared by congruent dissolution. In the in vitro flow-through system, 8 μm diameter fibers of most known commercial glass fiber compositions exhibited 10% breakage in less than 60% of the time calculated for complete dissolution. Fiber breakage in these two in vitro systems apparently resulted from leaching-induced weakness and mild stress generated by the somewhat interwoven nature of sample webs (Figure 7). In the lung, fibers would be too dispersed to generate forces upon each other in this way; however, movement of air, fluid, mobile cells and expanding and relaxing motions of the alveoli could generate mild flexion

and stress on lung fibers. Thus, these in vitro data suggest that, in the lung, these glass compositions could fragment into shorter segments long before they would disappear by complete dissolution, and over time these segments could break into small pieces that could be translocated out of the lung by macrophage-mediated clearance. Incongruent dissolution was also demonstrated in vitro for three of the five animal inhalation study fibers, MMVF10, 11 and 22; in contrast, very little or no leaching was observed in MMVF21 and RCF1. Thus, while some, maybe most SVF compositions undergo incongruent leaching, other compositions apparently undergo simple (congruent) dissolution and may completely dissolve before they break (Figure 1). In these latter compositions, breakage may not be a significant factor in biopersistence. Nonetheless, the in vitro data demonstrate that fiber leaching and breakage must be considered as well as dissolution in any complete model of lung fiber biopersistence and clearance.

Conclusions

In the rat chronic inhalation studies of five SVF compositions, it was shown that lung fiber dose, dimension and disappearance rate are not the only determinants of lung toxicity. The short-term inhalation data strongly suggest that SVF but not crocidolite break in the rat lung. Additionally, electron microscopic analysis of lung fibers indicated that MMVF10, 11, and 22 (nontoxic in the animal studies) underwent incongruent dissolution (leaching), while the three toxic fibers (crocidolite asbestos, RCF1 and MMVF21) underwent very slow or imperceptible, congruent dissolution.

The in vitro fiber degradation studies also demonstrated that glass fibers break long before they completely dissolve and that the degree of leaching (incongruent dissolution) correlates well with the rate of breakage. Taken together, these data demonstrate a relationship between the ability of SVFs to be leached and broken and their lack of toxicity to the lung.

The tendency of a fiber to be physically and chemically transformed in physiological solutions could influence its potential toxicity to the lung by affecting either biopersistence or bioreactivity. In the simplest scenario, fibers that dissolve very rapidly and disappear in a matter of days or weeks would induce little or no toxicity because their lung residence time is too brief to have much biological impact. Fibers that undergo a high rate of incongruent leaching may also be less toxic because they tend to break into smaller pieces that can be removed from the lung within a few weeks by macrophage-mediated clearance. Short fibers have also been shown to be intrinsically less toxic at the cellular level (Hart et al., 1994). In the animal studies discussed here, there was a clear association between decreased leachability and toxicity of fibers. This suggests that leaching, in addition to making the fibers more breakable, may alter the bioreactivity of the fiber's surface. Leaching-induced changes in fiber surface chemistry could affect, among other things: stimulation of cellular release of inflammatory mediators; the ability of macrophages to adhere to, phagocytize, and translocate fibers; and/or the tendency of the fiber surface to form destructive free radicals.

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Preparation of test fibers for in vivo studies by B. Fitzpatrick; electron microscopy analysis of fibers by R. Hamilton and F. D'Ovidio; chemical analysis of fiber leachate by B. Law.

TABLE 1. RAT LUNG PATHOLOGY: CHRONIC INHALATION STUDIES

Test Fiber	Exposure Fibers >5μm[d] /cc	Lung Fibrosis	Lung Tumors	Mesotheliomas
Air Controls[a]	0	–	1--3 %	0
MMVF 10[a] 901 Insualtion Glass	232 ±56	–	5.8%	0
MMVF 11[a] Insulation Glass	246 ± 76	–	2.6%	0
MMVF 21[b] Rock Wool	243 ± 67	+	4.4%	0
MMVF 22[b] Slag Wool	213 ± 62	–	2.6%	0
RCF1[c] Refractory Cer. Fiber	187 ± 53	+	12.4%*	1.7%*
Crocidolite[b] **Asbestos**	1,600 ± 1,000	+	13.2%*	0.9%*

[a]Hesterberg et al., 1995b;[b]McConnell et al., 1994. [c]Mast et a., 1995. [d]Fibers longer than 5 μm.
*Significantly different from air controls; t test at 0.05 probability.

TABLE 2. LUNG FIBER CLEARANCE HALF TIMES, $T_{1/2}$

Number of post-exposure recovery days required to reduce lung burden by 50%.

Fiber	$T_{1/2}$ Days, by Fiber Length Category			
	Short Fibers, <5 μm	>5μm	>10 μm	Long Fibers, >20 μm
MMVF10	111	89	83	44*
MMVF11	46	35	22	6
MMVF21	174	111	84	53
MMVF22	118	75	18	5
Crocidolite	44	234	142	986**

* MMVFs: T1/2 decreases with increasing fiber length.
** Crocidolite: T1/2 increases with increasing fiber length

TABLE 3. LUNG RETENTION OF LONG FIBERS

Fiber	Fibers >20m per lung X 10^6		
	Recovery Day 1	Recovery Day 365	% Retained after 365 D.
MMVF10	0.14	0.002	1%
MMVF11	0.97*	0.002**	<1%**
MMVF21	0.55	0.020	4%
MMVF22	0.40	0.001	<1%
Crocidolite	0.95*	0.790**	83%**

* On recovery Day 1, MMVF11 and Crocidolite numbers of long fibers/lung were the same.

** After 365 d. recovery, MMVF11 long fibers are mostly gone; crocidolite long fibers are mostly retained.

Fig. 1. Dissolution of Synthetic Vitreous Fibers: Congruent v. Incongruent

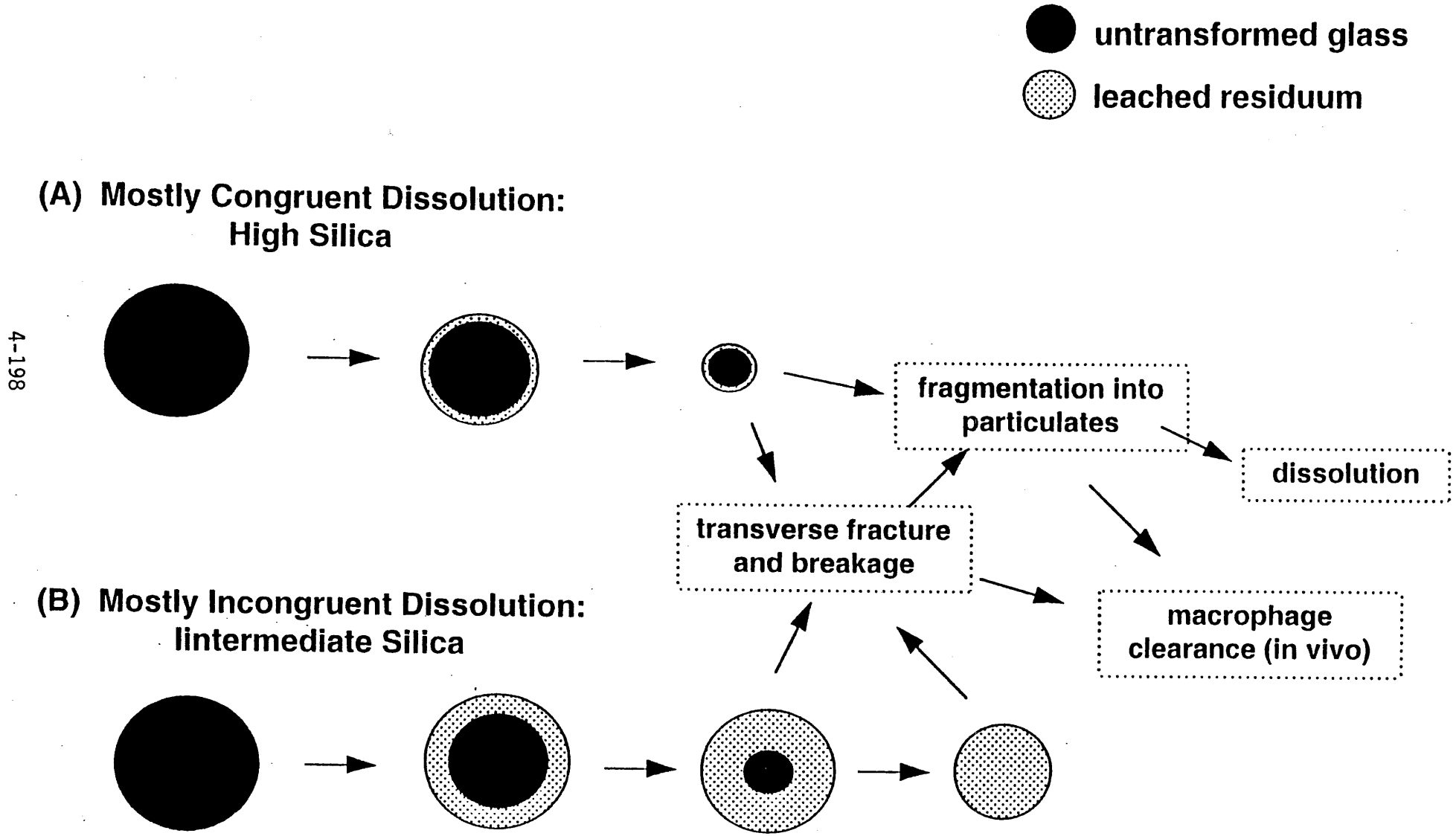


Fig. 2. Changes in Fiber Lengths During Lung Residence

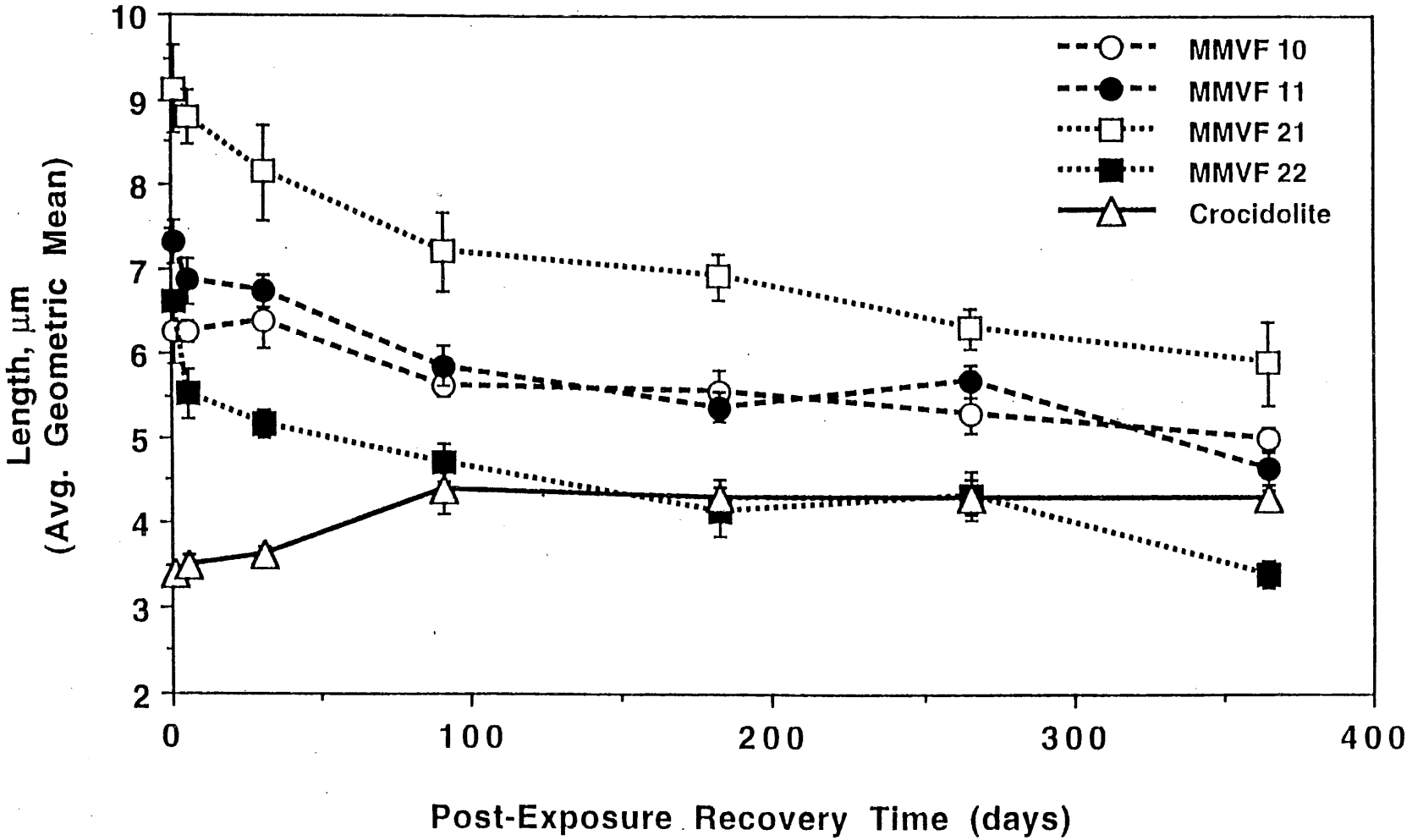
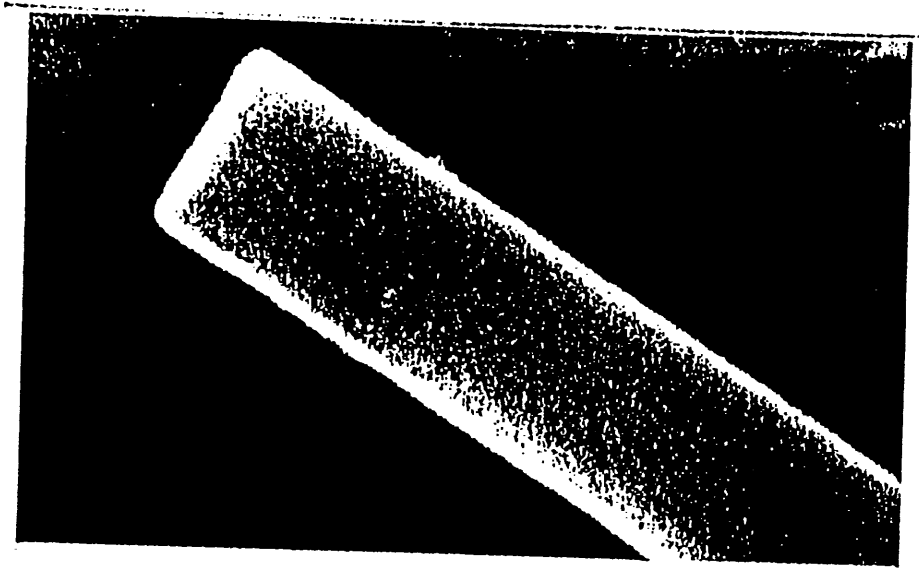
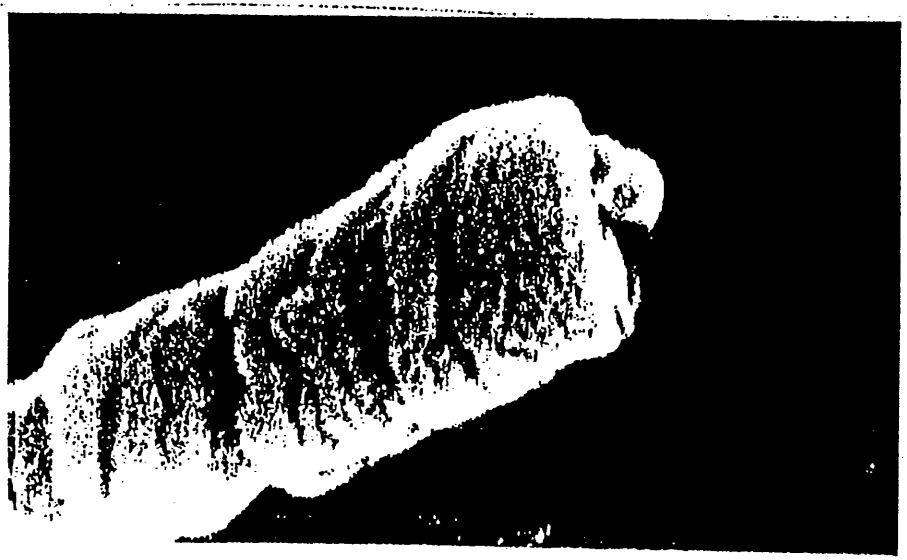


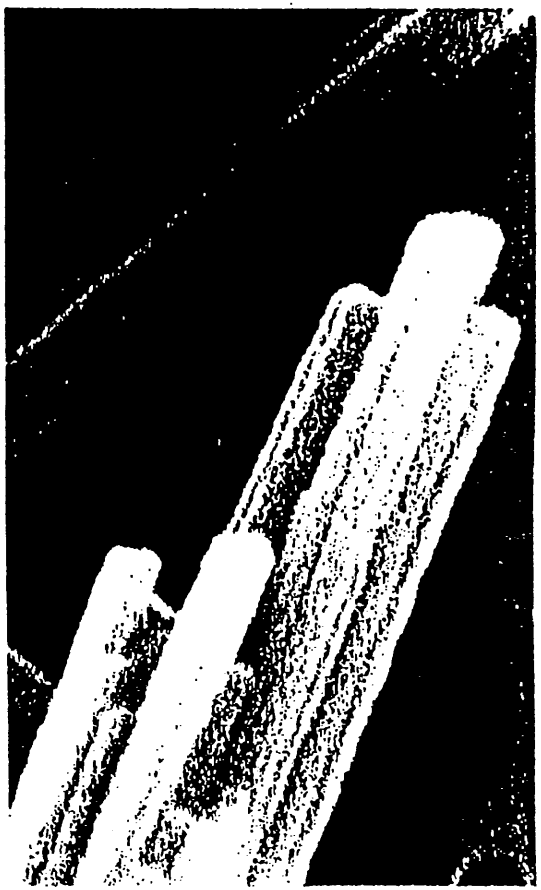
Fig. 3. Fibers After 6 Months in the Rat Lung



A. MMVF21: No visible change.



B. MMVF22: Visible degradation.



C. Crocidolite Asbestos: No visible change.

X52,000

Fig. 4. In Vitro Glass Fiber Breakage and Disappearance

In Vitro High Volume Dilution System

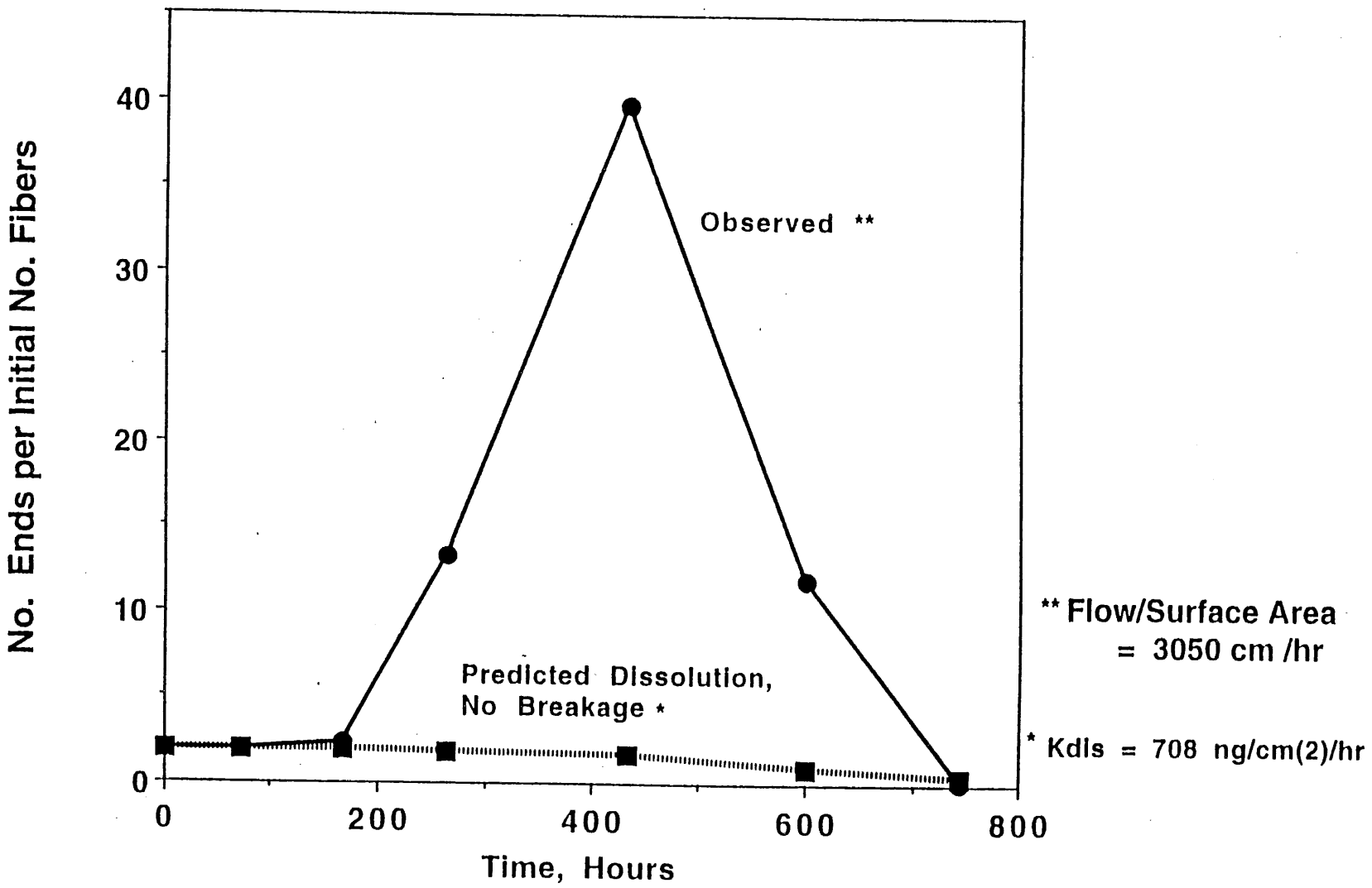
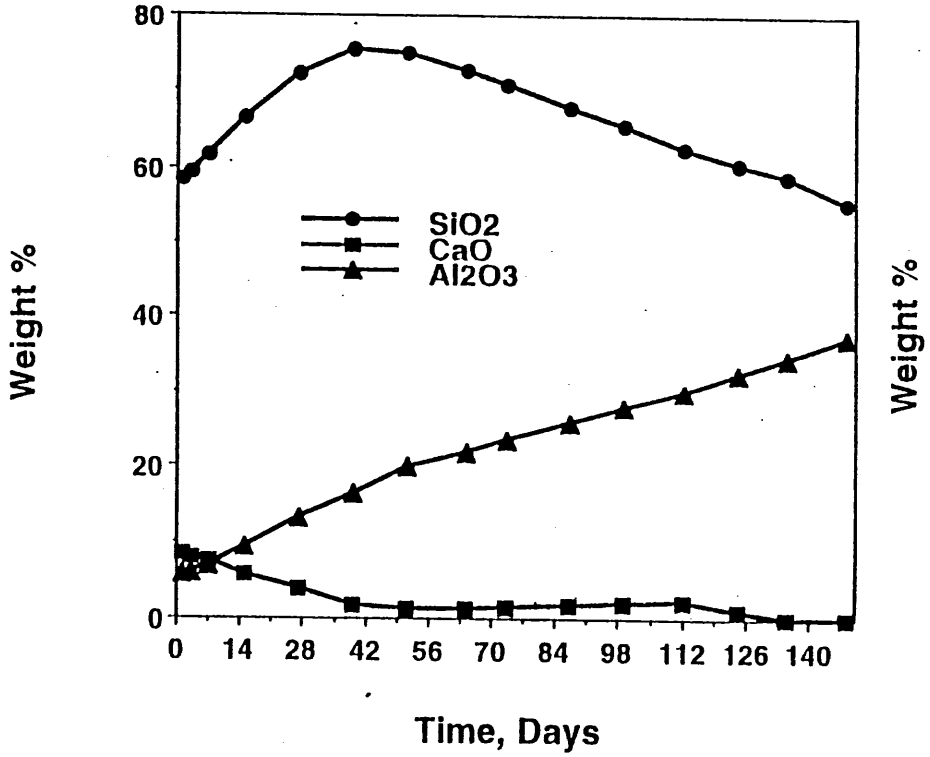


Fig. 5. Leaching of Glass Fiber: In Vitro v. In Vivo

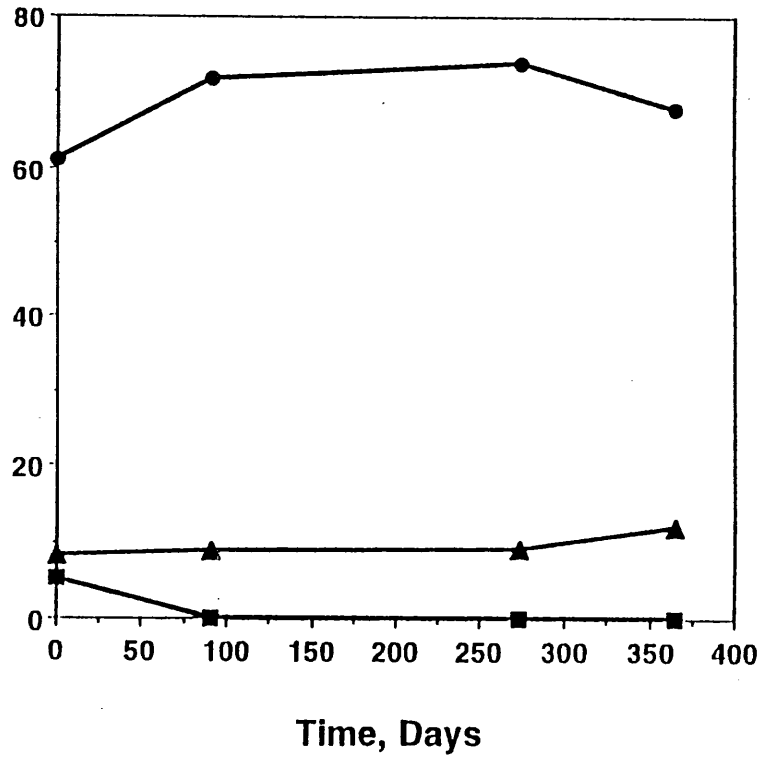
A. In Vitro, 5 Mo.

901 Glass*; Flow-through model



B. In Vivo, 12 Mo.

MMVF10: Rodent Inhalation Model



*Schuller 901 glass composition is similar to MMVF10.

Fig. 6. Glass Fibers Break Before They Dissolve

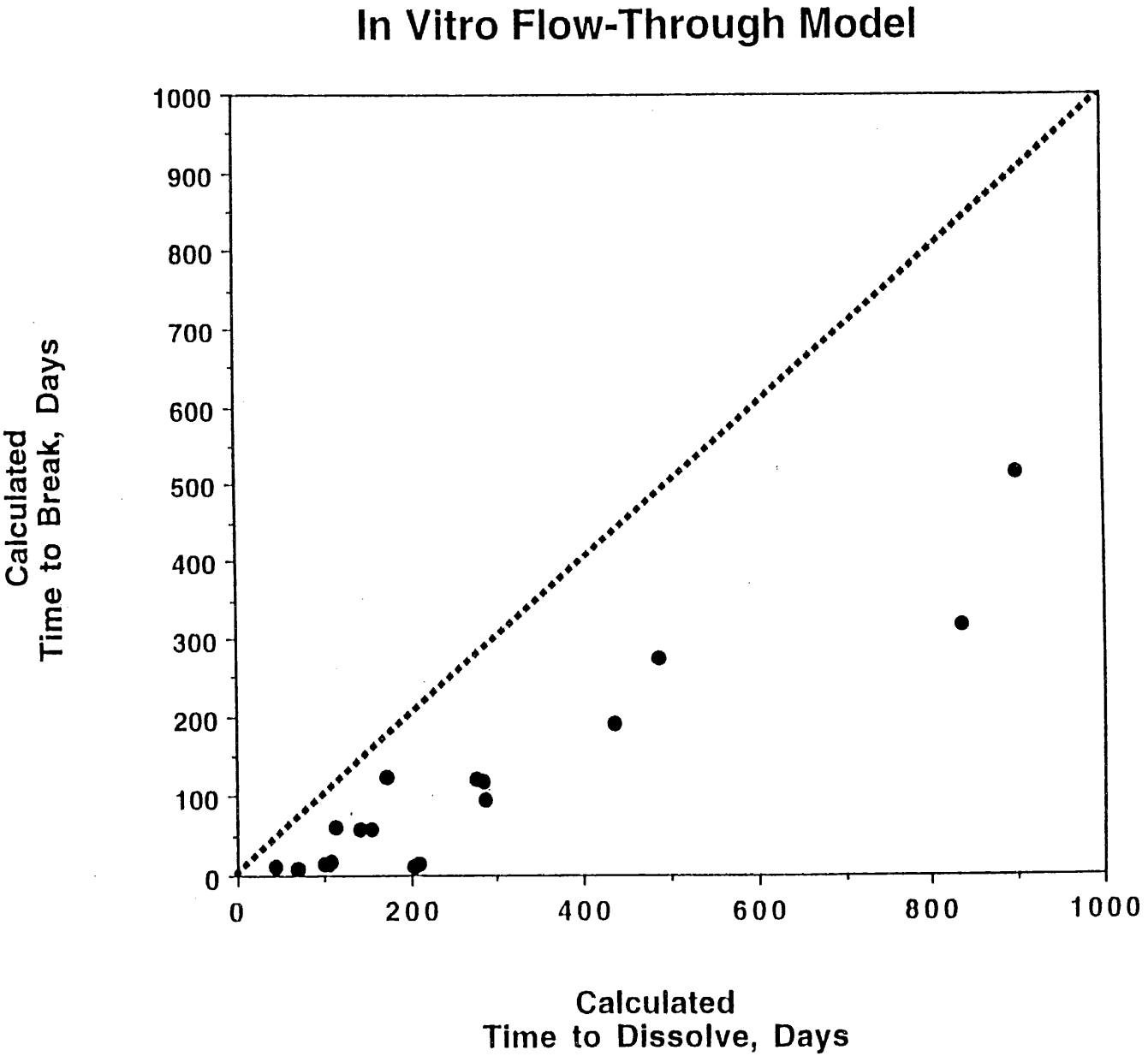
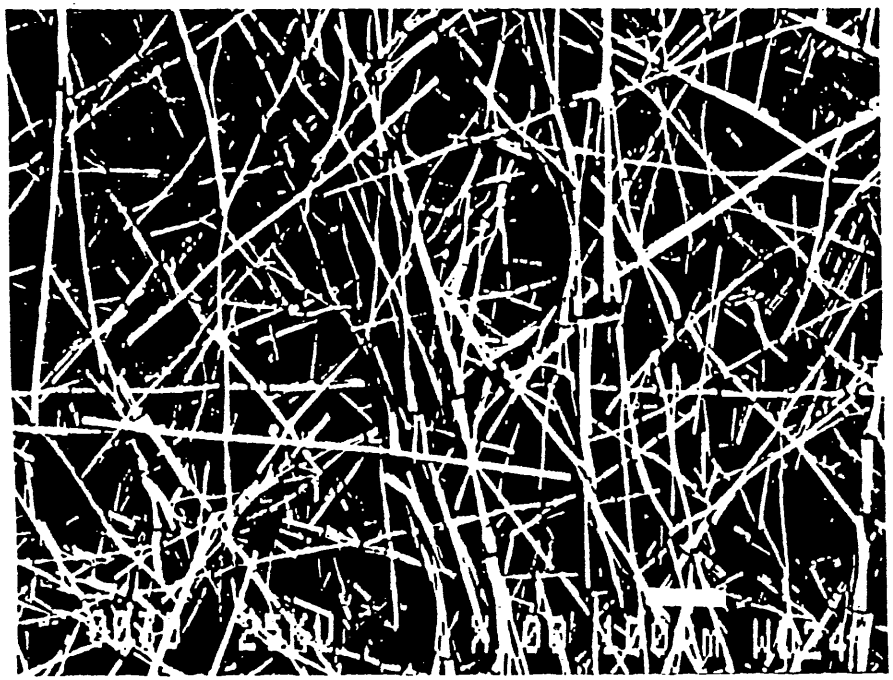
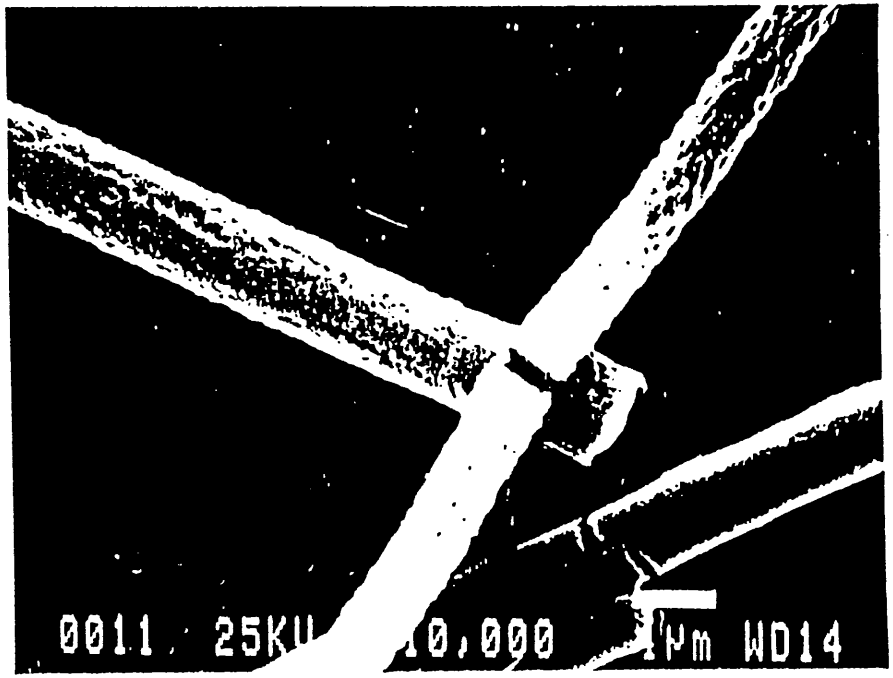


Fig. 7. In Vitro Glass Fiber Breakage

901 Glass after 430 Hr. in the In Vitro Flow-Through System



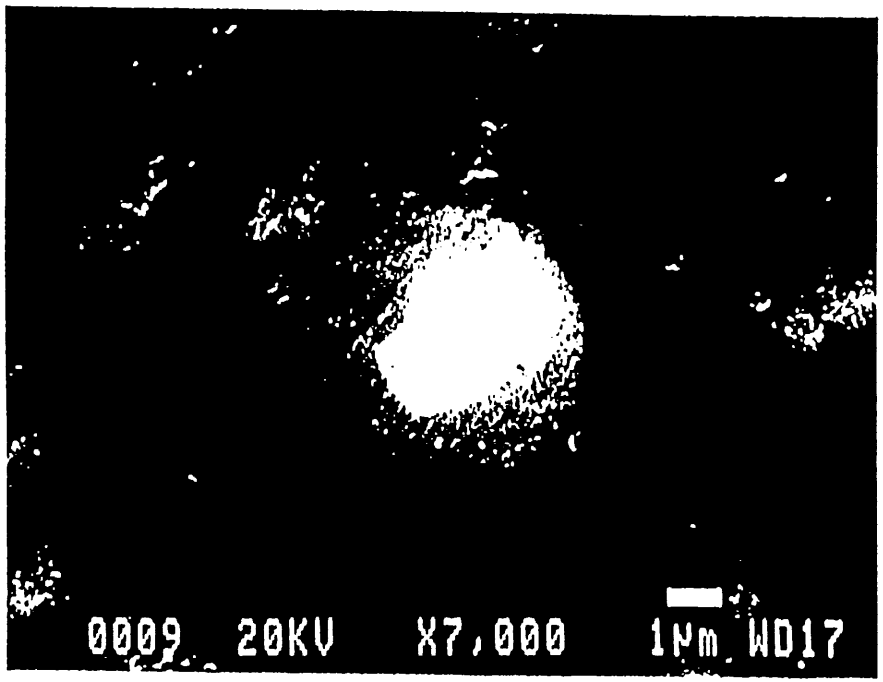
X100



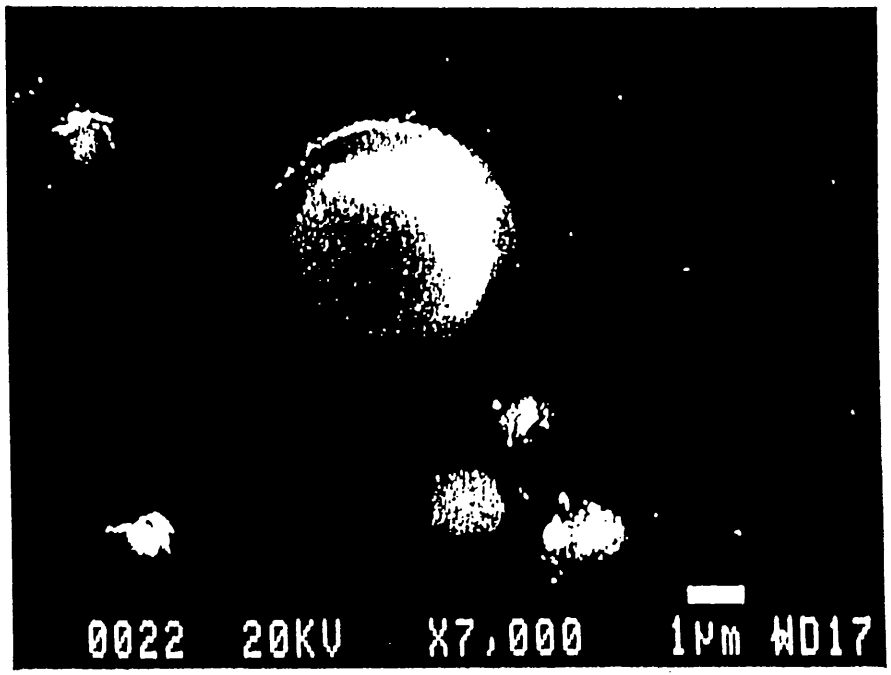
X10,000

Fig. 8. Fiber Persistence: Incongruent Dissolution

In Vitro Flow-Through System, 500 Hr.

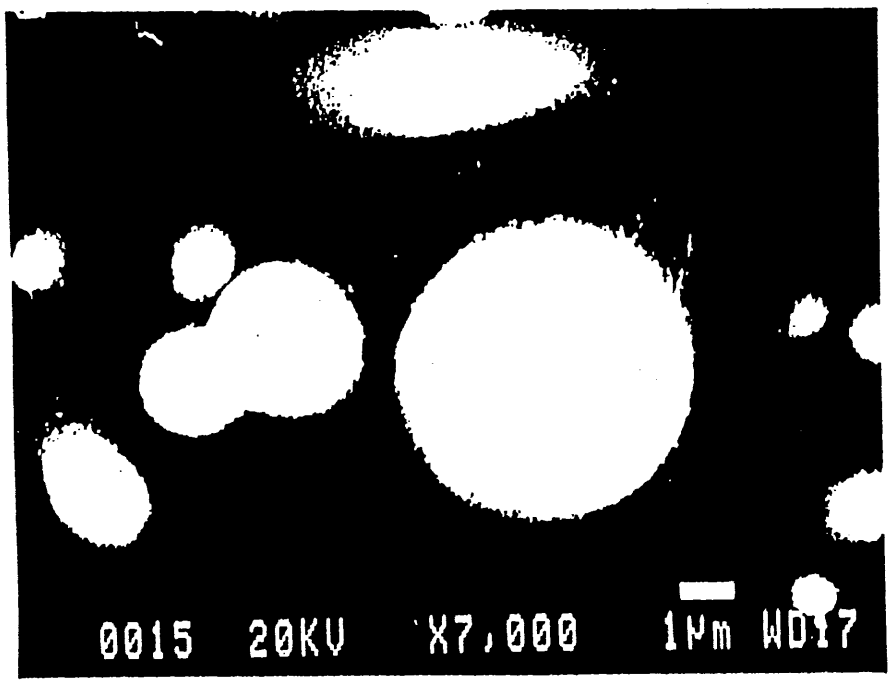


A. Rapid Leaching,
MMVF10



B. Moderate Leaching,
MMVF22

(Fig. 8. Continued)



C. No Leaching,
MMVF21

Negative Health Effects of Environmental Odor Pollution

- A Review -

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ABSTRACT

Malodors may impact upon human health through direct neurotoxic or indirect (stress) effects. Persons with impaired olfactory ability often perceive malodors as more annoying than do persons with normal olfaction. Malodors may induce depression, nausea, vomiting, headaches, coughing, insomnia, impaired appetite, exacerbation of asthma, permanent olfactory loss, cardiovascular effects and immune function compromise. Chronic exposure to intermittent malodor near a Navy landfill in Washington was associated with cortical and subcortical dysfunction as manifest by encephalopathy, limbic encephalopathy and cephalgia. Reported psychiatric effects of malodors include: aggression, confusion and depression, as demonstrated by numbers of motor vehicle accidents, family disturbances, psychiatric hospital admissions and 911 emergency calls. Persons undergoing major stress or suffering chronic diseases may be more vulnerable to these psychological effects. On days that malodor wafted from a mulching site southeast of Chicago to the school across the street, children's behavioral problems at the school increased. Community exposure to unpleasant odors reportedly increases helplessness and frustration, reduces task performance, learning ability, motivation and capacity to cope with other stressors, and promotes familial disharmony. These effects combine to induce disadvantageous social conditions for the stability of the family unit and rearing of children.

Key words: Air pollution, Malodors, Neurotoxic effects, Psychologic effects, Stress.

Introduction

In studies I conducted over the past ten years, ambient odors affected human emotions, behavior, and physical health in various ways. Odorants can directly impact on neuromechanisms or they can indirectly affect the physical health of the individual through their psychological consequences.[1] In either case, the individual's state of health before the exposure is a factor. Chronic disease states or emotionally stressful conditions render persons especially vulnerable to toxic effects, and persons on medications may, as a side effect, perceive odors in a distorted manner.

Negative Health Effects

A number of studies indicate that exposure to malodorous emanations, besides being an annoyance, induce true physical effects. In 1980, Miner[2] described the results of exposure to the odor of livestock waste; the various effects included annoyance, depression, nausea, vomiting, headache, shallow breathing, coughing, insomnia and impaired appetite.

Malodorous chemical pollutants have various negative effects. To mention a few that have been studied, trichloroethylene, a universally present air pollutant, can cause cephalgia.[3] Acute exposure to nitrogen tetroxide can cause cephalgia[4] and chronic neurotoxicity.[5] Acute exposure to chlorine gas can cause neurotoxicity.[6] In 1991, Neutra[7] reported that people living around hazardous waste sites reported more physical symptoms at times when they detected malodors than at times when they were unaware of such odors. Shusterman[8] demonstrated that even at levels considered nontoxic, chemical odors can cause physical symptoms.

Physical health effects of malodors can be divided into six categories: respiratory, chemosensory, cardiovascular, immune, neurologic and psychologic.

Respiratory effects occur most notably among asthmatics. Any strong odor may induce an attack in persons with unstable asthma.

Chemosensory. Chronic exposure to malodors from pulp mills can cause permanent olfactory loss.[9]

Cardiovascular. Malodors can induce an adrenocortical and adrenomedullary response leading to elevation of blood

pressure and subsequent increase in stroke and heart disease.[1]

Immune. Immune function may be compromised either directly, as a result of olfactory/neural projections to lymphoid tissue,[1] or indirectly, as a result of malodor-induced depression and other negative mood states.[10]

Neurologic. In a recent study, chronic exposure to intermittent malodors from a Navy dump site induced cortical and subcortical dysfunction manifested by encephalopathy, limbic encephalopathy and cephalgia.[11]

Psychologic effects of odors, recognized for centuries and noted by Freud and others, vary widely among individuals. Persons experiencing major stressful events are particularly vulnerable to psychological effects of malodorous air.[1] And those with a distorted or impaired olfactory sense are often annoyed by odors that most persons usually consider pleasant.[1]

It is logical that odors influence moods and emotions because the olfactory lobe, which is the part of the brain believed to account for smell, anatomically belongs to the limbic system, which is the seat of the emotions.[12] Thus, the olfactory sense is the one sensory system that, more than any other, has the potential to affect brain functioning.

Psychophysiologically, odors may impact upon human emotions through any of three mechanisms: 1. by inducing a Pavlovian conditioned response, 2. through olfactory evoked recall or nostalgia,[13] and 3. by direct action upon the brain, in a manner similar to that of a drug.[14] This last mechanism is demonstrated by measurements of subjects' EEGs, or brain wave frequencies.[15]

Certain bad odors irritate nasal passages and resultant trigeminal stimulation releases adrenalin, leading to a tense and angry state.

Thus bad odors can produce aggression which may then be covertly expressed. In one experiment college man were instructed to apply varying degrees of electric shocks to their colleagues, supposedly for the purpose of training them; these men chose to inflict greater degrees of pain upon their colleagues when bad odors were present.[16] And on days when malodorous air pollution is high, the numbers of motor vehicle accidents also is high, indicating that

persons drive more aggressively in a polluted atmosphere.[17]

In studies of residents exposed to malodors from nearby commercial swine operations, subjects reported that they suffered increased tension, fatigue, confusion, depression and anger and that their vigor decreased.[18]

Ambient pollutants can detract from personal attraction, according to one study.[19] And in a German urban area, the moods of young adults fluctuated according to fluctuations in the daily ambient air quality, a correlation especially marked among more emotionally unstable individuals.[20] Further, daily diary entries showed that the psychological well-being of women in Bavaria varied according to variations in ambient air quality; the correlation was particularly marked among women suffering from chronic diseases such as diabetes.[21,22] Similarly in Israel, negative health effects were significantly associated with levels of urban pollution.[23]

Also linked to malodors in the environment, as determined by ozone levels, were the numbers of family disturbances and the numbers of 911 emergency psychiatric calls.[24] In several cities, the numbers of psychiatric admissions paralleled the quality of environmental air.[25]

In our study of the malodorous emanations from a mulching site southeast of Chicago, undertaken for the Illinois EPA, Illinois Attorney General's Office, on days when the miasma wafted from the site to the school across the street, children's behavioral problems at the school increased.

Community and Social Effects

The fatigue and annoyance caused by ambient malodors reduce persons' capacities to function normally. Thus their abilities to tolerate frustration, to learn, and to cope with other stressors are impaired. These effects can act together to increase familial and community disharmonies[1] to the detriment of the nurturance of families, the growth and well-being of individuals and society.

Human awareness, concern and motivation to change these conditions are problematic. Migrants from rural areas are apt to notice the poor quality of urban air and judge odor pollution as serious,[26] but prolonged exposure leads to attitudes of helplessness to remedy the situation. In a laboratory study, subjects exposed to unpleasant odors experienced increased feelings of helplessness and their

motivation was reduced.[27] Besides, the longer people live in a polluted atmosphere, the less they notice it.[28] Many long-time city dwellers no longer even bother to take precautions in response to air pollution advisories.[29] The future looks hazy indeed.

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A Continuous Denuder for Acid Aerosols and Gases

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Abstract

A continuous flow denuder has been developed to extract water soluble acid aerosols and gases from the atmosphere prior to analysis. To avoid interaction between the aerosol or gas to be measured and the surface walls of the denuder, it has been designed so that there is minimal surface interaction prior to extraction. This denuder body is constructed of plexiglas^{R} G acrylic material. Extraction medium is pumped to the denuder entrance at a rate of 3.0 milliliters per minute using a miniature solenoid pump. Sample air is drawn through the denuder at 2.5 liters per minute by means of a vacuum source. The air and liquid meet at the denuder entrance and are immediately drawn into the extraction chamber where turbulent flow conditions exist. This mixture can be analyzed by any real-time detection device; however, this continuous denuder was designed specifically to support the real-time halogen acid aerosol/gas analyzer developed by the Army. The advantages of this device are that it provides for a small, non-breakable, continuous flow denuder which can be operated in any orientation. The extraction efficiency of this device compares favorably with results obtained using a midget impinger for sampling various halogen acid aerosols and gases.

Introduction

During the use of halon and halon replacement candidates to extinguish fires exposure to significantly high acid aerosol and gas concentrations may occur and be episodic in nature. Accepted procedures that recommend sampling with midget bubblers[1] and sorbent tubes[2] collect a time-weighted-average sample that provides time-weighted-average exposure information. The peak value of the exposure level tends to be averaged with the lower values; thus, actual exposure assessment can be inaccurate. In order to accurately assess health effects from exposure to acid aerosols and gases under these

situations, real-time monitoring instrumentation is needed. Any real-time continuous monitoring instrumentation which analyzes air toxics in the aqueous phase needs a continuous extraction device. Many gas analyzers sample through a length of tubing because the sampling environment can be hostile. For the same reason impingers and sorbent tubes often sample through tubing under field conditions. It has been reported that significant halogen acid gas sample loses can occur with most types of tubing.(3) Therefore, the best way to avoid these loses is to reduce the amount of surface the sample gas is exposed to before it makes intimate contact with the extraction medium. The continuous denuder described here is designed in such a way that there is almost no opportunity for the sample gas to interact with any surface prior to making intimate contact with the extraction media.

Experimental

This minimal surface continuous denuder was designed specifically to support the real-time halogen acid aerosol and gas analyzer developed by the Army.(4) It will support any analyzer which requires extraction of an aerosol or gaseous analyte into aqueous solution prior to analysis. The denuder body is constructed of Plexiglas^{R} G acrylic material. Figure 1 shows a diagram of the minimal surface continuous denuder. Trapping solution is pumped to the denuder entrance at a rate of 3.0 milliliters per minute using a 50-microliter solenoid pump from The Lee Company. Sample air is drawn through the denuder at 2.5 liters per minute by means of a vacuum source. The air and liquid meet at the denuder entrance and are immediately drawn into the extraction chamber where turbulent flow conditions exist. Any aerosols or gases in the air sample that are soluble in the trapping solution are extracted from the air into the liquid phase in the extraction chamber.

Sampling and Analysis

To validate the performance of this denuder it was used along with midget

impingers to sample gases and aerosols at various concentrations. Midget impinger samples were analyzed with a Dionex^R ion chromatograph. Plastic impingers were used to collect HF gas samples and glass impingers equipped with fritted glass nozzles were used to collect aerosol samples.

Gas and Aerosol Generation

Hydrogen fluoride, hydrogen chloride, and hydrogen bromide gases in N_2 were obtained from a local supplier. They were diluted to various levels with house nitrogen using Sierra electronic flow controllers. Hydrogen iodide gas was not commercially available and had to be generated by a controlled chemical reaction between KI and H_3PO_4 developed under contract by the University of Florida.(5) Aerosols of the sodium salts were generated with a medication nebulizer that was operated at 13 psi and 5.8 LPM and measured with a Grimm model 1.104 real-time aerosol monitor.

Results

This continuous denuder is an integral part of the halogen acid gas analyzer and has been extensively tested under laboratory conditions using both gases and aerosols. Various concentrations of HF, HCl, HBr, and HI gases and aerosols were generated and sampled. The particle size distribution of the aerosol generator is provided in figure 2. As indicated on table I, good agreement is obtained between the midget impinger samples and the gas analyzer values equipped with the continuous denuder.

Reynolds numbers calculated for the denuder with air flows from 2.5 to 4 liters/minute ranged from approximately 16000 to 26000. This indicates the denuder is operating under turbulent flow which is needed to obtain high extraction efficiencies. A detailed drawing of the denuder is available from the author.

Conclusions and Recommendations

The novel feature of this device is that the well and extraction chamber have been designed so that there is almost no surface interaction between the sample gas and the surface of the device prior to extraction. In addition, the device is small, non-breakable, and can be operated in any orientation. The extraction chamber has a demonstrated high extraction efficiency for both gas and aerosol halogen acid samples.

This minimal surface continuous denuder will provide a means to continuously extract air toxics from the atmosphere in support of real-time monitoring devices which are used to monitor acid aerosols and gases resulting from the use of halogenated fire suppression agents, from the launching of the Space Shuttle and similar rocket systems, and from the demilitarization of perchlorate based solid rocket fuel and nerve agent.

This device also can be used in compliance monitoring to trap air toxics in hostile environments such as inside the stack of a hazardous waste incinerator. This would eliminate the losses currently experienced by sampling though long lengths of plastic tubing.

Acknowledgment

The author wishes to thank Mr. Stan Kneiss and Ms. Jennifer Hornsby for assisting with the laboratory testing of this device and Mr. Louie Martin for timely fabrication support.

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Table I. Comparison of halogen acid gas analyzer and midget impinger results for gases and aerosols. All values are reported in mg/m^3.

	HF		HCl		HBr		HI	
Phase	Impinger	Analyzer	Impinger	Analyzer	Impinger	Analyzer	Impinger	Analyzer
Gas	2.4	2.3	16.1	16.8	32.3	34.5	38.5	42.4
	4.5	4.0	48.7	47.8	55.2	60.8	48.4	51.9
	57	59	59.2	61.6	324	273	68.1	75.2
					766	816		
Aerosol	149	144	77.7	77.1	8.4	9.0	84	64
			165	164	45.5	43.3	219	200
					61.8	62.0		
					151	134		

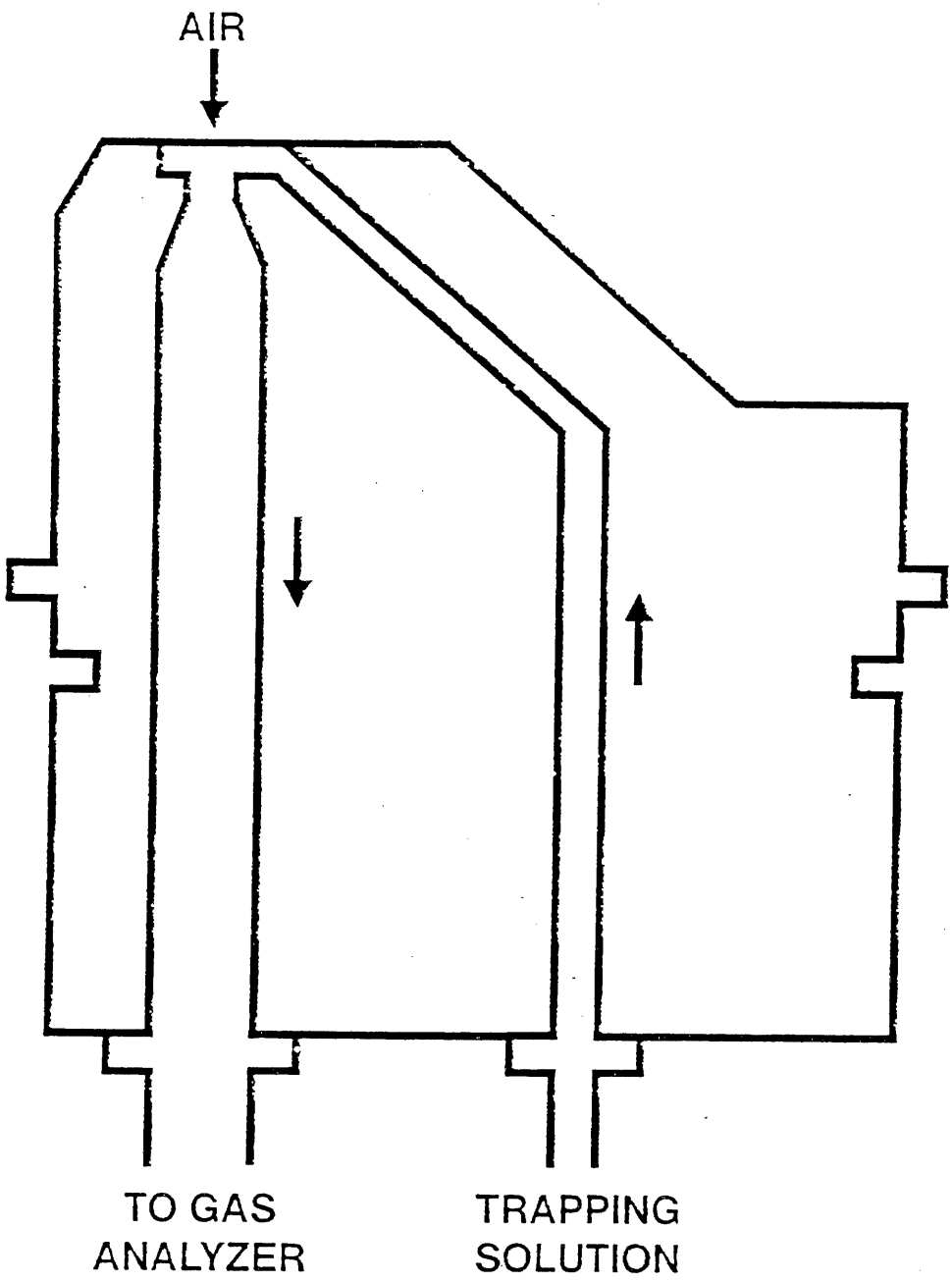

Figure 1. Diagram of the minimal surface continuous denuder with 0.036-inch diameter throat.

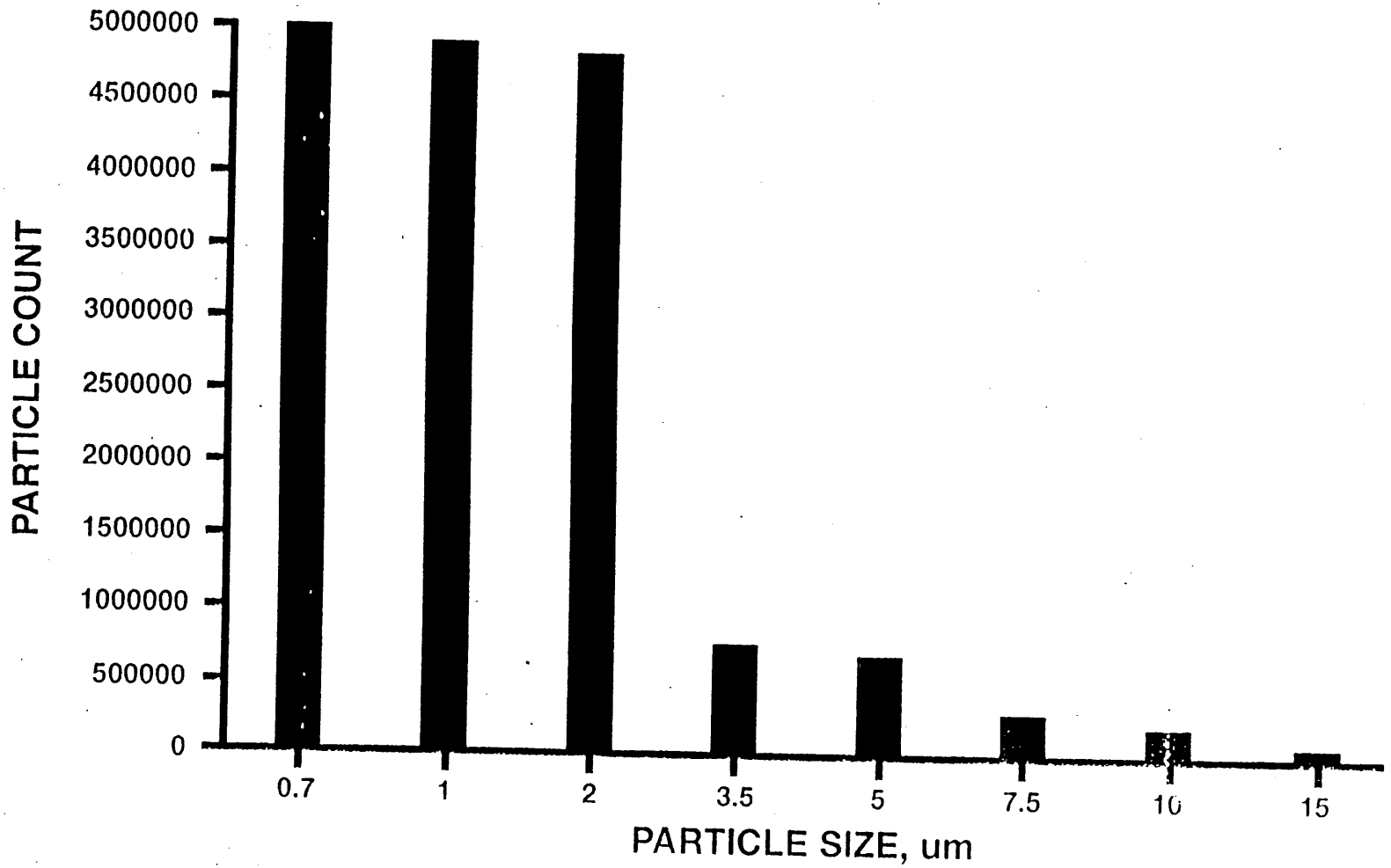

Figure 2. Particle size distribution from medication nebulizer measured with a Grimm Aerosol monitor.

Issues in the Interpretation of Exposure/Response Curves in Time-Series PM-Health Effects Studies

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Abstract

A number of time-series studies have reported significant associations between particulate matter (PM) and both morbidity and mortality in various locales in the U.S. and in other countries. These studies have typically reported short-term excess increases in deaths or hospital admissions as the percent increase of total deaths or admissions per unit PM concentrations (e.g., relative risk per 100 μg/m3 of PM10). Some of these studies also reported estimated exposure-response curves for ranges of PM levels. However, there remain unresolved issues that may be critical in properly interpreting these relative risks and exposure-response curves for risk assessment. These include: 1) differences between cities in statistical power to detect health effects; 2) relative exposure errors (i.e., spatial variability) among PM, co-pollutants, and weather variables within metropolitan areas; 3) inter-comparability of the short-term risks estimated; 4) exposure misclassification and underestimation for at-risk sub-populations. In this paper, these issues are outlined and illustrated using example PM10, copollutants, temperature and mortality data from selected U.S. cities. Results include: the effects of small datasets (both in terms of the number of days and daily mortality counts available) on the statistical power to detect a given PM slope size; differential spatial variabilities for PM, co-pollutants, and temperature; comparison of short-term relative risks. Systematic and quantitative evaluation of these issues should provide valuable input for the interpretations of time-series observational studies.

Introduction

Increases in daily death counts and hospital admissions were documented for historical air pollution episodes such as the 1930 Meuse Valley, Belgium smog episode,[1] and the December 1952 London, England smog episode.[2] Such associations were also found in relatively "non-episodic" period in London by others.[3-5] These classic air pollution conditions were characterized by elevated levels of particulate matter (PM) and sulfur dioxide (SO_2), due to mostly coal burning during temperature inversions in winter. More recently, a large number of studies have reported associations between PM and mortality or hospital admissions in various regions of U.S. and other countries,[e.g., 6-10] and a consistency of estimated risks have been asserted by some researchers.[11-13] However, in contrast to the classic air pollution episodes, these contemporary air pollution conditions are not always related to the winter temperature inversion or primary aerosols from coal burning. Furthermore, for PM10, the associations have been reported for levels well below the current National Ambient Air Quality Standard of 150μ/m^3. At such levels with chemically varied PM mixtures, the causal mechanisms speculated for classic air pollution, such as acute anoxia from brochospasm,[2] may not be plausible. Experimental researchers therefore have focused on an elucidation of plausible mechanism(s) by examining specific size ranges (e.g., ultrafine particles) and specific chemical components (e.g., acid aerosols) and mixtures thereof. While establishment of a plausible biological mechanisms is important to the causality of PM effects, the observational air pollution epidemiology also faces several critical issues that need to be addressed so that the estimated risks can be used most appropriately for policy decisions.

The critical issues in the interpretation of the PM exposure/response curves are generally related to the limitation of the data used in the studies. It should be noted that most of the time-series studies on PM-health outcomes utilized existing mortality or morbidity records, air pollution, and weather data collected by local, state, or federal agencies. In contrast to designed prospective cohort studies, the use of these data for epidemiological purpose can suffer from potential exposure misclassification, measurement errors, multi-collinearity, unmeasured confounders, etc. Nevertheless, the advantage of the ecologic time-series studies is that they consider the entire population's health outcomes in a given city, and therefore the results can be a direct input for public health risk assessment.

This paper raises critical issues in interpreting the estimated risks and exposure/response curves in the time-series studies using examples and illustrations, and identifies future research needs. The specific issues to be discussed are: 1) statistical power; 2) differential exposure errors of explanatory variables; 3) population-at-risk or exposure misclassification, and; 4) risk estimate interpretation.

Issue: Statistical Power of Data Needed to Detect a Given Effect Size

Time-series PM-mortality or morbidity studies typically report estimates of "relative risk" (RR) per unit increase in PM, based on a Poisson regression coefficient (e.g., RR=1.04 per 50μg/m^3 increase in PM10). A review of recent studies found that the range of total daily death RR for PM10 is 1.015-1.085 per 50μ/m3 increase.[14] Because these RRs are not "very large" (more discussion on this later), and their associated significance are not "enormous" (ranging in t-statistics from 1 to 6), such effects are unlikely to be statistically significant in areas with small populations, given the typical PM sampling frequency (every-6th-day). It should be noted that most of the past time-series studies had many years of daily data. This is not the case for most U.S. cities today.

For a given effect size, the significance of PM coefficient in a Poisson regression in the time-series data depends on its standard error (S.E.), which is itself a function of : 1) the number of observation (days) available; 2) daily mean counts of outcome (mortality or hospital admission); 3) day-to-day variance of PM; and 4) model specification. For the first three items, the standard error (S.E.) of PM is a function of their inverse square-root:

$$S.E._{\beta}=\frac{k}{\sqrt{n}\sqrt{m}\sqrt{var_{pm}}}$$

where k= a constant that depends on the model specification; n=number of days available; m=mean daily number of deaths or hospital admissions; var_{pm}=daily variance of PM.

One such example, using PM10 and mortality data from Steubenville-Weirton/Wheeling, OH-WV MSAs between 1985-1990, is shown in Figure 1, in which the S.E. of PM10 coefficient was examined as: (a) a function of the number of days used in the regression (mean death count and variance of PM10 were held approximately constant by randomly resampling varying number of days from the entire data); and (b) a function of mean death counts (by using various cause specific categories). In this example, the Poisson regression also included the hot-and-humid and season indicator variables, as was done in Schwartz and Dockery's original Steubenville TSP-mortality study.[9] It can be seen that the standard error of the PM10 coefficient is a inverse square-root function of the number of days available or the mean daily death counts.

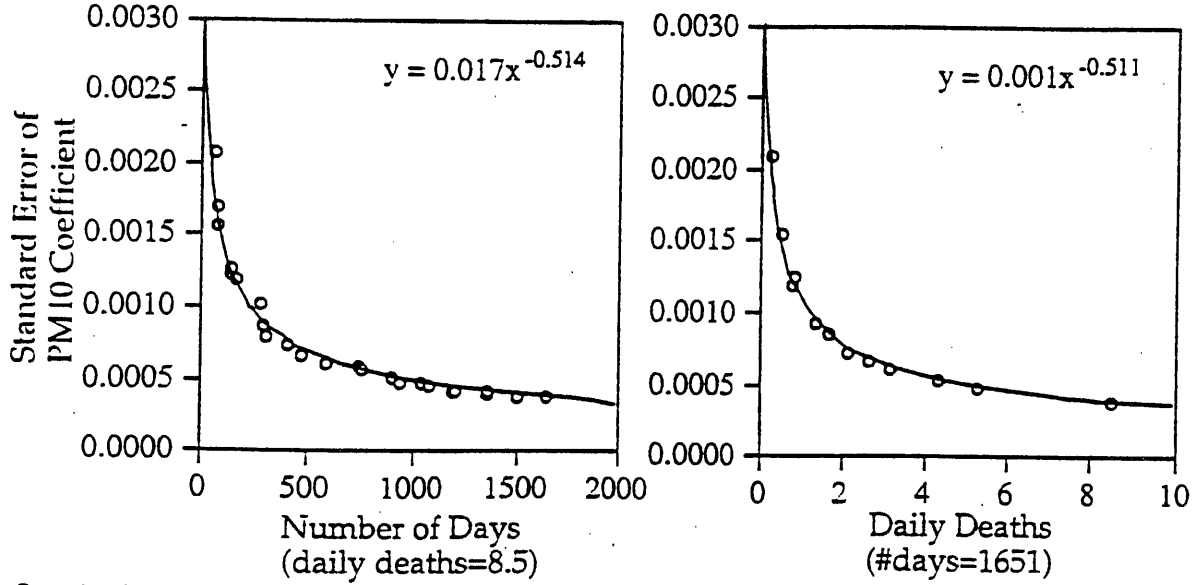

Figure 1. Standard Error of PM10 regression coefficients as functions of number of days and daily death count. See text for explanation.

Suppose that the S.E. of PM10 coefficient could be predicted from the population size, the number of days on which PM10 data are available, and the variance of the PM10, based upon the previous example. What does this tell us about the power of detecting the reported range of PM10-mortality effects using the currently available PM10 data in the U.S.? Figure 2-(a) shows the distribution of PM10 sampling stations in the U.S. in 1990, as well as their means of daily values, and the number of sampling days. The mean values appear to range widely (Figure 2-(b)), but for most of major MSAs (e.g., New York, Chicago, Atlanta, Houston, San Francisco, etc.; Los Angeles and its vicinity being exception), the average PM10 ranged between 30 to 40 μ/m^3 during this period. The variance in this range changed approximately proportionally to the mean, and therefore is not the major factor in determining the power in most major cities. The number of PM10 sample days, however, is a major factor in determining the power of the data. As seen in Figure 2-(c), a majority of PM10 stations collect data using the standard every-6th-day schedule; and only a small number of stations collect data every-other day or every day. Thus, the difference in sampling schedule alone affects the t-statistics by a factor of square-root of six. The effect of the difference in population size (and, consequently, the mean number of deaths or hospital admissions) among cities can be also important. For example, a difference in the daily mean number of deaths between a small MSA with mean daily deaths of 3 (e.g., Steubenville, OH) and a large MSA with mean daily deaths of 150 (e.g., Los Angeles) can result in a factor of square-root of 50 in t-statistics if everything else remained the same.

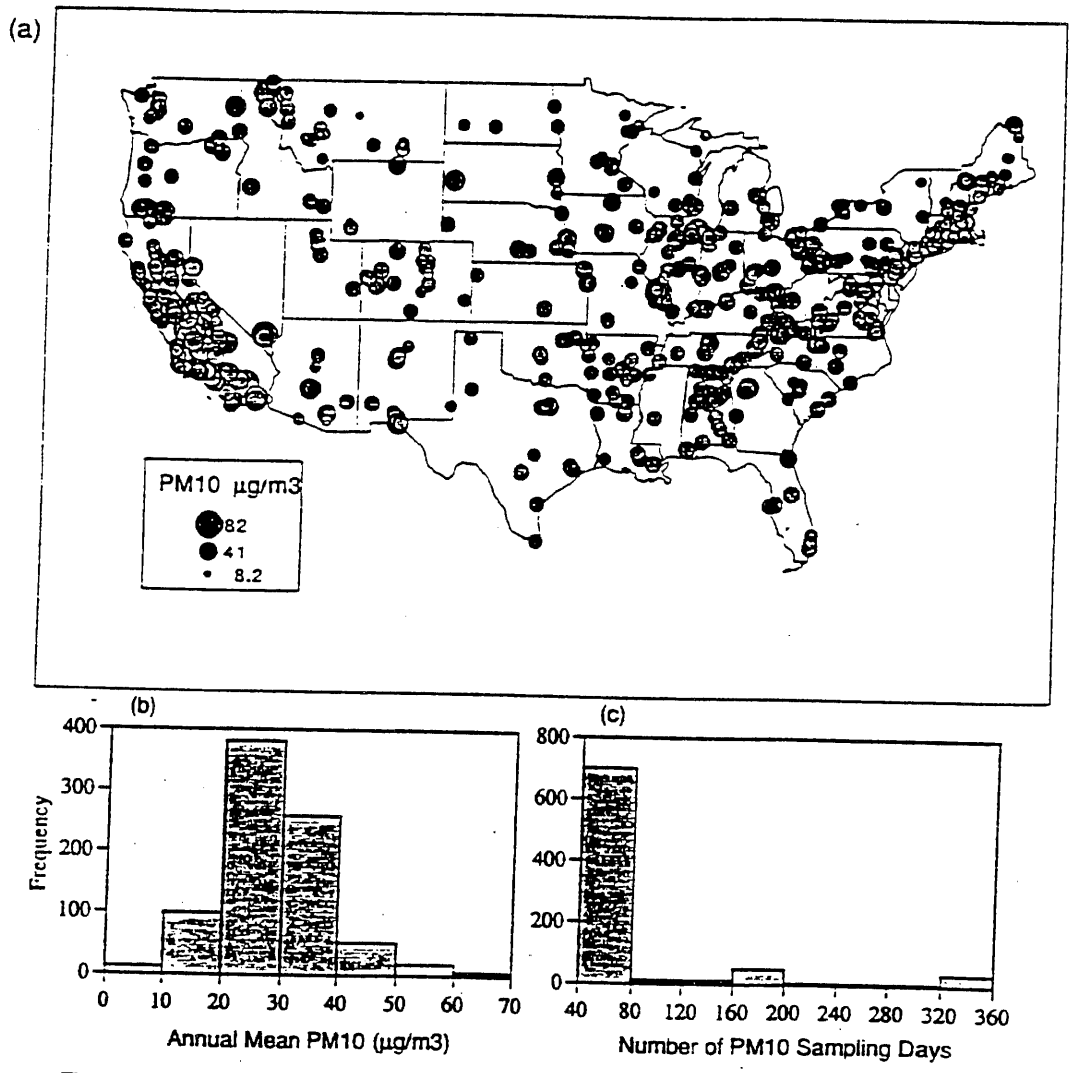

Figure 2. The location of PM10 monitoring stations in the U.S., the distribution of their annual means, and the sampling days available in 1990.

Figure 3 shows a hypothetical power curve to detect RR=1.04 per 50μg/m^3 increase in PM10 (approximately the middle point of the reported range) as a function of daily death counts and the number of days PM10 are available, based on the previous example (Figure 1), assuming that the variance of PM10 are equal to that in the Steubenville-Weirton/Wheeling MSAs, and using the same model specification. The dotted line indicates the complete 10-year sampling with every-6th-day schedule (PM10 sampling started around 1985, so by now we have 10 years of data). It can be seen that even with this length of data, the MSA needs to be at least the size of Atlanta, GA in order to detect the effect size with power of 80%.

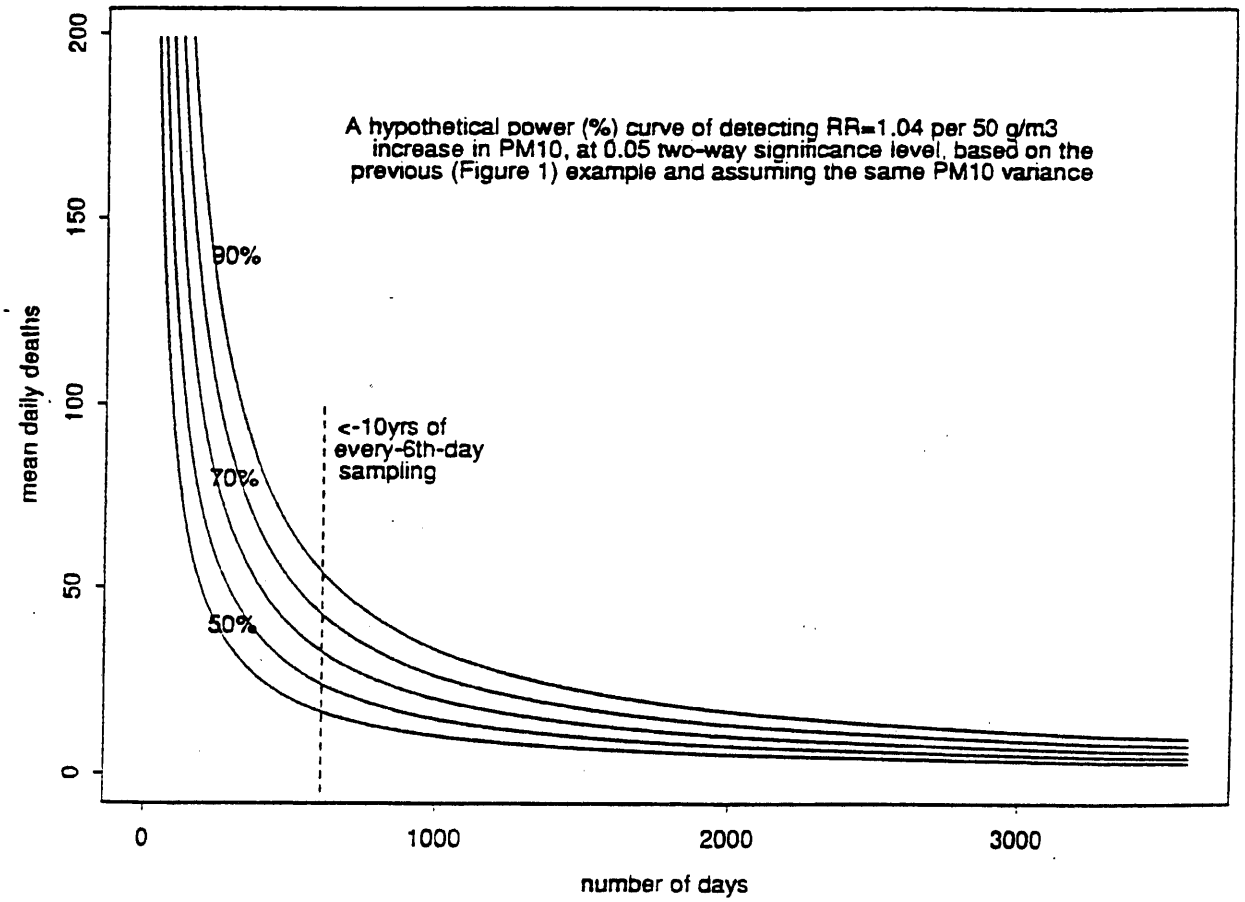

Figure 3. Hypothetical power (%) contour of detecting mortality RR of 1.04 per 50μg/m^3 increase in PM10 at 0.05 significance level, based on the previous results (Fig 1), and assuming the day-to-day PM10 variance is equal to that in the example dataset from Steubenville-Weirton/Wheeling MSAs.

Issue: Differential Exposure Errors of Explanatory Variables

When more than one air pollutant or weather variables are considered either separately or simultaneously in a mortality or morbidity regression, the relative significance of these explanatory variables are often discussed in the context of relative causal role. For example, PM indices have been often shown to be more significantly associated with mortality than SO_2.(e.g., 3,4,9,15) While such observations and subsequent interpretation may be supported by reasoning external to the data (e.g., poorer indoor penetration of the reactive gas than PM; "unlikely" causal effects at the SO_2 levels observed, etc.), the face value interpretation of the relative significance of health-effect association as relative causality is adequate only if all the air pollution and weather variables are measured with equal precision.

Precision error includes both analytical and spatial variability.(e.g.,16) Spatial variability reflects errors in estimating the population exposure of large metropolitan area used for observational studies. It 's possible that the apparent consistency of particulate matter (PM)-mortality associations vs. less consistency for other pollutants may reflect the higher spatial uniformity for PM. If more significant health effects associations were found for air pollutants (or weather variables) with higher spatial uniformity,

then the association may be reflective of better population exposure estimates of "generic" air pollution or weather, rather than specificity of a causal factor. Such differential exposure errors have rarely been examined in the context of time-series health effects analyses. There are a few examples in earlier literature, however, in which the spatial variability errors for PM and other pollutants were considered.[17,18] In Stalker et al's study in Nashville, Tennessee, a lower spatial precision was found for SO_2 than TSP.[17] More recently, in Kochmar et al.'s study of five U.S. cities, fine particles were found to be more spatially uniformly distributed than coarse particles.[19] Some epidemiological studies have also described the spatial variability of sulfates and ozone,[20] and PM10,[21] by plotting the temporal correlation of the data from multiple sites, as a function of separating distance. .

It should be noted that the information pertinent to the significance of coefficients in time-series analyses is the spatial variability of temporal fluctuations, not the difference in absolute levels (i.e., constant gradient) within an MSA. The spatial variability of the absolute level may bias the coefficient, but it does not affect the significance, as long as their temporal fluctuations correlate well. An examination of this type of error is often difficult because of the limited number of monitoring stations collecting data for an extended period of time within an MSA.

The air pollution data for Steubenville-Weirton and Wheeling, OH-WV MSAs, as available from U.S. EPA's Aerometric Information Retrieval System (AIRS), provided an opportunity to examine the issue of spatial variability, as multiple monitoring sites were operated for an extended period of time, 1985-1990, and were available for PM10 (8 sites) and SO_2 (7 sites). Smaller numbers of sites were available for ozone (3 sites), nitrogen oxide (3 sites), and carbon monoxide (2 sites). Correlation of daily fluctuations for each pair of sites were calculated, and plotted against their separation distance. The result is shown in Figure 4. Excluding the correlations with one site in Mingo Junction (open circle), the majority of the values for PM10 were above 0.5, while the majority of SO_2 correlations were below 0.5. Thus, PM10 appears to be more spatially uniform than SO_2 in this locale. The correlations among O_3 were higher than those for NO_2 (measured at the same sites as O_3) for the three sites. Thus, the poorer temporal correlation of SO_2 than PM10 may partly explain the lower, or lack of, significance for SO_2 -mortality associations found in past studies.

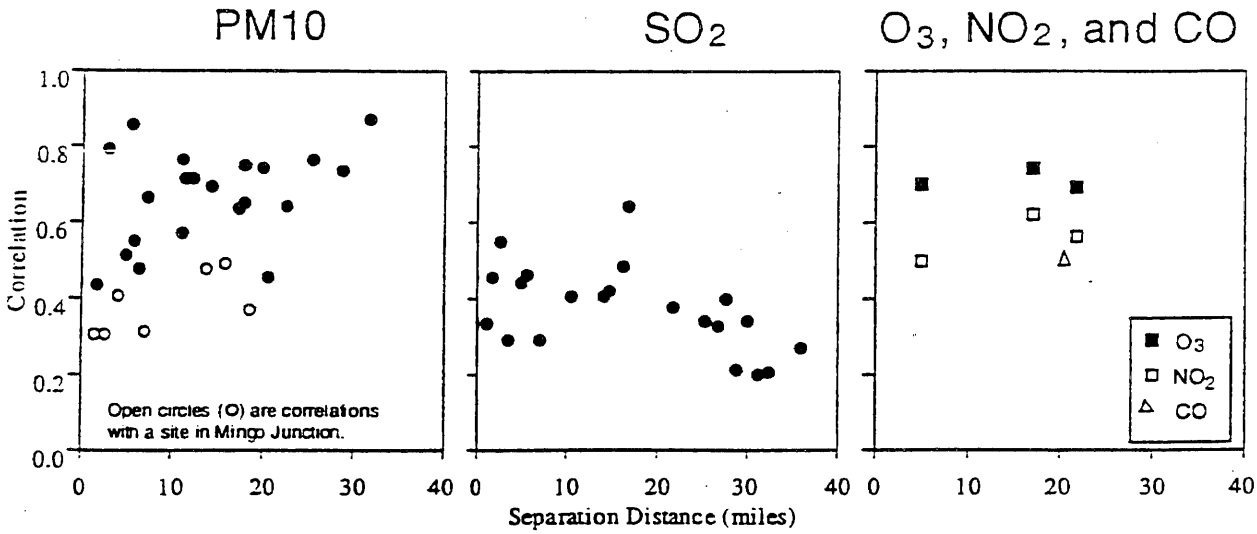

Figure 4. Correlations (over time) among the monitoring sites' air pollution vs. their separation distance

The issue of spatial variability also applies to the relative significance of weather vs. air pollution health effects. Extreme (hot and cold) temperature has been known to cause excess mortality and morbidity,[e.g., 22-24] and temperature is often shown to be more significant predictor of mortality than air pollution.[e.g., 25,26] While the biological plausibility of temperature effects on mortality (e.g., hyperthermia and hypothermia) have been accepted (in contrast to unclarified mechanism of PM effects), the issue of differential measurement errors of weather vs. air pollution has not been examined to date.

This may be because the weather variables used in time-series studies are usually data from airports, and there are not more than one or two airports in and around each MSA.

In order to determine the differential spatial errors (of temporal fluctuations) for PM10 and temperature with sufficient number of monitoring stations, data were procured for a much larger geographical scale than an MSA: seven central and eastern adjacent states including Illinois, Indiana, Michigan, Ohio, Pennsylvania, Wisconsin, and West Virginia during 1988-90. Temperature data were retrieved from compact disks from Earth Info,[27] which compiled National Climatic Center's nationwide surface hourly observation data. There were 45 temperature stations in these seven states. PM10 data were retrieved from U.S. EPA's AIRS System. The mean daily temperature data did not have missing values, while the PM10 data were not complete for many sites, and some sites collected more frequently than the standard every-6th-day. Therefore, in order to make the sample size more consistent, the sites with less than 90% of the every-6th-day sampling days were eliminated, and only the every-6th-day schedule days of each site were analyzed. This resulted in 72 PM10 sites. Likewise, temperature data were sub-sampled for the PM10 every-6th-day sampling days.

Figure 5-(a) and (b) shows the site-to-site correlations for each pair of temperature and PM10 data, plotted against their separation distance. The negative correlation/distance slope is shallower for temperature than for PM10, and the scatter around the slope is also much narrower for temperature, indicating a better spatial precision of temporal fluctuations. Such correlation-distance relationships have been previously analyzed by Burnett and colleagues for the Toronto, Ontario region for ozone and sulfates.[20] The slope and intercept for PM10 shown in Figure 5-(b) ($r = 0.721 - 0.0007$*miles) are comparable to those for sulfates and ozone, adjusting for miles, reported by Burnett et al.,[20] but the scatter for PM10, especially in the range less than 100 mile, appear to be greater for PM10 than for ozone or sulfates, possibly reflecting greater impacts of local sources on PM10 than on more chemically specific regional air pollutants such as sulfates or ozone.

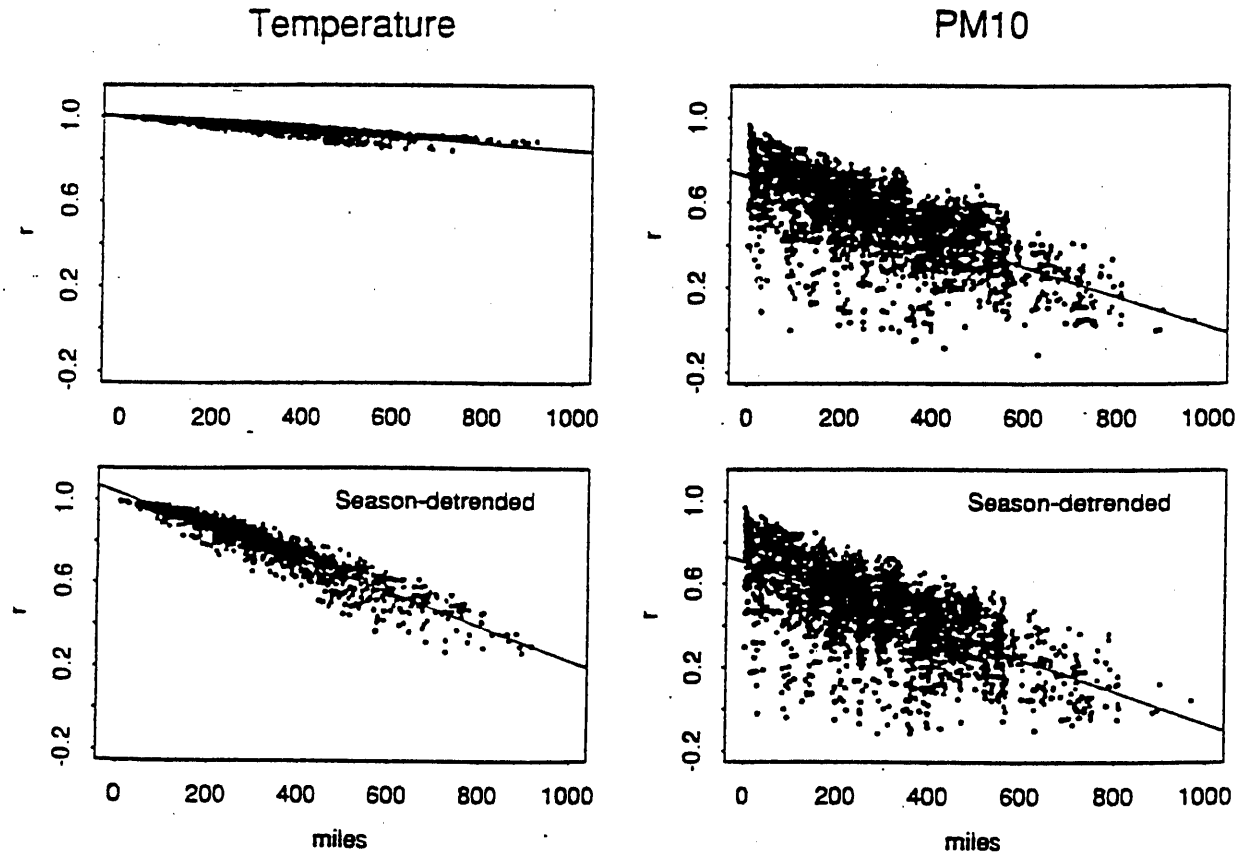

Figure 5. Correlation/separation distance relationships for temperature (45) and PM10 (72) stations in seven Central/Eastern states during 1988-1990.

It should be noted, however, that a major fraction (> 50%) of the temporal variance of temperature in the central and eastern U.S. is due to the seasonal cycles, while a lesser fraction (< 20%) of PM10 temporal variance is explained by seasonal cycles. That is, the higher correlations among the temperature stations is partially explained by the strong seasonal influence. Since the seasonal cycles of health outcomes are controlled in the Poisson regression, it is not the component of the variance of interest in assessing the exposure error of PM10 and temperature. Therefore, the correlations were also calculated after first eliminating the seasonal cycles, as estimated by local smoothing on time,[28] down to approximately one-month cycles, from each of temperature and PM10 series.

The results of the correlation-distance relationships for the season-detrended series are shown in Figure 5-(c) and (d). The slope for temperature is reduced, and more comparable to that for PM10, but the scatter is still much larger for PM10. Note this difference for the scale of an MSA, typically 30-100 miles in diameter. Two stations within this scale for temperature correlate almost perfectly, whereas, for PM10, the correlation may be as high as 0.9, or as low as zero, presumably depending on the local PM source impacts. Thus, in general, temperature temporal fluctuations are more uniform than those for PM10 within an MSA, even after controlling for season, possibly explaining temperature's generally more significant health outcome associations. It should be noted, however, that there are additional factors influencing exposure errors on the personal level, such as air conditioning and activity patterns, which may further complicate the differential exposure errors for air pollution and weather variables.

Issue: Can we compare the short-term risks to other types of risks?

One of the difficulties that risk assessors, policy makers, or even air pollution epidemiologists have when interpreting a short-term PM "relative risk" is its intercomparability with more conventional risks. The short-term relative risks reported in the literature appear to be consistently "small" (i.e., 1.025-1.085 for non-accidental deaths per 50 $\mu g/m^3$ increase in PM10), compared (at a face value) to the relative risks in other types of studies. In cancer epidemiology, for example, some consider a relative risk of 1.7 as weak support, "at most", for a causal inference.[29] However, these two types of relative risks are not comparable. The relative risk used in these short-term studies are not only *acute* in its exposure/response relationship, but also *indirect* cause of deaths. A healthy person does not develop a respiratory disease and die from an exposure to 100$\mu g/m^3$ PM10 in one day. A more plausible hypothesis is that people with chronic respiratory or cardiovascular diseases, who may be nearly dying from the conditions, are pushed to death prematurely by the additional stress on the respiratory system imposed by an increased level of air pollution through a yet unclarified mechanism. This is in contrast to a cancer risk from exposures to a chemical agent, through which a perfectly healthy person may develop cancer and die at the age of 50, when otherwise the person may have lived up to 70 years old. This difference may be obvious to the researchers analyzing these data, but it needs to be clarified when such 'risk estimates' are communicated to people who are not informed about the nature of the short-term risk. Therefore, one cannot say that these risks are "small" compared to cancer or other long-term risks.

One can, however, compare these short-term air pollution risks to other short-term risks. These include the risk estimates for the explanatory variables that are simultaneously included in the regression of health outcomes on PM. Figure 6 shows one such example derived from a Poisson regression to model daily (total non-accidental) mortality in Cook County, IL using 1985-1990 data.[30] While temperature was also modeled with continuous quadratic function in the study, quintile indicator variables were used for easier comparison. The cold temperature was two-day lagged, as the association was strongest at this lag. It can be seen that the relative risk estimated for a 50$\mu g/m^3$ increase in PM10 is roughly comparable to that for experiencing Monday, but somewhat smaller than those for the highest or lowest quintile of temperature. Of course, the choice of the 50 $\mu g/m^3$ increase for PM10 is, while consistent with those used in the recent EPA criteria document, arbitrary. Frequency based (e.g., use the increment whose frequency is comparable to once a week) comparison of relative risks may be "fair", but the difference in the nature of these risks and their cost or feasibility of preventive intervention (Monday cannot be

eliminated) makes a fair comparison difficult. Likewise, a comparison of relative risks from various air pollutants are also difficult, especially when their distributional characteristics are not comparable.

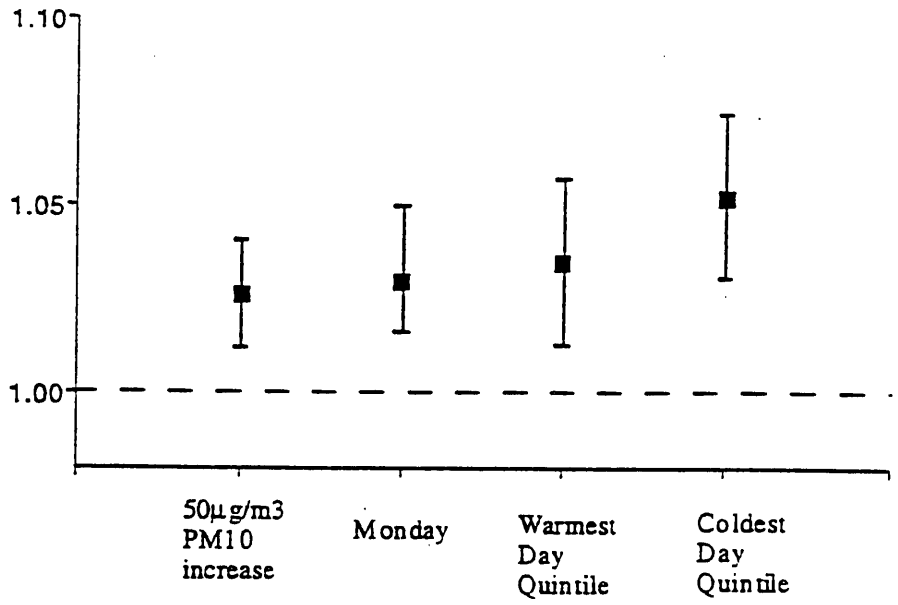

Figure 6. Some comprative short-term relative risks from Cook County, IL 1985-1990 analysys

As mentioned previously, if the stress of air pollution is pushing the already weakened people to their early deaths by a matter of a few days, then the short-term relative risks may not be simply added up in order to make it comparable to other long-term risks. The idea that an elevated level of air pollution kills and depletes a pool of available susceptible persons, and causes a subsequent 'deficit' in death in the following days, is sometimes called *harvesting*. While such a phenomenon should be more obvious in an episodic event, this was not the case in the 1952 London smog episode, in which a tail of elevated deaths persisted even after the pollution level subsided to normal levels. However, there is some suggestive evidence of this phenomenon in the literature. For example, an apparent harvesting was observed up to about 20 days following a heat-wave episode in New York City, 1966.[31] Spix et al., in their regression analysis of SO_2 and mortality reported that the negative coefficients for the product of SO_2 and moving average (up to 21 days) of mortality were indications of harvesting.[32] Since the extent of prematurity of death has a major implication to the interpretation of these short-term relative risks, further research is needed in this area. The methodological issues include modeling of the distribution of the extent (some people's prematurity of death may be a few days, while others may be years), the level dependence (air pollution must be sufficiently high to cause a "depletion"), and the distinction between the seasonal confounding and the long-wave deficit in mortality. In addition, the relationship between short-term effects and the annual excess deaths, as examined in cross-sectional studies, needs to be investigated. This issue has been discussed with hypothetical examples in the past,[33] but has never been examined in actual data. The mechanisms of chronic effects of air pollution need not be related to the mechanism of short-term effects, however. Therefore, the long-term mortality effects of PM, such as those reported in the recent prospective cohort studies, [34,35] may be independent of the accumulation of short-term excess deaths.

Issue: Population-at-risk and exposure misclassification

In addition to the exposure errors due to spatial variation of air pollutants within an MSA, personal- and neighborhood-level exposure estimation errors are expected. The extent of these errors, as yet unclarified, can have an important implication on the interpretation of the short-term risks reported for he overall populations. Figure 7 qualitatively illustrates how personal exposures can be related to outdoor temporal fluctuations of PM. In condition (a), there is no significant indoor PM sources, and the perfect penetration of outdoor PM makes the personal PM exposure highly correlated with outdoor day-to-day PM

fluctuations. In condition (b), a significant indoor PM source causes poor personal/outdoor PM correlation. If there are significant indoor PM sources and indoor penetration of PM is prevented, as in condition (c), the personal and outdoor PM levels have no association. There may also be a condition (d) in which there is no indoor penetration of PM and no significant indoor PM sources. Yet another possibility, as in condition (e), is that the impact from a strong local (neighborhood scale) PM source may be greater than the MSA-wide air pollution pattern, causing not only the personal but the neighborhood's PM exposure to be poorly correlated with the MSA-wide PM levels. In all these conditions except (d), PM, whether outdoor or indoor, may affect people's health outcome, but only in condition (a), the community (MSA) monitor's PM temporal fluctuation accurately reflects personal exposure. Reality is likely to be a mixture of these conditions with seasonal variation. If the exposures of only a small fraction of the population correlate with outdoor monitor's data, then the relative risk estimated for the entire MSA population may be a gross underestimation of the relative risk for that population. There have been several studies that investigated the correlations among personal, indoor, and outdoor PM correlations.[36,37] A review of these studies suggests that the "longitudinal" regressions showed consistently better relationships among the personal, indoor, and outdoor concentrations than the "cross-sectional" regressions, lending support for the air pollution-mortality association found in time-series studies.[38] The range of such correlations appear to be variable, however, and an estimation of the distribution of such correlations would be necessary for risk assessment.

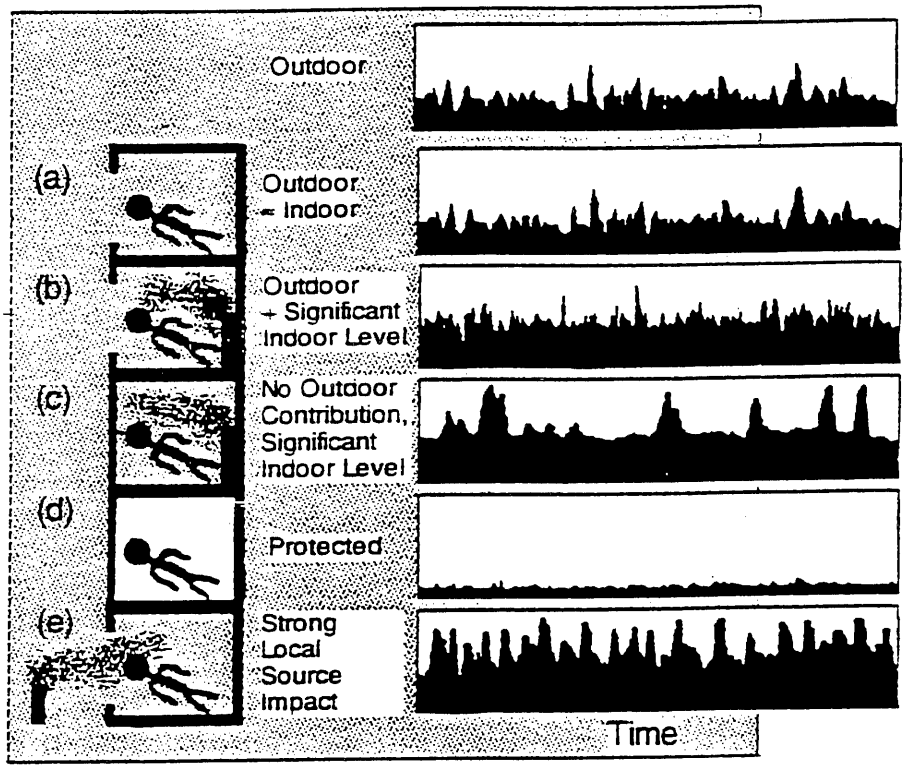

Figure 7. Illustration of the difference in temporal pattern between outdoor PM levels and personal PM exposures.

As shown in the previous examples (Figures 4 and 5), there are differential errors among weather and air pollution variables in estimating the day-to-day fluctuations of population exposure within a given city or MSA. Since the daily fluctuations within such geographical scales are influenced mainly by weather conditions and air mass movement, it is likely that weather variables (e.g., temperature) and regional air pollutants (e.g., sulfates and ozone) have less errors in estimating the area wide population exposures than more localized pollutants (e.g., CO and SO_2). Thus, a time-series analysis of the whole aggregate MSA population inherently cannot adequately identify localized air pollution problems. For example, if a sub-population of 50,000 persons, in a neighborhood within an MSA with five million

people, was affected by a strong local emission source, the health risks imposed on such sub-population would be either underestimated (if the temporal fluctuations of the local PM concentration correlate with that of the MSA), or not reflected (when there is no correlation between the local emission and the MSA-wide PM levels) in an MSA-wide time-series analysis. Because certain sub-populations, especially racial minorities and the economically disadvantaged, are expected to live closer to air pollution sources,[39,40] and these sub-populations are also known to suffer from poorer health status,[41] this issue needs to be investigated by monitoring PM levels in neighborhoods that are close to major PM sources.

Summary and Recommendations

The key issues discussed are: 1) statistical power; 2) differential exposure errors of explanatory variables; 3) risk estimate interpretation; and, 4) population-at-risk/exposure misclassification. Most of these issues can be quantitatively evaluated.

Limitation of a given dataset, in terms of sample size, should be discussed in interpreting the (lack of) significance of the results. Based on the expected size of effect, the number of days, daily mean counts of death or hospital visits, and variance of PM, researchers can evaluate the limit of a given data. Conversely, this information can be used to select a city for a time-series analysis when one has choices (i.e., power analysis).

Investigation of differential (temporal) exposure errors among explanatory variables is crucial when interpreting the relative significance of various air pollution and weather variables. Preliminary results presented in this paper suggest that PM10 may be "better" measured than SO_2, and that temperature may be better measured than PM10 within a scale of typical MSA. However, these differential measurement errors may vary from MSA to MSA, or region to region, depending their emission patterns and specific topological features (e.g., valley vs. flat field). Therefore, more systematic investigation of this issue is needed.

The apparently "small" short-term PM relative risks reported in the literature cannot be directly compared to long-term risk estimates. Since underestimation of the risks for sub-populations-at-risk are suspected, it appears premature to regard these numbers as "small". While determining the extent of "harvesting" is important in interpreting these short-term risk estimates, the control of long-wave components in the conventional time-series approach prohibits examination of harvesting beyond several weeks. Alternative approaches need to be developed to circumvent this problem.

The identification of populations-at-risk, by sub-category specific analysis, is difficult in the county-based mortality data usually analyzed, due to likely exposure misclassification within an MSA. Larger standard errors for the risk estimates for smaller sub-groups further weaken the statistical power. Analyses of hospital admission data (unscheduled/emergency visits) may be more powerful in identifying at-risk-sub-populations because the admission data often provide better spatial resolution (e.g., zip code of residence) that can be link to emission source information and census data. The counts for admission data are also generally larger than those for mortality. Careful targeting of a sub-population in a neighborhood with high PM exposures may be necessary for prospective studies in order to measure the extent of underestimation of risk estimated in the MSA-wide time-series studies.

Despite the potential problems, the results from time-series studies can be a direct input to the public health policy decisions, as they consider the entire population's health outcomes. These aggregate level studies are also relatively inexpensive to conduct, compared to other types of epidemiological studies, as the health outcome, air pollution and weather data have been already collected by federal or local agencies. Some of the issues raised in this paper (e.g., differential exposures and statistical power analysis) can be examined thorough analyses of existing data. Most of these issues apply to air pollution health effects studies in general. Quantification of these uncertainties will provide quantitative information that will help interpret the results from ecologic studies for evaluation of the National Ambient Air Quality Standard, further the understanding of the nature of health effects, and help develop a framework with which a network of population health monitors can be developed to guide effective interventions.

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DEATH FROM INHALATION OF FUEL OIL FLY ASH PARTICLES IN RATS WITH PRE-EXISTING PULMONARY INFLAMMATION

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Epidemiologic studies have found increased mortality associated with particulate air pollution. The objective of this study was to determine whether fly ash particles exacerbate pre-existing pulmonary inflammation, and whether mortality was associated with pro-inflammatory cytokine production in the lung and heart. We used monocrotaline-induced lung disease in rats and inhalation of combustion-generated oil fly ash to simulate adverse effects of complex ambient particles in sensitive human groups. Fuel oil fly ash particles were used because their chemical components and inherent toxicity are similar to urban air particles.[1] In addition, the fly ash has been well-characterized as to chemical composition and biologic responses in humans.[2] Monocrotaline injection results in acute inflammation with progressive lung injury in rats that can lead to pulmonary hypertension and right heart enlargement.[3]

Saline- or monocrotaline-treated rats (50 mg/kg subcutaneously; day 0) were exposed to aerosols of Wright Dust Feeder-generated dry fuel oil fly ash or filtered air for 6 hr on days 11-13. Animals were observed during the exposure period for unexpected deaths, and all surviving animals were sacrificed on day 14. Particle concentrations (mean $\pm$ SD) throughout the exposure were 580 $\pm$ 110 $\mu g/m^3$ with mass median aerodynamic diameter of 2.06 μm, σg of 1.57. Deaths occurred spontaneously only in monocrotaline-treated rats exposed to fly ash (42% mortality). On day 14, there was a significant increase in neutrophils in bronchoalveolar lavage (BAL) fluid in monocrotaline-treated rats with further increases induced by inhalation of fly ash. Northern analysis revealed that fly ash alone induced mRNA expression of the pro-inflammatory cytokine macrophage inflammatory protein-2 (MIP-2) in BAL cells from normal animals. MIP-2 mRNA was expressed in BAL cells, and MIP-2 immunostaining was positive in the heart and lungs of monocrotaline-treated rats exposed to either air or particles. Fly ash exposure enhanced MIP-2 immunostaining in the lung and heart of monocrotaline-treated animals. Positive, but less MIP-2 immunostaining was detected in the heart and alveolar macrophages of normal rats exposed to fly ash alone. MIP-2 immunostaining in the heart was detected in cardiac macrophages. These data suggest that deaths following monocrotaline treatment and fly ash exposure are associated with significant inflammation in the lung with pro-inflammatory implications in the heart.

Methods

Animal Model and Fine Fuel Oil Fly Ash Particle Exposure - Sprague-Dawley rats (CD; Charles River Laboratories, Wilmington, MA) weighing ~250 g were divided into four groups: 1) saline-treated plus filtered air, 2) saline-treated plus fly ash exposure, 3) monocrotaline-treated plus filtered air, and 4) monocrotaline-treated plus fly ash exposure. Monocrotaline-treated animals received a single subcutaneous injection on day 0 of 50 mg/kg monocrotaline (Sigma Chemical, St. Louis, MO) and control rats received sterile 0.9% saline.

The exposure chambers were 1000 L NYU design units. Up to 32 rats were placed in individual wire mesh cages and exposed to either fuel oil ash or filtered air (16 monocrotaline-treated and 16 saline-treated rats) for 6 h per day on 3 consecutive days. The 3-day exposure protocol was chosen because atmospheric conditions typically change in 3-day cycles. Exposures were conducted on days 11-13 post-monocrotaline or saline injection because pulmonary

inflammation is well-established at these times.[3,4] Complete autopsies were performed on animals that died prior to euthanasia.

The aerosol was generated with a Wright Dust Feeder (Model MK-II, L. Adams Ltd., London, UK). Power plant fly ash was obtained from the pollution control system (air heater and electrostatic precipitator) of a Boston area power plant during overhaul of the power plant. The dust was stored in sealed containers. For use in these studies, it was dried overnight at 120°C and ground using a mortar and pestle to break up visible aggregates. The ground fly ash was packed into the dust feeder cylindrical holder with a stainless steel scraper head. A stream of air (14 L/min; 6 PSIG) was passed along the head to carry the scraped dust onto an impactor plate. The spindle rotation rate was set at 0.182 RPM. The air stream, containing fly ash aerosol, was passed through a Harvard Marple Impactor to eliminate particles larger than 2.5 μm.[5] The aerosol was isokinetically fed into the chamber.

Particles were sampled continuously throughout the exposure. Concentration was determined gravimetrically from the mass change on 0.2 μm Millipore filters. The particle concentration during exposures was also controlled by using a Real-Time Aerosol Monitor (Model RAS-1; MIE, Inc., Bedford, MA). The particle size distributions in the chambers were determined periodically during the exposures using an aerosizer (Model MACCII, API, Inc., Amherst, MA). To determine particle composition, aerosol dust was collected using double-stick conductive carbon tape, coated with carbon, and analyzed by an Amray 1000A scanning electron microscope with energy dispersive x-ray spectroscopy using a Kevex μx 7000 system.

Bronchoalveolar Lavage and Northern Blot Analysis - On the day following the last exposure (day 14 post-monocrotaline or saline injection), rats were euthanized and cells were collected by bronchoalveolar lavage (BAL).[6] Viability and total cell counts were determined by hemocytometer counts of aliquots diluted in trypan blue solution. Cell type was determined from modified Wright-Giemsa-stained cytocentrifuge preparations. Remaining cells were prepared for total RNA extraction using a modified guanidinium method.[7]

Northern blot analysis for the proinflammatory cytokine macrophage inflammatory protein-2 (MIP-2) was performed for all treatment groups. MIP-2 (1.4 kb)[6] and human glyceraldehyde-3-phosphate dehydrogenase cDNA (1.2 kb; internal standard) were ^{32}P-labeled by random priming. These methods have been described elsewhere.[6]

MIP-2 Immunolocalization - Rat lung and heart tissues were embedded in O.C.T. compound (Miles, Elkhart, IN), and immediately snap frozen in dry ice-methylbutane. Cryostat sections (7-8 μm) were fixed in 2% paraformaldehyde/0.5% glucose in phosphate-buffered saline (pH 7.4) for 5 min at room temperature, dehydrated in a graded scale of alcohol, post-fixed in pre-cooled methanol for 10 min, preincubated in serum and incubated overnight in the primary antibody. Polyclonal rabbit anti-rat MIP-2 antibody (BioSource International, Camarillo, CA) was used at a concentration of 0.2 mg/ml of dilution buffer (0.1% bovine serum albumin, 0.1% sodium-azide in PBS, pH 7.3). Controls included use of antibody dilution buffer alone or dilutions of nonspecific purified rabbit IgG. Positive staining controls used in the lung included rat anti-keratin diluted 1:10 in antibody dilution buffer. After blocking endogenous peroxidase with a methanol-hydrogen peroxide solution, endogenous biotin sites were blocked by sequential incubations with unlabeled avidin and biotin (Biotin Blocking Kit; Vector Laboratories, Burlingame, CA). Specific binding was detected using a biotin-conjugated goat anti-rabbit IgG, avidin-biotin peroxidase complex (Vector Laboratories), and a substrate solution of H_2O_2 (0.03%) and diaminobenzidine (2 mg/ml) in 50 mM Tris-saline, pH 7.6, with 1M imidazole and 0.3% azide. The slides were counterstained with hematoxylin, dehydrated in a graded scale of alcohol and xylene, mounted, and coverslipped.

Results

Exposure Data and Mortality - The fuel oil ash concentration throughout the 3 day exposure was 580 ± 110 μg/m^3 (mean ± SD). The mass median aerodynamic diameter was 2.06 ± 0.17 μm (σg = 1.57 ± 0.06). Particle analysis by x-ray spectroscopy showed sulfur, silicon, iron, calcium, aluminum, vanadium, nickel, and magnesium to be primary elemental constituents.

Saline- and monocrotaline-treated rats were exposed to the same fuel oil ash for 6 hr on 3 consecutive days. There were no deaths in saline-treated rats exposed to air or fuel oil ash and no deaths in monocrotaline-treated rats exposed to filtered air alone. However, 5 of 12 (42%) of the monocrotaline-treated rats died during exposure to fine particle fuel oil ash. No visible signs of irritation or distress were observed during the exposure as most of the animals appeared to sleep throughout most of the exposure. Thus, when animals died during the exposure, it was often not immediately apparent. At autopsy, the animals that died unexpectedly did not have evidence of lung infection or pneumonia. However, these animals did show some indication of bronchoconstriction as manifested by visible buckling of airway epithelium. Overall, pulmonary inflammation was similar to the sacrificed animals of this group. The heart had no evidence of acute inflammation. Other organs had no gross pathologic changes.

Cytologic Analysis of BAL Cells - BAL was performed one day after the last exposure in all four treatment groups. Two-factor analysis of variance was used on log-transformed data to compare BAL cell counts and differentials among animals groups exposed to filtered air or fuel oil fly ash, followed by unpaired Student's *t*-test for selected comparisons.[8] Differences were considered significant when $p < 0.05$. BAL data are summarized in Table 1 below.

TABLE 1. Total nucleated cells and differential cell counts obtained by bronchoalveolar lavage from saline- or monocrotaline-treated rats exposed to fine fuel oil fly ash particles or air for 6 h on 3 consecutive days.

GROUP	Total Nucleated Cells (10^6)	Macrophages (%)	Neutrophils (%)	Lymphocytes (%)	Eosinophils (%)
Saline/Air	10.3	99.0 ± 0.3	0.9 ± 0.3	0	0.1 ± 0.1
Saline/Ash	15.4	99.6 ± 0.2	0.3 ± 0.2	0.1 ± 0.1	0
Mono/Air	6.7	46.7 ± 6.1*	49.1 ± 5.2*	3.2 ± 1.0	1.0 ± 0.8
Mono/Ash	10.7	48.4 ± 7.5*	41.6 ± 7.2*	0.5 ± 0.3	9.5 ± 8.8

Data is mean ± SEM; n=5-8 animals in each group.
* $p<0.05$ compared to control animals injected with saline and exposed to filtered air.

Monocrotaline treatment caused a significant decrease in the total number of macrophages recovered in BAL of rats exposed to either air or fly ash compared to saline-treated animals. The number of neutrophils was significantly increased in monocrotaline-treated rats exposed to filtered air compared to saline-treated animals. Although fuel oil fly ash increased neutrophil numbers in BAL fluid of monocrotaline-treated rats, the difference did not achieve significance ($p = 0.05$).

Northern Analysis of Cytokines - Total RNA (5 μg total RNA/lane) from rat BAL cells (n = 5-6 animals in each group) was analyzed for mRNA expression of the pro-inflammatory cytokine MIP-2 and G3PDH (internal control) mRNA expression. Results from a representative animal in each of the four groups is shown in Fig. 1. MIP-2 mRNA was not detected in BAL cells from control animals exposed only to filtered air (SALINE/Air). Some MIP-2 mRNA expression was

detectable in 4 of 6 saline-treated animals exposed to fly ash (SALINE/Ash). MIP-2 mRNA was expressed at relatively high levels in all monocrotaline-treated animals whether or not they were exposed to fly ash particles (MONOCROTALINE/Air and MONOCROTALINE/Ash).

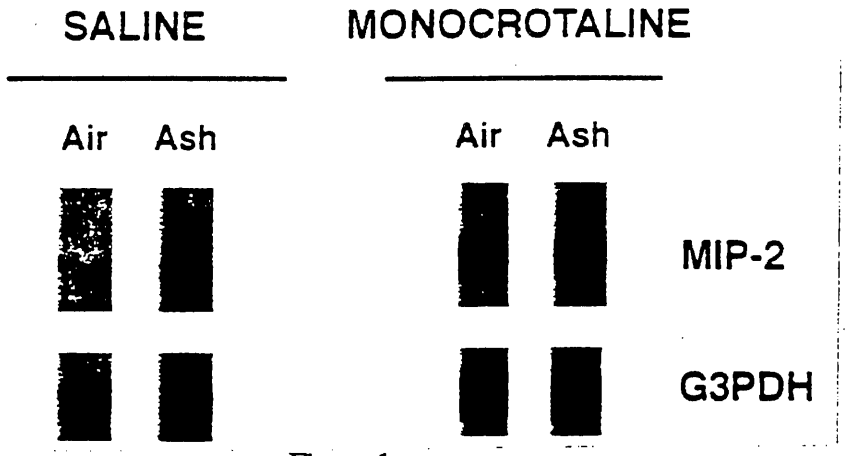
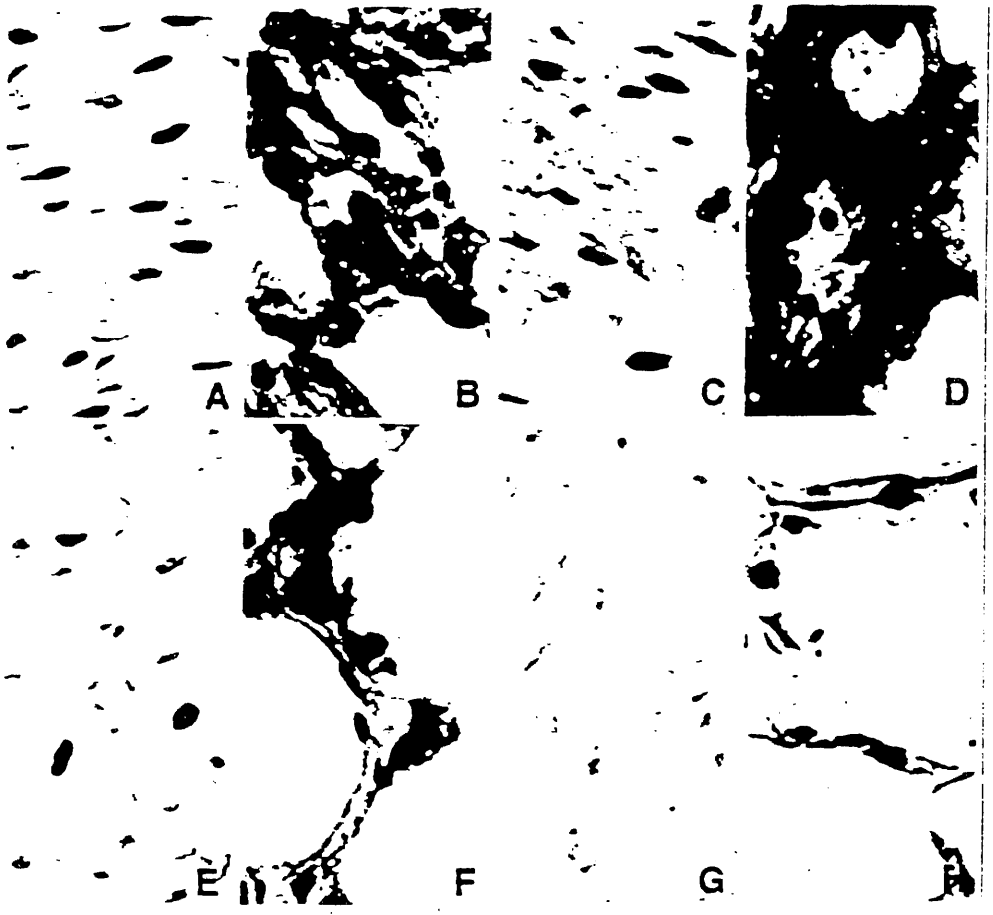


Figure 1

Immunolocalization - Figure 2 illustrates representative heart and lung sections obtained from the four treatment groups in which MIP-2 positive cells were computer-enhanced. Positive MIP-2 staining was identified in cardiac macrophages in monocrotaline-treated rats exposed to fly ash (A). In the same rats, staining was detected in areas of inflammation in cells in alveolar walls and interstitium of the lung, around blood vessels, and in macrophages (B). MIP-2 was also detected



in cardiac macrophages (C), and in blood vessels and the lung interstitium of monocrotaline-treated rats exposed to filtered air (D). MIP-2 was detectable, but to a much lesser extent, in the heart (E) and alveolar macrophages (F) of saline-treated controls exposed to fly ash particles. Staining was not detected in the heart (G) or lungs (H) of control animals exposed to air. Similarly, staining was not detected in monocrotaline-treated heart processed with control antibody (data not shown).

Discussion

This study was designed to model the epidemiologic observations that increases in ambient air particulate are associated with increased morbidity and mortality, especially in humans with pre-existing cardiorespiratory disease. Indeed, exposure to fine fuel oil fly ash particles collected from a Boston power plant resulted in significant mortality only in rats with monocrotaline-induced cardiorespiratory disease. Boilermakers exposed to the same dust occupationally had significant alterations in pulmonary function.[2] Exposure of these workers, monitored with personal samplers, found PM_{10} concentrations of 3.22 ± 1.42 mg/m^3 (mean $\pm$ SD). The fine fuel oil ash concentration in these animals experiments throughout the 3 days of exposure was 0.58 ± 0.11 mg/m^3. Therefore, deaths occurred in rats with pre-existing disease at concentrations considerably lower than measured occupational exposure levels.

We chose the monocrotaline model of pulmonary inflammation because it is rapid in onset, reproducible, and has been studied for over 3 decades.[3] Our hypothesis was that underlying pulmonary inflammation was a component of the air pollution-mortality relationship detected in humans, so we used an animal model in which leukocyte activation and neutrophil influx has been described in BAL and lung tissue.[3, 4, 9, 10] We detected a significant neutrophil influx but macrophage counts were significantly decreased in monocrotaline-treated rats exposed to air or fly ash. Although this decrease in absolute numbers of BAL macrophages is in contrast to the findings of Schultze et al.,[4] it is likely that our findings are related to decreased lavageability rather than decreased numbers of cells. There was no decrease in cell viability in these BAL samples, and histopathologic examination in our experiments revealed mononuclear perivascular hypercellularity and increased number of macrophages in the alveoli and interstitium, which were not seen in saline-treated animals. These histopathologic findings may account for the decreased numbers of macrophages in BAL in our experiments. Similar differences between BAL cell counts and lung histopathology in hamsters with pulmonary inflammation induced by ultrafine copper particle exposure have been reported,[11] suggesting that BAL may not always reflect the lung's response to inflammatory stimuli.

MIP-2 is a major rodent C-X-C cytokine, which has been shown to mediate neutrophil chemotaxis and activation both *in vitro* and *in vivo*.[6] MIP-2 is expressed by many cell types including lung macrophages, pulmonary epithelial cells, and fibroblasts,[6, 12] which makes this cytokine a putative candidate for a role in exacerbations of pre-existing disease in animals exposed to air particulates. MIP-2 mRNA is not normally detected in healthy, control animals, but expression is induced in pulmonary cells in response to inflammatory stimuli.[6, 12] Monocrotaline treatment induced marked MIP-2 mRNA expression in BAL cells, suggesting that MIP-2 is involved in neutrophil recruitment into monocrotaline-inflamed lungs. Fuel oil fly ash inhalation increased MIP-2 mRNA expression in some, but not all animals.

Increased MIP-2 mRNA and protein expression in BAL cells and lung, respectively, suggest that this cytokine contributes to pulmonary neutrophil activation and influx in monocrotaline-induced lung disease. We are not aware of any studies that examine intracellular cytokine protein expression in the heart in relationship to lung inflammation. The heart was of interest because pre-existing cardiovascular disease increases the risk of air pollution-associated death, and people who

die following air pollution exposure die of "cardiorespiratory" causes.[13] Immunohistochemistry revealed the presence of MIP-2 in the heart of monocrotaline-treated rats exposed to air or fly ash, and to a lesser extent in control rats exposed to fly ash. MIP-2 protein was expressed in cylindrically-shaped cardiac macrophages, which are found closely associated with the surface of cardiac myocytes, and are considered to be normal residents of the adult rat heart.[14, 15] The role of macrophages in the myocardium is speculative.[14, 15] Nevertheless, the definitive presence of MIP-2 in cardiac macrophages raises the possibility of these cells and this cytokine playing a previously unrecognized role in cardiac pathophysiologic responses.

Cytokines are extracellular signaling proteins secreted by immunocompetent cells as well as nonimmune cells such as vascular endothelium.[16] Although these intercellular peptide mediators have long been known to play an important role in the regulation of inflammation by controlling recruitment and activation of various responsive cell populations, it is only recently that cytokines have been proposed to have a role in the triggering and perpetuation of a variety of other conditions such as atherosclerosis, congestive heart failure, and during myocardial infarction.[16-18] Indeed, the potential role of cytokines in the generation of cardiac arrhythmias has been appreciated from *in vitro* studies in which cytokines have been added directly to isolated cardiac myocytes.[19] Since neutrophils were not found in histologic sections of the myocardium, we are uncertain as to the function of the MIP-2 in the heart. However, we suspect that MIP-2 could potentially contribute to fatal arrhythmias. Although the significance of elevated levels of cytokines in a variety of clinical cardiovascular conditions, as well as the cardiac MIP-2 immunostaining detected in our experiments is uncertain, it is becoming increasingly apparent that proinflammatory cytokines may play a fundamentally important role in terms of modulating the structure and function of the heart in health and disease.

In conclusion, significant mortality occurred only in monocrotaline-treated animals exposed to fly ash particulate. Exposure of control rats to fine particle fuel oil fly ash results in detection of pro-inflammatory chemoattractant cytokines in both the lung and the heart. MIP-2 mRNA expression was also detectable in BAL cells in the absence of pre-existing disease in saline-treated animals exposed to fly ash. Significant neutrophil recruitment was detected in the BAL of monocrotaline-treated rats exposed to filtered air, and this influx tended to increase with fly ash exposure. Therefore, in the presence of pre-existing cardiorespiratory disease caused by monocrotaline, inhaled fly ash particles provide an external stimulus to increase pulmonary inflammation, enhance intracellular detection of the cytokine MIP-2 in the lungs and heart, and cause significant mortality.

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A Comparison of Indoor/Outdoor PM_{10} Concentrations Measured at Three Hospitals and a Centrally Located Monitor in Utah

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Abstract

This research measured daily 24-hour PM_{10} concentrations at various locations in Salt Lake City, Utah from December 1994 to May 1995. Between four and six indoor locations were sampled at each of three hospitals. Indoor data were compared to outdoor roof data of each respective hospital and to the City's central monitoring location. The study goals were to: 1) evaluate variation of PM_{10} concentrations at four different outdoor sampling locations across Salt Lake valley; 2) determine if a centrally located monitor can predict PM_{10} concentrations across the valley; 3) evaluate variation in PM_{10} concentrations inside hospitals to see if a single indoor sampler can estimate exposure for an entire hospital; 4) compare indoor/outdoor roof concentrations at three hospitals to determine if an outdoor roof sampler can be used to predict indoor concentrations;and 5) determine if a centrally located monitor can predict concentrations indoors in the three hospitals. Results from outdoor samplers indicate that variation occurred between the four sites. When regressed against the central sampler, the slopes of each hospital were linear but statistically different. Because the three hospitals had similar y-intercepts, at low outdoor PM_{10} concentrations the central monitor predicted hospital roof concentrations. As outdoor PM_{10} concentrations increased, the central monitor had higher concentrations and overestimated PM_{10} relative to the three hospital sites. Results from indoor samplers indicate large variation in PM_{10} concentrations both within and between hospitals. Data indicate that one indoor location does not adequately represent the variation in indoor PM_{10} concentrations and that outdoor PM_{10} account for a varying percentage of indoor PM_{10} concentrations. Finally, it appears that PM_{10} concentrations at different indoor hospital locations cannot be predicted by one central outdoor PM_{10} sampling location.

Introduction

The Environmental Protection Agency amended the National Ambient Air Quality Standard for Total Suspended Particulate pollution in 1987 to include only particulate matter with a 10 micrometer (μm) aerodynamic cut-point (PM_{10}). Municipalities often use PM_{10} measurements from one "worse-case" sampling site for compliance purposes even though air pollution levels may significantly fluctuate within micro-geographical areas and/or air sheds.

Outdoor PM_{10} levels also may not be a good indicator of indoor PM_{10} levels.[1] Indoor studies have focused on the home environment; demonstrating that indoor particulate

exposure varies greatly depending on both indoor and outdoor sources.[2] In addition to infiltration of outdoor PM_{10}, significant domestic sources contributing to indoor PM_{10} include smoking, woodstoves, cooking, fabric fibers, etc.[3,4,5,6]

Individuals move between indoor and outdoor microclimates, spending on average 80-90% of their time indoors.[7] A variety of indoor and outdoor environments, in combination with behavioral factors, determine overall 24 hour PM_{10} exposure. A single, fixed position, outdoor PM_{10} monitor located for compliance purposes does not consider the spatial and indoor/outdoor concentration difference so that data generated from such a site may not be an accurate estimate of personal exposure. Epidemiological studies have historically relied on data collected from municipal compliance sampling sites for outdoor point estimates of PM_{10} air pollution concentrations to estimate individual exposure for an entire area. Studies using this type of data have indicated that a relationship may exist between ambient PM_{10} levels and a broad range of health effects. Health end points evaluated include fatal lung disease,[8] respiratory disease,[9,10,11] hospital admissions for respiratory ailments,[12] decreased lung function,[13,14] and increased asthma medication use.[15,16]

Hospitals are unique facilities and factors including heating, ventilation and air conditioning (HVAC) design, non-porous washable flooring, daily housekeeping programs, foot traffic, no-smoking policies, etc. are very different from domestic home environments. Hospitals also have specific subpopulations which may be more susceptible to the effects of particulate air pollution; very young and old as well as those with pre-existing respiratory conditions. Lyon, et al. demonstrated the largest contribution to excess mortality attributed to PM_{10} was in the population aged 75+, occurs in a hospital, and that up to 50% of this population resided in the hospital for more than five days prior to death.[17] The potential for centralized mortality in these populations occur. A hospital environment thus has an at risk population with limited mobility and limited changes in PM_{10} exposure prior to the mortality event. No studies have attempted to measure exposure to PM_{10} in hospitals.

This project was undertaken to provide an estimate of individual PM_{10} exposure for high risk groups residing in hospitals; focusing on Intensive Care Units (ICU's) of both general and pediatric nature. The objectives of this study were to: 1) examine the relationship between four outdoor sampling sites within an airshed; 2) examine the relationship between numerous sampling sites within a hospital and 3) examine the ability to predict PM_{10} concentrations indoors in three hospitals located in Salt Lake City, Utah from outdoor PM_{10} concentrations during winter 1994-1995.

Sampling Methods and Materials

Indoor and ambient outdoor PM_{10} levels were studied at three hospitals in Salt Lake City, Utah. Outdoor PM_{10} samples were also collected at the State of Utah, Division of Air Quality (DAQ), Downtown Salt Lake City Air Monitoring Station for comparison. The three hospitals are each located at different elevations in the Salt Lake Valley. The location and elevation of each hospital and the DAQ is shown in Figure 1. Daily 24-hour samples were collected from November 10, 1994 through May 1, 1995 on an approximate noon to noon schedule. At each hospital, one PM_{10} sampler was located on the roof. These roof samplers were located close to the building air intakes but as far from exhaust vents as feasible. The indoor sampler locations and number of indoor samplers varied among the three hospitals (Table 1). In all three hospitals samplers were located in at least one intensive care unit.

PM_{10} samples were collected using Airmetrics Minivol v. 4.01 samplers. The Airmetrics samplers were calibrated to run at five liters per minute. Samplers were equipped with a preseperator using a virtual impactor designed with a 50% collection efficiency of 10 μm, aerodynamic diameter. Filters were pre and post conditioned for 24 hours at an average relative humidity of 30 % ± 2 % and an average temperature of 26 degrees Celsius (°C) ± 5 °C. Filters were weighed prior to and after sampling using a Cahn C-35 microbalance. The filters were handled using stainless steel forceps and were carefully exposed to a Polonium-210 source to reduce error associated with electrostatic charge build-up on the filter. Following the preweighing, filters were placed in an Airmetrics filter holder/pre separator. A filter holder rotation was designed to minimize any systematic errors which may be associated with individual pre-separators. The majority of this study, January 4, 1995 to May 1, 1995, was done using Schleicher and Schuell G30 47 millimeter binderless borosilicate filters. Prior to January 4, 1995 Whatman quartz QMA filters were used, but were discontinued because the filters were often friable resulting in lost samples.

Statistical Methods

All reported analysis was performed using SAS. Descriptive statistics showing the sampler location, number of samples per location, mean PM_{10} concentration at each location, standard deviation and concentration range at all indoor and outdoor locations are given in Table 1.

Mean hospital roof PM_{10} concentrations were compared for the four sampling locations. Daily differences in PM_{10} concentrations were compared by pairing all outdoor locations. After adjusting for autocorrelation up to order three, a one sample t-test was performed.

Adjusting for autocorrelation is conservative; increasing the standard error estimates without changing the estimated mean differences.

Regression techniques were used to evaluate how well daily PM_{10} measurements at DAQ predict daily PM_{10} measurements at hospital roof locations. It was hypothesized that the relationship between DAQ measurements and hospital roof measurements might not be linear, so an initial nonparametric regression technique was performed (using smoothing splines). After it was determined that the relationships were linear, the daily hospital roof PM_{10} concentration at each hospital roof location was regressed on the daily DAQ PM_{10} concentration. The residuals from an initial least squares regression were found to have first order autocorrelation, and the regression was adjusted for this correlation. Adjustments for minimum daily temperature was considered but determined not to be necessary. To determine whether the slopes of the above regression lines were statistically significantly different, the difference in daily hospital roof PM_{10} concentrations for each pair of hospitals was regressed on DAQ PM_{10} concentrations. Autocorrelation up to order three was controlled for in these regression models.

A linear regression of the daily PM_{10} concentration at each indoor site was performed comparing daily hospital roof PM_{10} at the same location. Residual analysis indicated that it was necessary to adjust for first order auto correlation. It was again determined that adjustment for minimum daily temperature was not necessary.

Results and Discussion

Correlation among outdoor PM_{10} samplers

Outdoor concentrations of PM_{10} demonstrated variation among the four sites (Table 1). The downtown DAQ location had the highest mean value. This sampler was located on a roof of a single story building, next to a major traffic egress route from the city center. Significant mobile source (gas and diesel vehicles) likely contributed to the PM_{10} at this sample location. Hospital A had the lowest mean value. This hospital is located at the highest elevation and experiences minimal mobile source activity.

Regression models were created comparing each hospital roof site to the centrally located DAQ site (Table 2-A, Figure 2). Hospital roof sites had similar intercepts. To test wether the slopes of the hospitals were different, daily differences between hospital roof measurements were regressed on DAQ. (Table 2-B). Two slopes were statistically different from each other ($p < 0.05$). The exception was the comparison of hospital A to B ($p = 0.193$). At low outdoor PM_{10} concentrations, the centrally located DAQ monitor is an adequate predictor of roof PM_{10} concentrations for all three sites. Meteorological

conditions typically associated with low outdoor PM_{10} concentrations in Salt Lake City include good atmospheric mixing (e.g., wind) and support a more uniform PM_{10} concentration in the airshed. As outdoor PM_{10} concentrations increase, the concentrations at DAQ become significantly higher and the centrally located monitor overestimates PM_{10} concentrations relative to the other three outdoor sites. Meteorological conditions typically associated with high outdoor PM_{10} conditions in Salt Lake City are poor atmospheric mixing (i.e., stagnating inversion). These conditions accentuate micro-climatic variability among the four sampling sites.

Correlation of Outdoor Ambient PM_{10} Concentration to Indoor PM_{10} Concentration

The specific contribution of outdoor PM_{10} to indoor PM_{10} in hospitals is highly variable. Regression models were created for indoor sites at each hospital as a function of their respective roof (outdoor) PM_{10} concentrations (Table 3, Figures 3, 4, and 5). Based on slopes, at some locations the effect of outdoor PM_{10} is negligible (i.e., bone marrow transplant unit at Hospital A and some intensive care units), and others the effect of outdoor PM_{10} is considerable (i.e., nursery and maternity at Hospital C).

Heating, ventilation and air condition (HVAC) configurations varied in the three hospitals. The bone marrow transplant unit (BMT) in Hospital A has a highly sophisticated and well maintained high efficiency particulate air (HEPA) filtration system to minimize the potential for infection in immunocompromized patients. Thus, the sampling location in the non-occupied BMT room with minimal human activity was, in essence, the indoor PM_{10} concentrations representative of absolute background levels.

Using an auto-regressive model allowed the estimation of indoor PM_{10} at a given hospital sampling site for the given hospital's outdoor concentration of PM_{10}. Figures 3, 4 and 5 graphically represents the regression of data comparing indoor sampling locations to their respective roof locations. At low outdoor PM_{10} concentrations, there exists a small amount of indoor PM_{10}. These indoor PM_{10} levels during low outdoor PM_{10} levels represent a background level of indoor PM_{10} which are the likely result of indoor sources. By extrapolating the data it is possible to estimate the amount of indoor PM_{10} that would theoretically exist with zero outdoor PM_{10}.

The theoretical existence of PM_{10} concentrations indoors even with no outdoor PM_{10} represents background indoor PM_{10} concentrations. When indoor PM_{10} levels exist in excess of these background levels, the proportion of indoor PM_{10} attributable to outdoor PM_{10} infiltrating into the hospital is the difference between total indoor PM_{10} and background indoor PM_{10} levels. Results of the regression estimate for outdoor concentrations of 10, 50, and 100 $\mu g/m^3$ are presented in Table 4. For most locations,

there is substantial variation in both indoor PM_{10} concentration and the contribution from outdoor PM_{10} as the outdoor PM_{10} concentration increases.

Variation in PM_{10} Concentrations Among Indoor Samplers

Results from indoor sampling indicate a large variation in indoor PM_{10} concentrations both within and between hospitals (Table 1 and 3) and suggest that one indoor location does not represent the indoor PM_{10} concentration in a hospital. The analysis of variance between different units of the same hospital and between similar units of different hospitals demonstrate that both the type of unit is important (Table 5) and the building itself is important when comparing the same type unit (Table 6). Critical building components would include geographical location, specific building materials depending on requirements of patient care unit, HVAC age and design, etc.

Comparison of Indoor PM_{10} to Outdoor PM_{10} at High Outdoor PM_{10} Concentrations

The outdoor DAQ site exceeded PM_{10} concentrations of 100 $\mu g/m^3$ on eight separate days. For these days, PM_{10} data from each hospital's ICU units were pooled and analyzed. Number of samples, mean PM_{10} concentrations and standard deviations are presented in Table 7. Results demonstrate that indoor PM_{10} concentrations, specifically in ICUs, are substantially lower than outdoor PM_{10} concentrations. Patients residing in these units have a considerably lower exposure to PM_{10} pollution than would be estimated based on outdoor concentrations.

Conclusions

If excess mortality or morbidity due to PM_{10} pollution is to be studied via epidemiological investigation, an accurate estimate of exposure is desirable. Prior studies have suggested excess mortality associated with ambient PM_{10} air pollution and that hospitals are a location where excess mortality occurred. Thus, estimating indoor PM_{10} concentrations in hospitals is a starting point for exposure estimates prior to the mortality event.

One result of this study was the identification of significant variability of outdoor measurements across the Salt Lake City airshed. The centralized DAQ monitoring site predicted PM_{10} concentration at three other Salt Lake Valley sites (3 to 16 kilometers from DAQ) under low PM_{10} conditions. However, the same DAQ monitoring site failed to accurately predict PM_{10} concentration at the three sites under high PM_{10} conditions. Conditions of high atmospheric PM_{10} concentrations is when accurate and precise evaluation of PM_{10} is critical and under these conditions in Salt Lake City, require more

than one monitor. When ambient PM_{10} concentration data is used as a predictor of individual exposure, more than one centralized monitor is absolutely necessary.

With respect to indoor PM_{10} concentrations in hospitals, significant variations were observed both within and between hospitals. Indoor variation appears to be a function of meteorology, outdoor PM_{10} concentrations, specific building design characteristics, and activity patterns. Results indicate that an internal source of PM_{10} was present at all indoor locations sampled. Outdoor PM_{10} contributed to indoor concentrations to a varying degree based on building design and outdoor concentration.

Indoor PM_{10} levels within intensive care units, where most critically ill are exposed, had mean concentrations ranging from 10.6 to 21.3 $\mu g/m^3$. For eight days, conditions of high outdoor PM_{10} (> 100 $\mu g/m^3$) existed. Average indoor PM_{10} concentrations in intensive care units for all three hospitals remained substantially lower during these periods. Hospitalized patients, who are the largest contributors to the association of PM_{10} and excess mortality, are exposed to substantially less PM_{10} pollution than outdoor PM_{10} concentrations would suggest.

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Figure 1. Outdoor PM10 sampler locations (relative to downtown Division of Air Quality - Air Monitoring Station) and elevations in Salt Lake City.

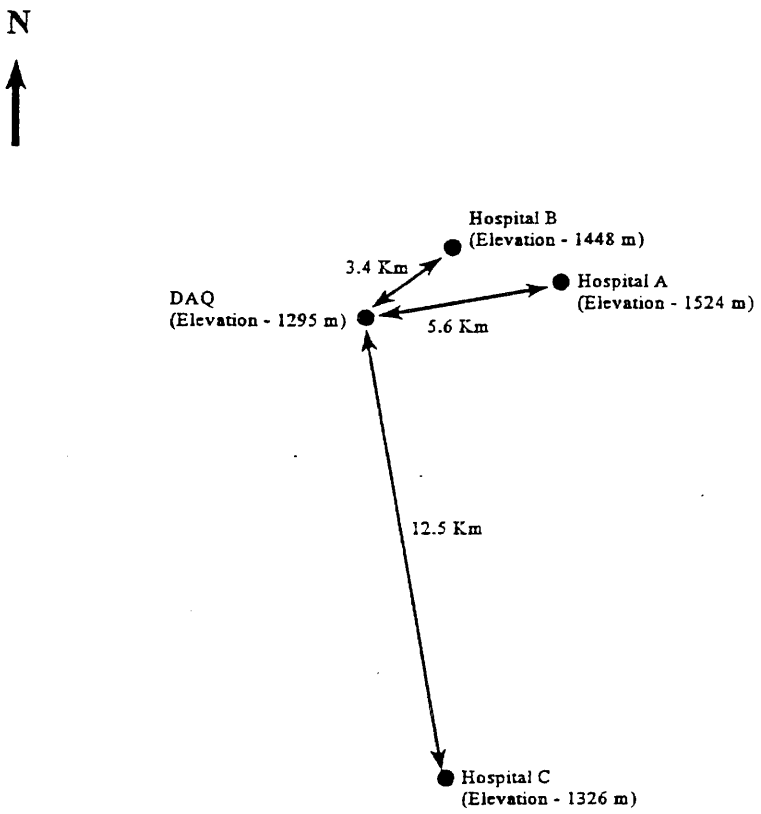

Table 1. Descriptive Statistics of location, sample size, mean value, standard deviation and range for indoor/outdoor PM_{10} sampling 11/28/94 - 4/29/95.

Hospital	Location	days	Mean(mg/m³)	Std Dev	Range
A	**Roof**	**130**	**21.7**	**17.2**	**0.78-130.7**
	ICU[A] 1	144	16.8	6.4	2.8-55.9
	ICU 2	143	17.7	7.0	1.7-70.7
	ICU 3	143	21.3	7.3	2.7-49.0
	ICU 4	143	17.4	6.4	2.7-48.1
	BMT[B] 1	143	11.5	4.9	1.6-28.3
	BMT 2	143	9.7	5.0	0.5-26.7
B	**Roof**	**138**	**26.5**	**19.0**	**3.4-134.8**
	ICU 1	150	12.9	8.7	0.6-99.8
	ICU 2	145	13.5	5.6	3.3-38.0
	ICU 3	148	16.0	5.0	3.3-39.9
	ICU 4	148	10.6	4.2	2.1-22.1
C	**Roof**	**140**	**29.5**	**20.0**	**1.3-111.9**
	Nursery 1	147	15.8	7.7	3.8-52.7
	Nursery 2	152	23.7	13.6	4.0-87.0
	Maternity 1	148	14.8	10.2	1.9-82.4
	Maternity 2	148	14.3	5.8	1.4-34.9
	ICU 1	150	12.1	5.3	1.0-28.8
	ICU 2	146	12.6	5.7	1.5-32.0
State Monitoring Station (DAQ)	**Roof**	**128**	**43.6**	**30.7**	**1.0-159.5**

[A] - Intensive Care Unit (ICU)
[B] - Bone Marrow Transplant (BMT) Unit

Table 2-A. Regression coefficients for Roof PM_{10} Measurements as a Function of Division of Air Quality PM_{10} Measurements. Computed from an Autoregressive AR(1) Model.

	Intercept (SE)	**Slope (SE)**
Hospital A	4.42 (2.18)	0.39 (0.039)
Hospital B	7.07 (2.18)	0.45 (0.038)
Hospital C	6.32 (0.034)	0.55 (0.034)

Table 2-B. Regression coefficients for differences in roof PM_{10} Measurements regressed against Division of Air Quality PM_{10} Measurements.

	Intercept (SE) **p - value (*)**	**Slope (SE)** **p - value (*)**
Hospital A - Hospital C	3.43 (1.05) p = 0.0016	0.396 (0.0194) p = 0.0442
Hospital B - Hospital A	-0.753 (2.29) p = 0.7429	-0.0430 (0.0328) p = 0.1933
Hospital B - Hospital C	-3.93 (2.40) p = 0.1044	-0.0923 (0.0419) p = 0.0301

Figure 2. Regression of the three hospital roof PM_{10} values on the DAQ PM_{10} values.

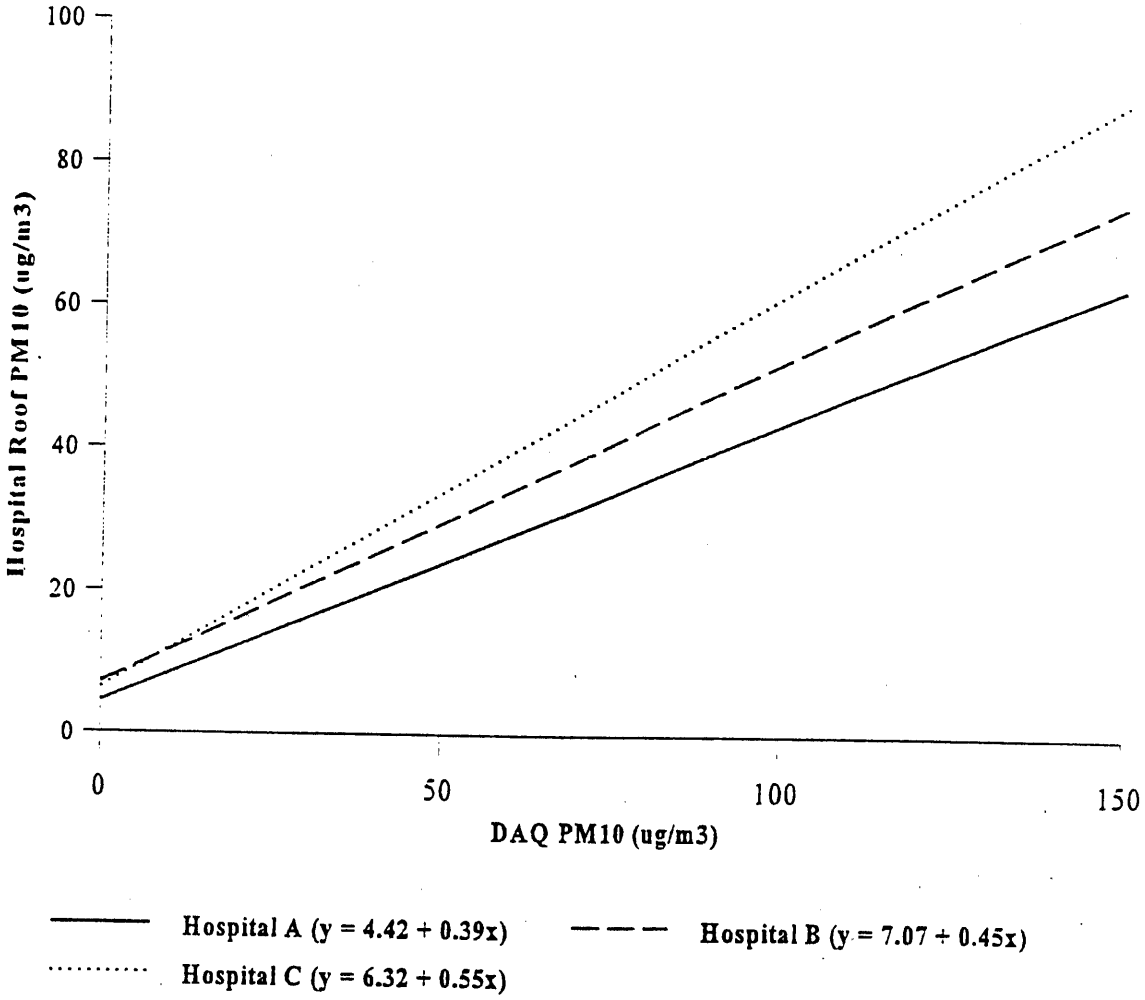

Table 3. Regression coefficients comparing indoor PM_{10} to roof PM_{10} measurements at various sites.

Hospital	Location	Intercept (SE)	Slope (SE)
A	ICU 1	15.08 (0.837) p = 0.0001	0.079 (0.030) p = 0.0116
	ICU 2	17.42 (1.079) p = 0.0001	0.030 (0.039) p = 0.4501
	ICU 3	17.18 (1.011) p = 0.0001	0.183 (0.035) p = 0.0001
	ICU 4	14.05 (0.920) p = 0.0001	0.163 (0.032) p = 0.0001
	BMT 1	11.60 (0.828) p = 0.0001	0.015 (0.033) p = 0.6460
	BMT 2	7.75 (0.892) p = 0.0001	0.109 (0.034) p = 0.0020
B	ICU 1	10.85 (0.885) p = 0.0001	0.062 (0.028) p = 0.0249
	ICU 2	11.93 (0.873) p = 0.0001	0.059 (0.028) p = 0.0364
	ICU 3	16.06 (0.869) p = 0.0001	0.00158 (0.0156) p = 0.9510
	ICU 4	10.70 (0.706) p = 0.0001	0.00577 (0.0210) p = 0.7839
C	Nursery 1	9.57 (0.938) p = 0.0001	0.228 (0.026) p = 0.0001
	Nursery 2	11.83 (1.56) p = 0.0001	0.418 (0.043) p = 0.0001
	Maternity 1	7.48 (1.45) p = 0.0001	0.260 (0.041) p = 0.0001
	Maternity 2	10.23 (0.920) p = 0.0001	0.146 (0.025) p = 0.0001
	ICU 1	10.50 (0.955) p = 0.0001	0.059 (0.026) p = 0.0257
	ICU 2	11.54 (0.964) p = 0.0001	0.047 (0.027) p = 0.0803

Each row estimated from a separate autoregressive AR(1) model.

Figure 3. Regression of PM10 values at indoor sampling sites versus roof PM10 values of Hospital A.

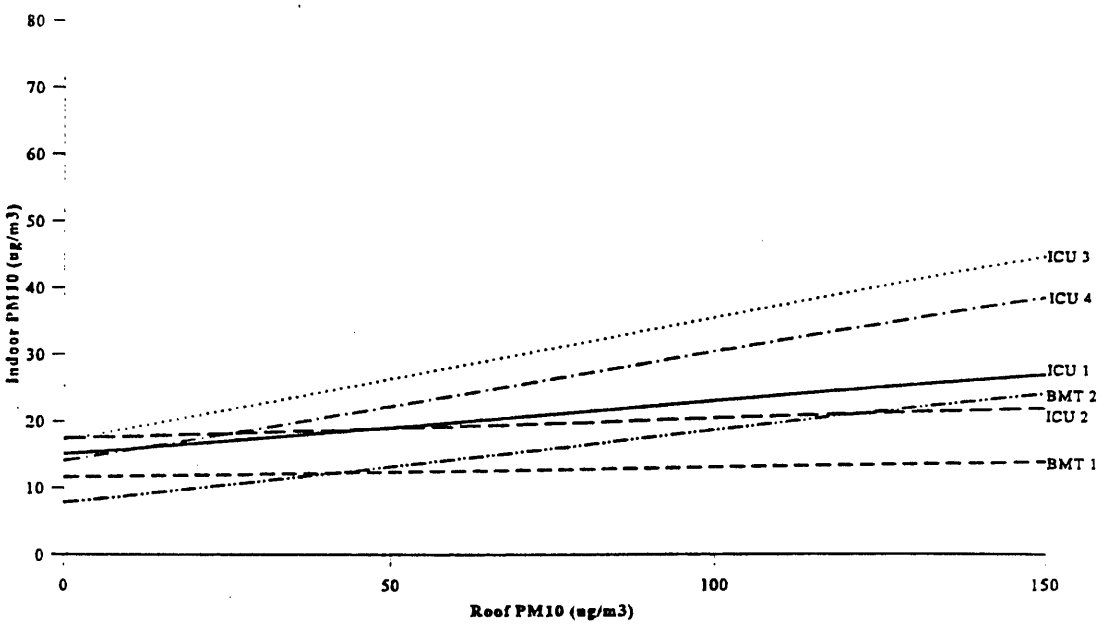

Figure 4. Regression of PM10 values at indoor sampling sites versus roof PM10 values of Hospital B.

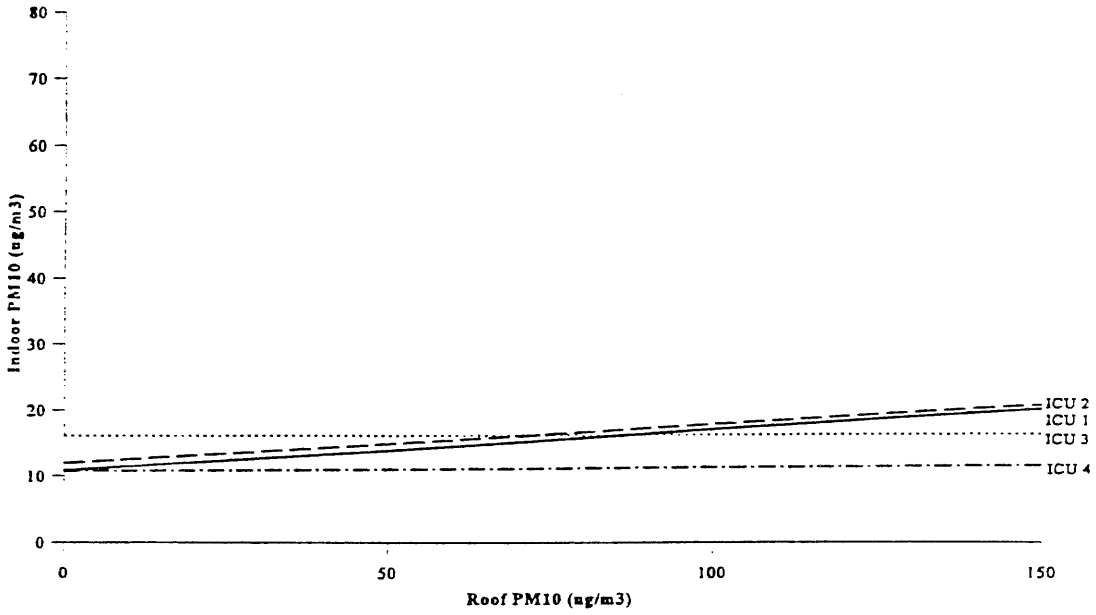

Figure 5. Regression of PM10 values at indoor sampling sites versus roof PM10 values of Hospital C.

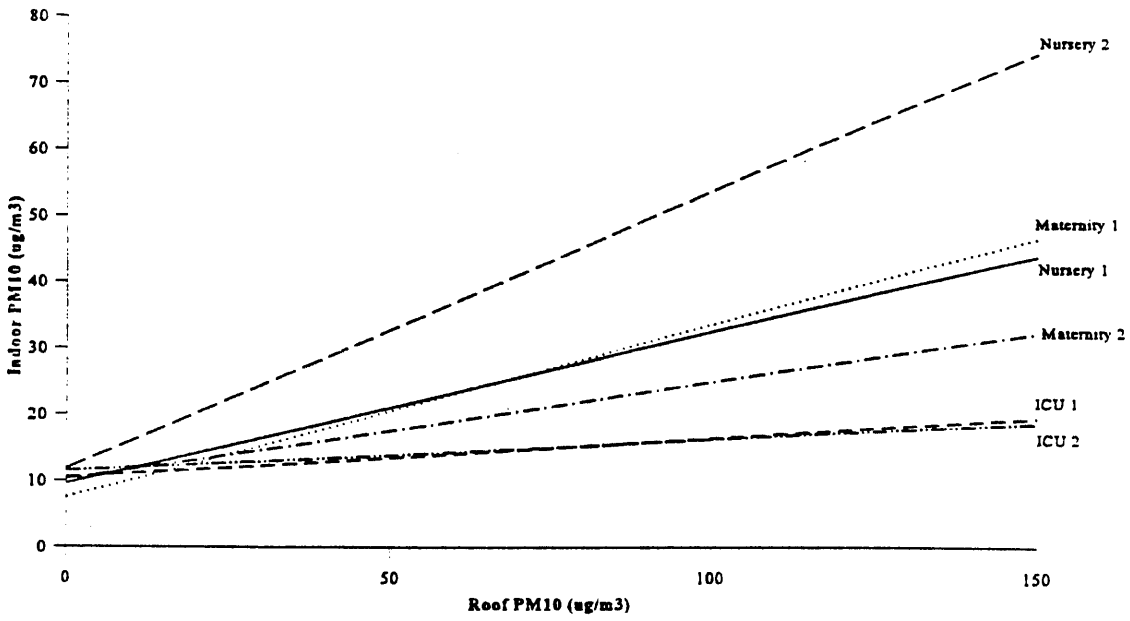

Table 4. Based on all data, mean indoor PM_{10} concentration ($\mu g/m^3$) and percent (%) attributable to outdoor (roof) PM_{10} concentrations. Expressed for Outdoor PM_{10} concentrations of 10, 50, and 100 $\mu g/m^3$. Estimated from autoregressive models.

T = Total Estimated PM_{10} at Location ($\mu g/m^3$).

O = Estimated Outdoor Contribution to Total PM_{10} ($\mu g/m^3$). [estimated total indoor PM_{10} at location - estimated total indoor PM_{10} at outdoor PM_{10} concentration of zero]

( ) = estimated percent contribution of outdoor PM_{10} to total indoor PM_{10}.

		Level of PM10 on Hospital Roof		
Hospital	**Location** **10**	**10 µg/m³**	**50 µg/m³**	**100 µg/m³**
A	ICU 1	T = 15.9 O = 0.8 (5.0)	T = 19.0 O = 3.9 (20.5)	T = 23.0 O = 7.9 (34.4)
	ICU 2	T = 17.7 O = 0.3 (1.7)	T = 18.6 O = 1.5 (8.1)	T = 20.4 O = 3.0 (14.7)
	ICU 3	T = 19.0 O = 1.8 (9.5)	T = 26.3 O = 9.2 (35.0)	T = 35.5 O = 18.3 (51.6)
	ICU4	T = 15.7 O = 1.6 (10.2)	T = 22.2 O = 8.1 (36.5)	T = 30.4 O = 16.3 (53.6)
	BMT 1	T = 11.8 O = 0.2 (1.7)	T = 12.4 O = 0.8 (6.5)	T = 13.1 O = 1.5 (11.5)
	BMT 2	T = 8.8 O = 1.1 (12.5)	T = 13.2 O = 5.5 (41.7)	T = 18.6 O = 10.9 (58.6)
B	ICU 1	T = 11.5 O = 0.1 (0.9)	T = 14.0 O = 3.1 (22.1)	T = 17.1 O = 6.2 (36.3)
	ICU 2	T = 12.5 O = 0.6 (4.8)	T = 14.9 O = 3.0 (20.1)	T = 17.8 O = 5.9 (33.2)
	ICU 3	T = 16.1 O = 0.0 (0.0)	T = 16.1 O = 0.1 (0.6)	T = 16.2 O = 0.2 (1.2)
	ICU 4	T = 10.8 O = 0.1 (0.9)	T = 11.0 O = 0.3 (2.7)	T = 11.3 O = 0.6 (5.3)
C	Nursery 1	T = 11.9 O = 2.3 (19.3)	T = 21.0 O = 11.4 (54.3)	T = 32.4 O = 22.8 (70.4)
	Nursery 2	T = 16.0 O = 4.2 (26.3)	T = 32.7 O = 24.1 (73.7)	T = 53.6 O = 41.8 (78.0)
	Maternity 1	T = 10.1 O = 2.6 (25.7)	T = 20.5 O = 13.0 (63.4)	T = 33.5 O = 26.0 (77.6)
	Maternity 2	T = 11.7 O = 1.5 (12.8)	T = 17.5 O = 7.3 (41.7)	T = 24.8 O = 14.6 (58.9)
	ICU 1	T = 11.1 O = 0.6 (5.4)	T = 13.5 O = 3.0 (22.2)	T = 16.4 O = 5.9 (36.0)
	ICU 2	T = 12.0 O = 0.5 (4.2)	T = 13.9 O = 2.4 (17.3)	T = 16.3 O = 4.7 (28.8)

Table 5. Analysis of variance for type of location within Hospital.

Source	DF	Mean Square	F Value	P Value
Hospital	2	944.25	0.96	0.4170
Type(Hospital)	3	9126.61	6.16	0.0121
Error	10	4938.87	-	

Table 6. Analysis of variance for ICU variation between Hospitals.

Source	DF	Mean Square	F Value	P Value
Hospital	2	3206.26	6.62	0.0243
Error	7	484.25	-	-

Table 7. Summary statistics of mean PM10 concentrations and standard deviations for all intensive care units within a hospital for the eight days when the measurements at the DAQ site exceeded 100 μ/m^3.

Site	n	Mean	Std. Dev.
DAQ	8	129.0	18.25
Hospital A	30	19.83	10.3
Hospital B	27	15.5	18.3
Hospital C	15	12.2	7.1

Field Evaluation of Airmetrics MiniVol PM_{10} and $PM_{2.5}$ Samplers

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Abstract

Airmetrics has recently designed a portable air sampler for particulate monitoring. The MiniVOL is a small, lightweight, battery powered, quiet, and relatively inexpensive sampler, ideal for research applications. Depending on the impaction type preseperator head used, a sampler can be set up to sample either Total, 10μm, or 2.5 μm cut size particle ranges. All the above features make this sampler an attractive research tool. It is ideal for both ambient saturation studies utilizing numerous sampling locations and indoor/outdoor monitoring studies where size and noise are a concern . During the winter of 1995 - 1996, six Airmetric samplers, three equipped with PM_{10} and three equipped with $PM_{2.5}$ sampling heads were run in the same location. The results were compared to an EPA equivalent method: a Sierra-Andersen Series 240 Dichotomous sampler. Fourteen 24-hour sampling events were captured. This study design allowed both intra-sampler variability of the Airmetrics and inter- sampler comparison of Airmetrics to an EPA equivalent method. Results revealed the Airmetrics PM_{10} sampler gave consistent but higher values (~ +11%) compared to the Sierra-Andersen at all conditions. The Airmetrics $PM_{2.5}$ sampler demonstrated a higher value but results revealed inconsistent variability.

Introduction

PM_{10} is defined as particulate matter with an aerodynamic diameter equal to or less than a nominal 10μm. $PM_{2.5}$ is defined as particulate matter with an aerodynamic diameter equal to or less than a nominal 2.5 μm. Under the current regulations of the U.S. Environmental Protection Agency (EPA), the PM_{10} standard is defined as a 24-hour maximum concentration not to exceed 150μg/m^3 three times in three years or an average annual arithmetic mean standard not to exceed 50μg/m^3.[1] An airshed which exceeds either of these standards is considered to be in "non-compliance". The EPA is currently contemplating adding a "fine particulate" standard which appears will be $PM_{2.5}$.

The EPA has established a "reference method" for PM_{10} sampling using "Hi-Volume" samplers and "equivalent methods". Some observations concerning theses reference methods include:

- the high cost of samplers.
- the high air volume these samplers require,
- the sampler's portability: the samplers often require a fixed position, and
- the noise these samplers emit.

These operating requirements make EPA reference and equivalent samplers less desirable for either saturation research (where large numbers of samplers are required) or indoor research (where noise is a concern). Airmetrics (Springfield, OR) has recently developed a portable sampler that meets some of the above concerns. Named the MiniVOL, the sampler is small, lightweight, battery powered, quiet, and relatively inexpensive. This research attempted to determine the applicability of the Airmetrics sampler compared to an EPA equivalent method under outdoor, winter field conditions.

Material and Methods

Sample Site Description

All samplers were located five meters above ground on a flat roof (Figure 1). Samplers were spaced minimally 1.5 meters apart. The elevation of the site is approximately 1530 meters.

Number of Samplers

A total of seven samplers were operational for each sampling event. Six Airmetrics samplers were used. They were divided in two groups: three PM_{10} samplers (#1-3) and three $PM_{2.5}$ samplers (#4-6). One Sierra-Andersen (Atlanta, GA) Dichotomous sampler (Model#240) was used for both PM_{10} and $PM_{2.5}$. The Sierra-Andersen is an EPA "equivalent method" and was considered the control sampler in this study.

Sampler Technology

AIRmetrics:

- The AIRmetrics sampler uses 47 mm glass-fiber filters (Schleicher & Schuell)
- The Sampler operates at a flow rate of 5 L/min.
- Particle separation is achieved by impaction.
- Following new recommendations from the manufacturer $PM_{2.5}$ samplers were equipped with a PM_{10} unit as a pre-preseperator head to minimize the chance of overloading the $PM_{2.5}$ preseparator.

Sierra-Andersen:

- The Sierra-Andersen Dichotomous sampler uses 37 mm Teflon filters (Millipore).
- The sampler operates at flow rates of 16.7 L/min for $PM_{2.5}$ and 1.67 L/min for PM_{10}.
- The sampler divides the incoming airstream into two portions which are sampled (filtered) as a 0-2.5μm (fine) and a 2.5-10 μm (coarse) fraction (separation is accomplished by virtual impaction).

Samplers were calibrated with a soap bubble meter. All filters were conditioned to stable conditions of 30% humidity and room temperature for at least 24 hours prior to both

initial and final weighing. The filters were weighed on a microbalance located in a humidity controlled room. After the initial weighing of filters, they were placed in individual, labeled plastic storage dishes. After sampling, the filters were replaced in their original dishes and returned to the filter conditioning room prior to final weighing.

Sampling Day Criteria

Sampling occurred for approximately 24 hours from noon to noon. Sampling occurred over a 60-day period from mid-January through mid-March, 1996. A series of multiple storms resulted in good air quality and only one extended atmospheric inversion. A total of 14 sampling events were captured during this study. Of these 10, sampling events for the PM_{10} study and 12 sampling events for the $PM_{2.5}$ study were chosen. Some samples were determined not valid because of single pump failures, timer failures and/or filter damage.

Weather Data

Air stagnation index data are shown in table I. These data were obtained from the National Weather Service in Salt Lake City. Air stagnation is a product of the depth of the air layer times the average wind speed through that layer and is obtained from daily soundings. The depth of the layer is calculated by determining at what altitude in the atmosphere a warm parcel of air is cooled to a point that intersects the ambient temperature and elevation are plotted on a graph. Air stagnation values at or above 1000 indicate well-mixed conditions, values below 250 indicate days with inversion conditions.

Results and Discussion

PM_{10} Results

PM_{10} results are presented in Table II. A two-way analysis of a variance was performed on the entire data set (α=0.05). Results indicate that there is a significant difference ($p<0.05$) between dates and between samplers. The difference between sampling events was not surprising. There was no expectation that the results of different sampling events (days) are equal.

In order to assess whether a difference exists between AIRmetrics samplers and Sierra-Andersen sampler, a second ANOVA for the ratios of the AIRmetrics versus Sierra-Andersen sampler were calculated. This analysis demonstrated that there was no significant difference within the AIRmetrics group ($p<0.05$). The mean ratio ρ is 0.1074 which means that the AIRmetrics values average about 10.74% higher than the Sierra-Andersen values. The 95% confidence interval for the ratio ρ (with $t_{0.025,29} = 2.045$ and $s_D = 0.165051$) is $\rho \pm t^* s_D/\sqrt{n} = (0.0457, 0.1690)$.

$PM_{2.5}$ Results:
$PM_{2.5}$ results are presented in Table III. A two-way analysis of a variance was performed on the entire data set (α=0.05). Results indicate that there is a significant difference ($p<0.05$) between dates and between samplers.

In order to assess whether a difference exists between Airmetrics samplers and Sierra-Andersen sampler, a second ANOVA for the ratios of the Airmetrics versus Sierra-Andersen sampler were calculated. This analysis demonstrated that there was no significant difference within the groups of Airmetrics samplers ($p<0.05$).

A significant difference between discrete sampling events was observed. The degree of difference between the Airmetrics and Sierra-Andersen sampler was dependent on the day. Therefore, no 95% confidence interval could be calculated for the ratio between the Airmetrics and the Sierra-Andersen sampler.

As a further test, the $PM_{2.5}$ values were divided into two groups of low (<40 $\mu g/m^3$) and high (>40$\mu g/m^3$) values. These individual ratios between Sierra-Andersen and Airmetrics samplers were evaluated. No significant difference within the low Airmetrics group was observed ($p<0.05$). The mean ratio ρ is 0.179 which means that the Airmetrics values are in average about 18% higher than the Sierra-Andersen values. The 95% confidence interval for the ratio ρ (with $t_{0.025,17} = 2.110$ and $s_D = 0.117229$) is $\rho \pm t^* s_D/\sqrt{n} = (0.1139, 0.2305)$. The high $PM_{2.5}$ values showed no significant difference ($p<0.05$) between the ratios of the samplers but did demonstrate a difference between the sampling events.

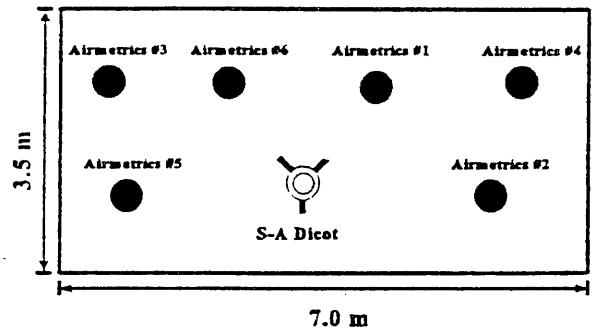
Conclusions

Airmetrics MiniVOL samplers, equipped with a PM_{10} preseparator-head, appear accurate. Sampling precision was approximately 11% greater than the Sierra-Andersen reference sampler. The $PM_{2.5}$ preseparator-head of the Airmetrics sampler were accurate but did not operate as precisely as the PM_{10} preseparator-head. Equipped with $PM_{2.5}$ heads, Airmetrics samplers were sampling approximately 18% greater than the Sierra-Andersen sampler in the low range (<40$\mu g/m^3$). On days with higher pollution three Airmetrics samplers sampled consistently higher, but the degree of variation was dependent on the day. Results indicate that the Airmetric samplers will provide an overall consistent estimate of PM_{10}. With respect to $PM_{2.5}$, the samplers are somewhat less consistent.

References

(1) Code of Federal Regulations Title 40, pt. 50. 1994.

Figure 1. Sampler Orientation



Samplers located:
- **5 meters above ground**
- **Minimally 1.5 meters apart**

Table I. Air Stagnation Index

Date	Air Stagnation Index	Date	Air Stagnation Index
2.1.96	100	2.12.96	20
2.5.96	60	2.13.96	40
2.6.96	30	2.14.96	40
2.7.96	70	2.15.96	28
2.8.96	40	2.16.96	80
2.9.96	25	3.1.96	900
2.11.96	15		

Table II. PM_{10} Sampling Results

Date	Andersen PM_{10}	AIRmetrics PM_{10}#1	AIRmetrics PM_{10}#2	AIRmetrics PM_{10}#3	Mean Row
2.6.96	63.64	69.04	70.99	75.27	69.73
2.7.96	25.21	31.53	31.8	15.78	26.08
2.8.96	41.19	51.96	53.69	54.25	50.27
2.9.96	56.69	64.5	54.04	67.2	60.6
2.11.96	44.27	57.67	47.13	58.66	51.93
2.12.96	56.21	69.19	69.08	66.86	65.34
2.13.96	76.58	73.72	93.43	95.32	84.76
2.14.96	73.01	89.62	93.87	93.77	87.57
2.15.96	86.27	80.69	92.55	96.19	88.92
3.1.96	10.63	9.849	10.5	12.04	10.75
Mean Column	53.37	59.77	61.7	63.53	59.61

Figure 2. PM_{10} Sampling Results

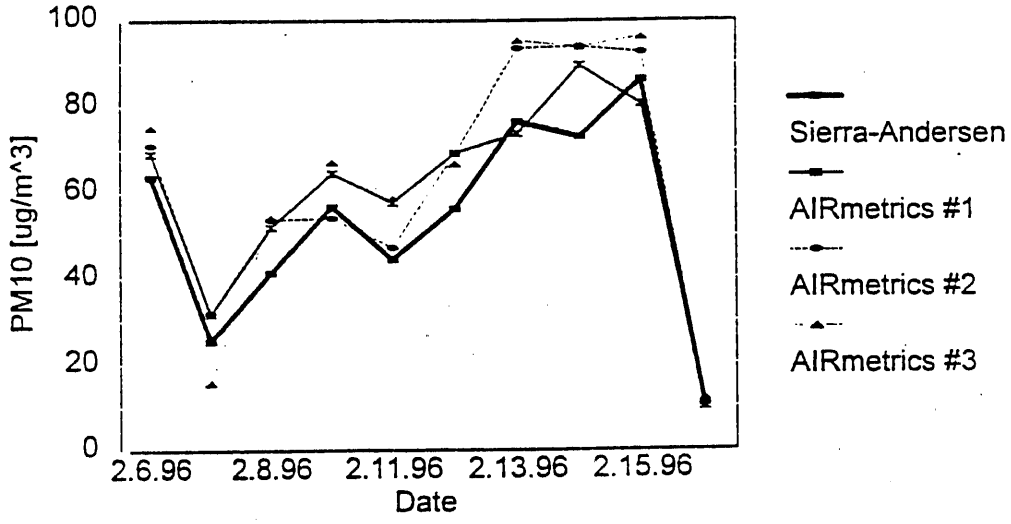
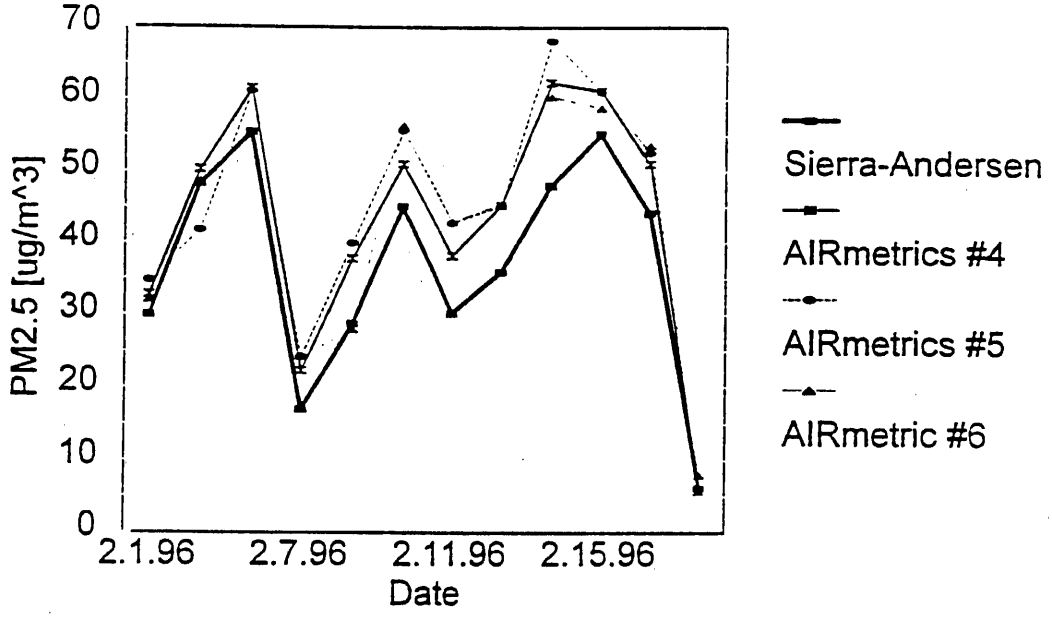


Table III. $PM_{2.5}$ Data

Date	Sierra-Andersen $PM_{2.5}$	Airmetrics $PM_{2.5}$#4	Airmetrics $PM_{2.5}$#5	Airmetrics $PM_{2.5}$#6	Mean Row
2.1.96	30.01	32.81	34.77	32.12	32.43
2.5.96	48.25	50.33	41.84	48.73	47.29
2.6.96	55.47	61.59	61.22	61.42	59.92
2.7.96	16.93	22.35	24.2	24.29	21.94
2.8.96	28.76	37.83	39.98	28.02	33.65
2.9.96	45.03	51.02	55.64	56.41	52.03
2.11.96	30.17	38.2	42.79	42.99	38.54
2.12.96	35.88	45.24	45.22	45.42	42.94
2.14.96	47.94	62.37	68.12	60.45	59.72
2.15.96	55.21	61.19	61.07	58.85	59.08
2.16.96	44.11	51.01	52.58	53.62	50.33
3.1.96	6.11	5.77	6.17	7.99	6.51
Mean column	36.99	43.31	44.47	43.36	42.03

Figure 3. $PM_{2.5}$ Sampling Results



SHORT-TERM PARTICULATE EXPOSURES AND HEALTH CHANGES IN LOS ANGELES RESIDENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD): A PRELIMINARY REPORT OF A PANEL STUDY

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ABSTRACT

To help understand the epidemiologic relationship between particulates and mortality/morbidity, we studied daily exposures, time-activity patterns, and health status in Los Angeles area residents with severe COPD. Volunteers (N = 45) recorded activity and symptoms in diaries, and measured lung function 3 times/day, for 4-day periods (Thursday a.m. - Monday a.m.) in summer or fall. Concurrent personal, inside-home, and outside-home PM_{10} measurements were taken during one 24-hr interval; $PM_{2.5}$ was measured during the preceding or following 24 hr. Background PM_{10} was determined from the nearest local monitoring station. Passive personal monitors estimated cumulative exposures to pollutant gases. Temperature and humidity were monitored inside and outside homes, and at nearest stations. Holter electrocardiograms were obtained for 24 hr in each subject. Preliminary air monitoring results (24-hr averages in $\mu g/m^3$) showed a mean (range) of 55 (23-174) for nearest-station PM_{10}, 53 (5-149) for outside-home PM_{10}, 37 (14-86) for inside-home PM_{10}, and 42 (17-105) for personal PM_{10}. $PM_{2.5}$ measurements averaged near 2/3 of corresponding PM_{10}. Nearest-station PM_{10} correlated highly with outside-home concentrations ($r = 0.77$ for PM_{10}, 0.71 for $PM_{2.5}$), less highly with indoor concentrations ($r = 0.30$ for PM_{10}, 0.64 for $PM_{2.5}$) or personal concentrations ($r = 0.38$ for PM_{10}, 0.29 for $PM_{2.5}$). Indoor and personal concentrations correlated ($r = 0.59$ for PM_{10}, 0.74 for $PM_{2.5}$), as expected since subjects spent >90% of their time indoors. Physical activity occupied ≈14% of subjects' time, but was of low intensity, judging from Holter electrocardiograms. Self-rated overall clinical status did not vary significantly day to day, and did not covary significantly with same-day PM_{10} at the nearest station. Some lung function indices varied significantly with time; most did not covary with PM_{10}, but peak flow declined with increasing PM_{10} according to some analytical models. Conclusions: Panel studies of short-term personal exposures and concurrent health changes are feasible in typical COPD patients. Current results suggest that Los Angeles area particulate monitoring stations provide good estimates of exposure outside subjects' homes, but less good estimates indoors.

INTRODUCTION

Exposures to particulate matter (PM) and/or accompanying environmental stresses are associated with increased rates of premature death or hospitalization in people with chronic cardiopulmonary disease, over a wide range of atmospheric and demographic circumstances [Bascom et al., 1996; Thurston, 1996; Pope et al., 1995; Dockery and Pope, 1994; Gong and Linn, 1994; Lipfert, 1994]. These health responses occur within 24-48 hr. If the relationship is causal,

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then such exposures presumably also cause more widespread, less serious health effects in the chronically diseased population [Bates, 1992]. We hypothesize that the mildest effects are sufficiently common to be detected by detailed concurrent exposure and health monitoring for comparatively short periods in comparatively small groups. If our hypothesis is correct, these small-scale studies of short-term exposures and health changes should help to sort out the specific pollutants or other associated factors which present the greatest risks. Identification of specific pollutants which affect health is usually impossible in larger epidemiologic studies [Lipfert and Wyzga, 1995].

This project was a pilot field study of short-term environmental stresses and concurrent health changes in a panel of elderly volunteers with COPD. Its goals were to demonstrate the feasibility of various sensitive exposure and health measurements in chronically ill subjects going about their everyday activities; and in the process, to obtain preliminary statistical estimates of short-term exposure-health relationships, which would be helpful in designing future field and laboratory studies.

METHODS

We studied daily exposures, time-activity patterns, and health status in 45 Los Angeles area volunteers with severe chronic obstructive pulmonary disease (COPD) - 24 men and 21 women, aged 61-82, recruited by advertisements and physician referrals. All subjects had forced expired volume in 1 sec (FEV_1) less than 50% of predicted; 13 subjects improved FEV_1 by >20% after inhaling a bronchodilator, but did not return to the normal range. Most were on respiratory medications, some also on medication for cardiovascular disease. Some lived in coastal communities with moderate temperatures and pollution, others in inland communities with greater extremes. Their dwellings included single-family houses, mobile homes, and apartments. About half had refrigerated air conditioning in all or part of the home; less than 10% had evaporative cooling; and the rest had no air conditioning.

During 4-day periods (Thursday through Monday mornings) in summer or fall 1995, subjects recorded activity and symptoms in diaries every waking hour. They measured their own lung function every morning, afternoon, and evening using Creative Biomedics L'Vision portable electronic spirometers. A Holter electrocardiogram was obtained for 24 hr in each subject. Concurrent personal, inside-home, and outside-home measurements of particulate matter less than 10 μm in aerodynamic diameter (PM_{10}) were taken for each subject, using Marple low-volume size-selective samplers, during one 24-hr interval within the 4 days. Fine particulate matter ($PM_{2.5}$) was measured similarly during the preceding or following 24 hr. Background PM_{10} was determined from the South Coast Air Quality Management District (SCAQMD) continuous monitor nearest the subject's home. Because no other continuous PM data were available, background PM_{10} was used in analysis of day-to-day health changes. Subjects wore passive personal monitoring badges to estimate their cumulative exposures to ozone (O_3) [Koutrakis et al., 1990] and nitrogen dioxide (NO_2) [Yanagisawa et al., 1990] over 4 days. Background O_3 and NO_2 were determined from the SCAQMD stations nearest subjects' homes (sometimes closer than nearest PM_{10} monitoring stations, because O_3 and NO_2 stations are more numerous). Temperature and relative humidity were monitored inside and outside homes with portable continuous recording hygrothermographs. Background outdoor temperature and relative humidity data were obtained from the nearest SCAQMD O_3/NO_2 monitoring stations.

Statistical analyses employed the BMDP software [Dixon, 1992]. Cross-sectional (between-subjects) analyses of related exposure measurements employed ordinary least-squares regression. Longitudinal analyses of health change versus exposure change employed repeated-measures analysis of covariance, with a health variable as the repeated-measures factor and an exposure variable as the time-varying covariate. Multiple analytical models were tested for each exposure-health variable combination of interest, by changing the form of the exposure variable, time lag, number of days included, or method of dealing with missing data (see Table 2 notes).

RESULTS

Table 1 summarizes PM monitoring results. Outside-home PM_{10} averaged similar to, and correlated highly with, nearest-station PM_{10}; while inside-home PM_{10} concentrations averaged somewhat less than outside-home concentrations, and were not highly correlated with station readings (Figure 1). Both indoor and outdoor $PM_{2.5}$ correlated with nearest-station PM_{10} ($r = 0.64$, 0.71 respectively). Indoor and personal concentrations correlated ($r = 0.59$ for PM_{10}, 0.74 for $PM_{2.5}$), as expected from subjects' diary reports, which indicated that they spent more than 90% of their time indoors. Four-day personal NO_2 exposure concentrations, as estimated from badges, showed a mean of 43 ppb (range 3-109), and correlated significantly ($r = 0.57$) with concurrent levels at nearest stations (mean 48 ppb, range 15-98). Comparable data for O_3 showed a similar correlation of personal and station readings ($r = 0.55$), but estimated personal exposures (mean 6 ppb, range 1-19) were well below station levels (mean 24 ppb, range 11-46). Note that the aforementioned correlations are cross-sectional, and do not address the question of how personal exposures track station data longitudinally.

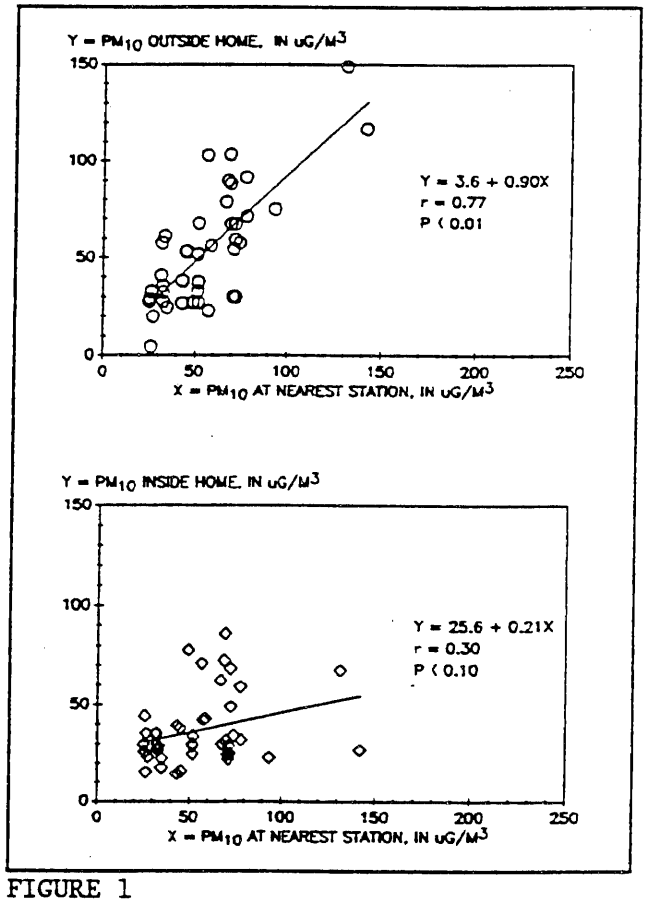

FIGURE 1

Outdoor temperatures at nearest stations ranged from 47° to 101° F during the study period. Hot days were dry, with relative humidity usually well below 50%. Most homes demonstrated reasonably good climate control. Nevertheless, some stressful indoor temperatures were documented - extremes were 59° and 92°. There were multiple instances of indoor temperature above 80° and relative humidity above 60%, some apparently deliberate. For the entire panel, indoor maximum or minimum temperatures were significantly ($P < 0.05$) associated with outdoor maximum or minimum temperatures.

Lung function varied significantly ($P < 0.05$) over time, regardless of air quality. Forced vital capacity (FVC) and forced expired volume in one second (FEV_1) showed circadian variation, being lowest in mornings and highest in afternoons, as expected in chronic respiratory disease. Mean FVC also increased from day to day, but FEV_1 did not. Figure 2 shows mean lung function, adjusted for circadian variation, on Thursdays through Mondays (open symbols). Figure 2 also shows daily maximum hourly PM_{10} at nearest monitoring stations (solid circles), averaged across all subjects. Neither FVC nor FEV_1 varied significantly with PM_{10}, O_3, or temperature. Peak expiratory flow (PF) showed no significant circadian variation, but declined significantly from day to day. Daily mean PF appeared to decline significantly with increasing PM_{10} concentration on the same day, after allowance for the overall time trend, in some but not all statistical models (Table 2). Interpretation of the PF-PM_{10} relationship is complicated in that PM_{10} showed significant day-to-day variation which to some degree paralleled PF variation, trending downward from Thursdays through Sundays.

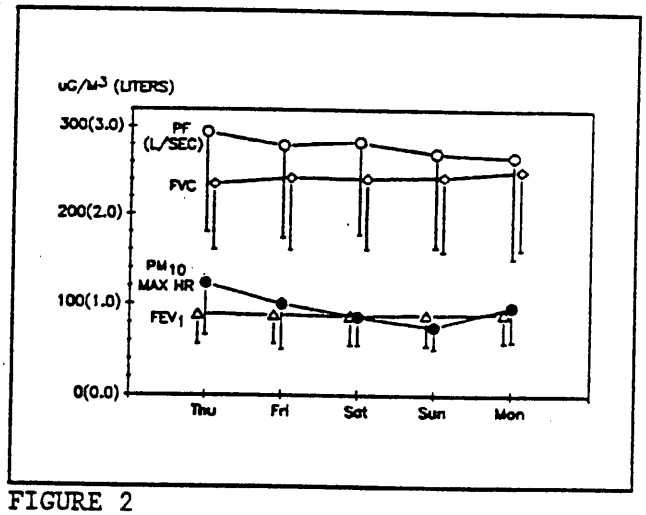

FIGURE 2

Self-rated overall clinical status (a simple numerical index based on diary reports of general feelings and medication needs throughout a given day) did not vary significantly day to day, and did not decline significantly with increasing PM_{10} or O_3 (Table 2). Overall clinical status did show a slight, marginally significant ($P = 0.05$) improvement with increasing daily maximum temperature outdoors. More detailed symptom evaluations, focusing on irritant symptoms likely to be triggered by air pollutants, showed no significant relationship to PM_{10}, O_3, or temperature.

Physical activity occupied about 14% of subjects' time, but was of low intensity, judging from diaries and Holter electrocardiograms. In about half the subjects, hourly heart rates from Holter records correlated significantly with diary activity records; other subjects either reported no activity, or their reported activity did not consistently increase heart rate.

Table 1.
Summary of Particulate Monitoring Findings*

Measure	Location	N	Mean ± SD	Range
PM_{10} Mass	Station†	45	55.1 ± 25.6	25.1 - 141.8
	Outdoors	42	53.5 ± 30.2	4.5 - 149.0
	Indoors	44	37.0 ± 17.9	14.3 - 85.8
	Personal	43	42.3 ± 20.3	16.8 - 104.6
	I/O Ratio	42	0.9 ± 0.6	0.3 - 3.4
PM_{10} Nitrate	Outdoors	42	13.0 ± 12.2	2.1 - 54.8
	Indoors	44	5.0 ± 5.4	0.7 - 25.6
	Personal	43	5.2 ± 5.7	0.8 - 30.0
	I/O Ratio	42	0.5 ± 0.4	0.1 - 1.9
PM_{10} Sulfate	Outdoors	42	5.8 ± 4.1	0.6 - 16.6
	Indoors	44	4.8 ± 3.0	1.1 - 15.2
	Personal	43	4.9 ± 2.9	1.2 - 11.1
	I/O Ratio	42	1.0 ± 1.2	0.4 - 8.0
$PM_{2.5}$ Mass	Station†	45	55.4 ± 25.2	23.8 - 174.8
	Outdoors	41	33.6 ± 18.5	5.9 - 96.3
	Indoors	44	26.4 ± 16.0	8.8 - 97.3
	Personal	45	28.2 ± 14.4	8.2 - 70.0
	I/O Ratio	40	0.9 ± 0.6	0.2 - 4.0
$PM_{2.5}$ Nitrate	Outdoors	41	9.1 ± 8.6	0.3 - 41.8
	Indoors	44	4.0 ± 4.4	0.4 - 15.9
	Personal	45	3.9 ± 4.1	0.3 - 14.2
	I/O Ratio	40	0.6 ± 0.4	0.03 - 2.3
$PM_{2.5}$ Sulfate	Outdoors	41	5.8 ± 3.1	0.8 - 14.3
	Indoors	44	4.6 ± 2.2	1.3 - 10.2
	Personal	45	4.6 ± 2.0	0.8 - 8.7
	I/O Ratio	40	0.9 ± 0.6	0.3 - 4.4
$PM_{2.5}$ Carbon‡ (Organic)	Outdoors	44	10.3 ± 4.8	3.3 - 29.8
	Indoors	44	13.5 ± 5.7	6.4 - 33.4
	I/O Ratio	43	1.4 ± 0.6	0.3 - 3.3
$PM_{2.5}$ Carbon‡ (Elemental)	Outdoors	44	1.3 ± 0.7	0.1 - 2.7
	Indoors	44	1.3 ± 0.7	0.2 - 3.0
	I/O Ratio	43	1.0 ± 0.3	0.7 - 2.1

*All measurements are in $\mu g/m^3$ except for indoor/outdoor (I/O) ratios, which are dimensionless. N is the number of usable samples.

†Averages of hourly data from continuous PM_{10} monitors at SCAQMD stations nearest subjects' homes, for the relevant 24-hr intervals of subject-oriented monitoring. (Note that stations do not monitor $PM_{2.5}$, all station data are PM_{10}.)

‡Carbon samples were collected over 48 hr, the PM_{10} monitoring interval plus the $PM_{2.5}$ monitoring interval.

Table 2. Summary of Repeated-Measures Analyses of Covariance Relating Health and Environmental Variables

- A + sign indicates a significant relationship; see footnote.
- A - sign indicates non-significant (P > .05) relationship.
- The figure in parentheses indicates the number of models tested. Model differences related to number of days included, use of daily mean or hourly extreme environmental variable, and treatment of 1-5 subjects with incomplete data (exclusion, or maximum likelihood estimation of missing values).
- Blank cell indicates that no analyses were done.

ENVIRONMENTAL VARIABLE	HEALTH VARIABLE						
	FVC	FEV_1	PEAK FLOW	OVERALL CLINICAL STATUS	TOTAL SYMPTOM SCORE	LOWER RESP. SYMPTOM	G.I. OR MUSCLE SYMPTOM
PM_{10} same day	- (5)	- (5)	+ note a	- (4)	- (3)	- (1)	- (1)
PM_{10} prev. day	- (5)	- (5)	- (6)	- (2)		- (1)	
O_3 same day	- (4)	- (4)	- (4)	- (2)	- (2)	- (2)	- (2)
Hi temperature same day	- (1)	- (1)	- (1)	+ note b	- (1)		+ note c
Low temperature same day				- (2)	- (1)		

NOTES:

a. 9 of 13 models showed significant (P < .05) decrease of peak flow with increasing PM_{10} at nearest station.

b. One of 2 models showed overall clinical status (based on general questions about subject's overall sense of well-being, activity, and medication use) improved with increasing outdoor maximum temperature at nearest station (P = .05).

c. Only model tested showed that GI and/or muscle symptoms (considered unrelated to air pollution) decreased with increasing outdoor maximum temperature (P = .02).

DISCUSSION

This pilot study demonstrated the feasibility of all the individual-oriented health and exposure measurements attempted, with the exception of outside-home temperature and humidity monitoring. Daytime direct sun exposure and morning dew sometimes invalidated outdoor hygrothermograph records, so monitoring station data appeared to provide a better record of outdoor temperatures. A question arises concerning how much the monitoring efforts themselves interfere with the normal daily activities and health changes being studied. Anecdotal reports from some subjects suggested that the need to wear monitoring devices may have inhibited some activities outside their homes. This issue should be investigated by comparing the results of minimally intrusive activity monitoring with and without concurrent personal exposure monitoring.

Important preliminary conclusions include the following:

- Our presumably typical Los Angeles COPD patients usually stayed indoors, but still had some exposure to particulate pollutants, NO_2, and weather stresses found outdoors.
- Most analyses of daily health vs. monitoring-station PM_{10} levels showed no statistically significant relationship; but peak flow appeared to decrease with increasing PM_{10}.
- Personal exposures to O_3 were consistently low, according to passive monitoring badges, but still correlated with outdoor O_3 levels.
- Analyses of daily health vs. monitoring-station O_3 or temperature levels showed no statistically significant relationships, except for a possible slight improvement in non-respiratory symptoms on warmer days.
- Physical activity levels were low; many but not all subjects' activity reports were corroborated by Holter heart rate recordings.

With respect to PM exposure, our findings seem reasonably consistent with previous findings in the general population of Riverside, an inland Los Angeles suburb [Ozkaynak et al., 1996], in that concentrations outside subjects' homes correlated well with monitoring-station data, while indoor and personal concentrations correlated less well with stations. Also, our findings seem reasonably consistent with findings in Nashville COPD subjects [Bahadori and Koutrakis, this conference], even though the latter subjects lived in air-conditioned single-family homes in a more humid area with lower outdoor PM levels.

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Trends in Airborne Particulate Matter in the United States
I. Emissions Trends

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Abstract - This paper examines trends in population exposures to airborne particles in the United States for the period 1940-1990, based on published emissions data from specified source categories. To address the question of trends by particle size, sources of particulate matter (PM) are segregated into two groups: those that emit primarily fine particles derived from combustion and industrial processes, and those that emit the larger particles typically produced by materials handling and fugitive dust. Downward trends are seen in both groups at average rates from 2-5% per year. A companion paper addresses trends in ambient concentrations of particulate matter, which are found to be comparable to trends in emissions. Epidemiological studies designed to study long-term or chronic health effects based on spatial contrasts must recognize these differential rates of air quality improvement in order to realistically represent long-term exposures.

INTRODUCTION

Airborne particulate matter (PM) was one of the first air pollutants to be given serious abatement consideration in the earlier part of this century, when "smoke" control became an important priority, especially in communities where soft coal was the predominant fuel for space heating. However, smoke was often considered mainly as a nuisance, because of the soiling capacity of airborne soot and the tendency of larger particles in urban air to be manifested as foreign bodies in the eyes.[1] Since that time, urban space heating has shifted to oil and gas, better PM control devices have been installed on point sources, and ambient air quality has improved by about an order of magnitude in major cities.

More recently, PM has been singled out in epidemiological studies as a potential major factor in environmental health; the relative importance of particle size and composition is one of the important issues.[2,3] Significant statistical associations have been reported for almost all PM measures with respect to premature mortality, excess hospital admissions, and respiratory symptoms.[4-6] Both acute (daily) and long-term (a year or more) responses have been inferred from these studies, even at today's greatly reduced exposure levels. However, the long-term epidemiological studies have largely been based on ambient air quality data concurrent with the periods of study (Abbey *et al.*[7] is a notable exception). Because of differences between coincident and cumulative exposures, the associations between long-term exposure to air pollution and either disease prevalence or creation of new cases of chronic disease remain problematic. For the trend analyses in this paper, we take "long-term" to mean one or more decades.

The U.S. Environmental Protection Agency (EPA) is currently considering revisions to the national ambient air quality standards (NAAQS) for PM. Tightened NAAQS levels would require further reductions in PM emissions. It is therefore of interest to consider the long-term trends in PM emissions that have already occurred over the years. Trends in emissions of other air pollutants, including those that provide precursors for secondary particles, are also examined as a means of providing context for the primary PM trends.

Sources and Types of Particles in the Atmosphere

Of the air pollutants regulated under the Clean Air Act, particulate matter is perhaps the most diverse, consisting of solid and liquid particles of many different types and origins, both anthropogenic and natural. One of the most important classifications is by particle size (aerodynamic diameter), since the size and the density of a particle influence its ultimate fate in the atmosphere and also the location of deposition within the human respiratory system. "Large" particles, typically greater than about 20 um in aerodynamic diameter, tend to settle out quickly

by gravity and thus have relatively short lives and travel times in the atmosphere. Extremely small particles, typically less than about 0.1 um, may behave essentially as gases, except for their tendency to agglomerate and to be subject to other physical forces. Particle sizes between these two extremes are currently of most interest for their potential health effects; they tend to form two size distribution modes, with median diameters of roughly 0.3 um and 5 um, respectively. Because particles in this overall size range can penetrate human nasal defenses, they are called "thoracic" or "inhalable" particles (IP) and are currently regulated as "PM_{10}", since the sampler used to collect them is designed for a nominal particle size cut-point of 10 um.

Fine particles comprise condensed combustion products (including soot) and industrial process emissions and products of atmospheric chemical reactions, in addition to some particles of natural and of mineral origin. The larger particles, which we refer to here as "coarse" particles, are formed primarily from mechanical processes such as grinding or abrasion and are usually rich in mineral content, although there may also be some organic and metallic coarse particles.[8]

Sources of Uncertainty in Long-Term Trend Analysis

Trends in national emissions are useful from their broad perspective; decomposition into regional emission trends can also be useful, but as smaller regions are considered, it becomes necessary to account for the influence of inter-regional transport. Also, the effect of a unit of emission on ambient air quality varies substantially with stack height, and thus decreases in emissions from one category may or may not be compensated by increases in another category with respect to ambient air quality. In addition, the methods used to estimate emissions have changed over the years, as discussed below. Emissions trends pertain most directly to primary emissions; the parallel effects of secondary particles formed in the atmosphere must be estimated separately.

DATA AND METHODS USED

Particulate Emissions Data

EPA[9] has compiled a convenient source of emissions data for trend analysis, covering the period from 1900 to 1994. The period from 1940 to 1990 is perhaps of most interest for long-term studies of adult health effects; this 50-yr period exceeds the suspected latency periods of most of the chronic diseases thought to be associated with air pollution (heart disease, cancer, and chronic respiratory disease) and is thus long enough to allow longitudinal studies of adults with various cumulative exposure periods.

Bases for Emissions Estimates. The general methodology used for estimating emissions of air pollution requires three data elements for each process considered: (1) a process or production rate (g/s, kw/y, etc.), (2) a pollutant production rate or emission factor (g/unit of production), and (3) a pollutant removal or control efficiency. Estimates of historical emission rates may thus be problematic, since they rest on historical production statistics and on physical process parameters that can no longer be verified. As an illustration, various EPA estimates of PM emissions for the year 1970 were compared; the 1995 estimate for 1970 was about half of the earliest (1972) estimate for 1970, with the largest reduction in stationary source combustion emissions (62%). We assume that the most recent EPA estimates are the most reliable.

Since coal-fired power plants have perhaps the largest potential emissions of PM, it is especially important to estimate their control efficiencies accurately. The historical values were used in the most recent EPA estimates are listed in Table 1. It is interesting to compare these assumptions with those that were made much earlier by Vandegrift et al.,[10] who assumed an average operating control efficiency of 0.936 for coal-fired utility boilers, presumably for the ca. 1970 period. The difference in the two estimates amounts to at least a factor of 2 in PM emissions from utility sources. It is also interesting to note that Vandegrift et al. estimated in 1971 that PM emissions from stationary sources would decrease from 18 to 3 million tons per year by the year 2000 according to the most optimistic forecast; EPA's current estimate for 1994 for these sources is less than 2 million tons/y.

Table 1 Assumed PM Control Efficiencies for Electric Utilities

year	anthracite	bituminous
1940	0.50	0.50
1950	0.50	0.50
1960	0.69	0.69
1970	0.85	0.86
1971	0.85	0.88
1972	0.85	0.90
1973	0.85	0.91
1974	0.85	0.92

source: P. Carlson, personal communication, March 1996.

PM Emissions by Particle Size. The most recent accounting of PM emissions[9] assigns them all to "PM_{10}". For the present analysis, a further breakdown is needed, to identify the primary emissions of fine particles. For this purpose, all fuel combustion emissions, chemical manufacturing, metal smelting, and vehicle exhaust emissions are considered to be fine particles. Emissions from grain handling, mineral industries, and fugitive dust would be considered "coarse." This is consistent with the determinations made for Philadelphia by Chow et al.,[11] as tabulated in the Appendix.

RESULTS

National Trends in PM_{10} Emissions

The data used in this section were taken from EPA.[9] Figures 1 and 2 show how the sources of airborne particles have changed since 1940. The dramatic change after 1970 was due to implementation of the Clean Air Act; important further reductions have taken place since 1980. In the figures, all of the source categories shown except "mineral industry" (cement production, quarrying, mining, etc.) would be considered to contribute primarily to fine particle emissions. Figure 1 shows trends for the major source categories that emit primary particles. Perhaps the most dramatic change has been in mineral industry emissions, but these larger particles would be expected to exert their maximum effects on air quality relatively near their sources and thus may not be very important for public health because of this limited dispersion.

Figure 2 shows the shares of emissions sources for 1950, 1970, and 1990. In the early years, emissions from the mineral industries were the largest single source, but they probably contributed relatively little to fine particle loadings. In 1950 (Figure 2a), railroads were the largest anthropogenic combustion source, but by 1970 (Figure 2b), this had shifted to coal-burning power plants (as discussed above, this share may be an overestimate). In 1990 (Figure 2c), "wildfires" and "other fuel", which are dominated by residential wood combustion, were the largest source categories, followed by emissions from utility sources (primarily coal burning power plants). Emissions from diesel-powered vehicles were another important source in 1990, especially considering their low height of emission and locations in populated areas. Sulfate particles (formed secondarily from SO_2 in the atmosphere) are not considered in this framework but are discussed further below.

Figure 3 compares the overall trends in annual emissions for the 5 major pollutant categories regulated under the Clean Air Act. Particulate matter (excluding agricultural and other fugitive dust sources in order to emphasize fine particles) has been on a steady decline over the whole period, with a nearly 75% decrease, even when residential wood combustion (which may be localized) is subtracted. Nitrogen oxides, on the other hand, increased steadily until 1980, in part because the growth in numbers of vehicles outpaced the reductions in emission from each vehicle. CO, SO_2, and volatile organic compounds (VOCs) show nearly parallel trends, peaking in 1970.

Figure 4 considers trends in secondary pollutants as well as in primary PM emissions. For the purpose of this illustration, we assume proportionality between the national average SO_4^{2-} air concentration and national SO_2 emissions, and between the national average non-SO_4^{2-} ambient fine particle concentration (taking SO_4^{2-} as $(NH_4)_2SO_4$) and national fine particle primary emissions, using 1980 as the baseline year. Then, using the ambient data from the Inhalable Particulate Network (ca. 1980), which are thought to be free of artifact, we derive a scale factor for use in other years that effectively assigns 10.4% of the SO_2 emissions to the particulate phase. Since the IP measurement technology used here is thought to capture only minimal quantities of nitrates and secondary organics, parallel estimation procedures cannot be used and we assume that 5% of the NO_x emissions become nitrate aerosol and 2% of the VOC emissions become organic particles, again, for the purpose of illustration of likely trends. Obviously, these percentages can only be rough estimates and they will vary by region and season. The annual decrease in primary PM emissions seen in Figure 6 is about 2.7%; with all secondary species included, it is about 1.5% and a sort of plateau is seen between 1960 and 1970 with higher rates of decrease after 1970. Although the relative importance of secondary particles appears to be increasing with time, the overall downward trend in total fine particles is controlled by the trend in reduced emissions of primary fine particles.

In considering emissions as a crude surrogate for air quality, one must also take into account seasonal and regional trends in both emissions and dispersion. For example, residential wood combustion is only important in winter and mainly in relatively thinly populated areas. Wildfires are unlikely to seriously impact major population centers. Large particles are likely to be important only near their sources. Sulfates tend to be more important in the eastern half of the country. Such differences must be examined through ambient air quality measurements, which are the subject of a companion paper.

CONCLUSIONS

This analysis has shown that the U.S. has benefited from a substantial reduction in airborne particle loadings since the middle of the century. These reductions appear to have occurred in all particle size classifications and in most types of emissions sources. All of these reductions are consistent with an overall decreasing trend of 2-8% per year. The downward trends in TSP and IP are generally well known, and our finding of parallel trends in fine particles suggest that particle size distributions in urban areas may have been relatively steady during this period of greatly improving air quality.

It follows that long-term epidemiological studies must consider the fact that ambient exposures to all particle size fractions were likely to have been substantially higher in previous years than they are currently. Studies that are intended to examine any roles that air pollution might have had in the development of chronic disease patterns must recognize these trends in estimating the appropriate long-term or cumulative exposures.

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Appendix - Emissions Characterization by Particle Size

Chow *et al.*[11] analyzed PM source contributions in a Philadelphia industrial area and characterized source types by particle size, as follows:

Predominantly fine (< 2.5 um) particles	
residual oil combustion	987 t/y
refinery heating	726
municipal incinerators	705
anthracite coal combustion	651
chemical manufacturing	109
copper smelting	96
natural gas combustion	51
paint production	44
zinc galvanizing	29
aluminum melting	7
lead smelting	3
motor vehicle exhaust	?
residential combustion	?
inflow from long-range transport	?
sum of known sources	3408 t/y

Predominantly coarse (> 2.5 um) particles	
feed & grain handling	404 t/y
mineral handling	108
cargo handling	44
forest products	34
carpet manufacturing	23
urban dust	?
continental dust	?
sum of known sources	613 t/y

Unknown particle sizes	
sugar cane processing	94
can label coating	50
roofing products	41
carbon black furnace	12
marine aerosol	?
sum of known sources	197 t/y

According to this accounting, which probably reflects control technologies of the mid-1970s, the bulk of the controllable emissions are in the fine size classification. Also, note that some of these categories are seasonal, but it is likely that the higher inflow of fine particles from summer long-range transport would more than make up for the reduced contributions from local space heating.

For earlier periods, it is likely that controllable emissions might have been larger, because of less effective controls that might have been used then. By the same token, we expect uncontrollable emissions to be about the same. Note that fugitive dust from unpaved roads would not be expected to be a major factor in urban areas in the 20th century.

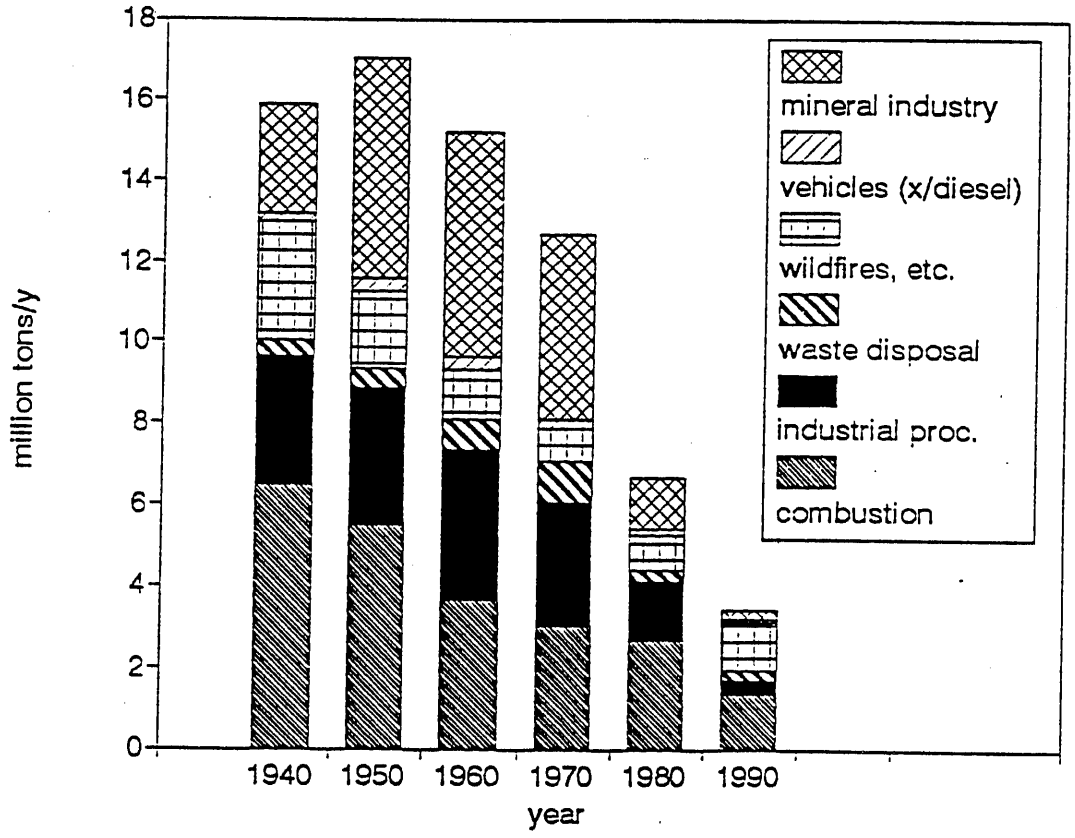

Figure 1. Trends in U.S. emissions of particulate matter from various source categories. Data source: U.S. EPA.[9]

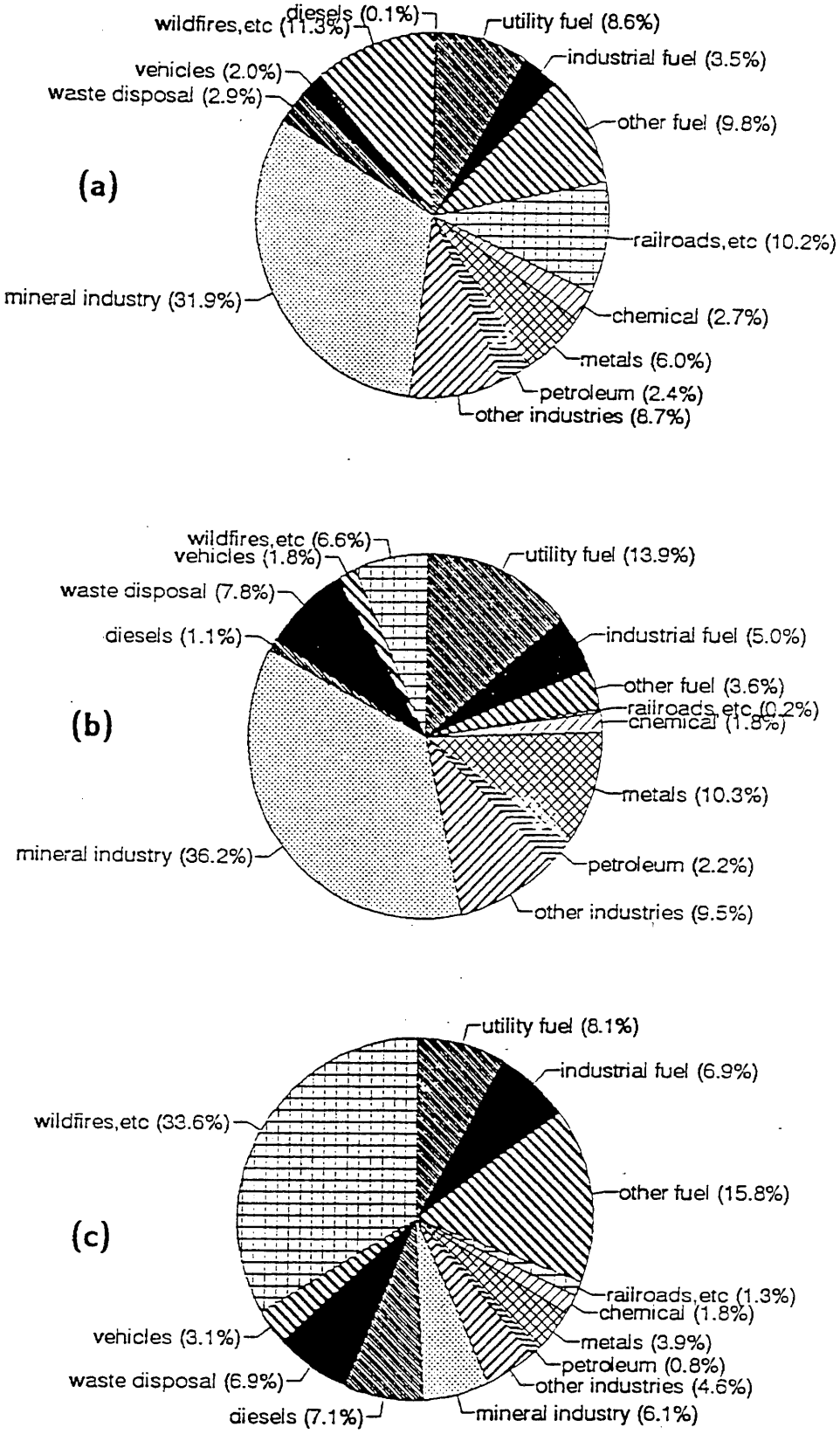

Figure 2. Shares of U.S. emissions of particulate matter. (a) 1950. (b) 1970. (c) 1990. Data source: U.S. EPA, 1995.

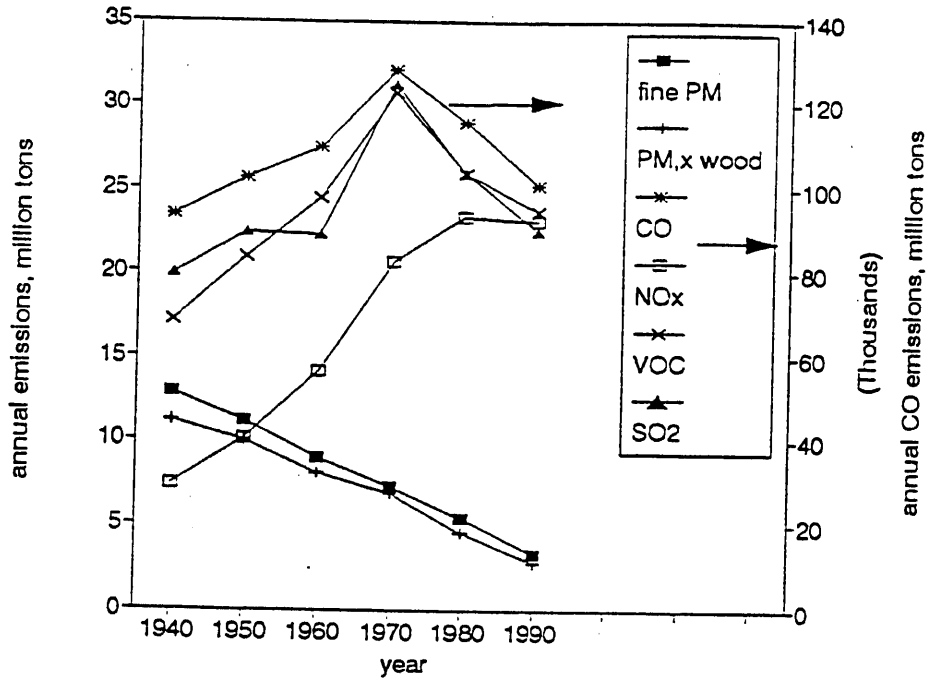

Figure 3. Trends in U.S. emissions of various air pollutants. Data source: U.S. EPA, 1995.

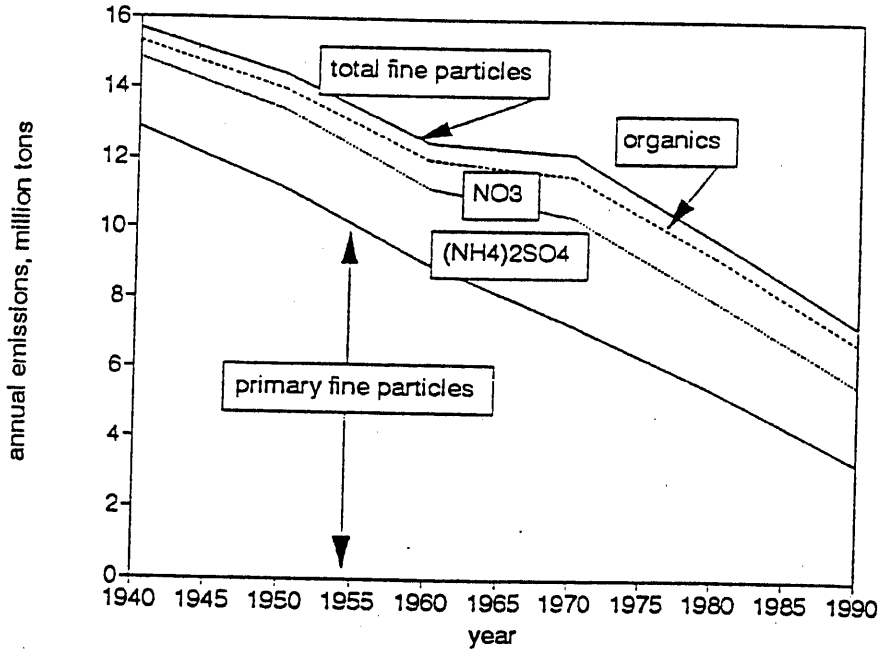

Figure 4. Trends in primary and secondary particles. Data source: U.S. EPA, 1995.

Trends in Airborne Particulate Matter in the United States
II. Trends in Ambient Air Quality

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Abstract - This paper examines trends in population exposures to airborne particles in the United States for the period 1950-1990. Ambient trend data are presented for total suspended particles (TSP) and for fine particles ($PM_{2.5}$); no consistent long-term network measurements are available for the latter, but data are combined from various sources to estimate the overall trends. Important exposure factors include the shift from winter to summer peaks in ambient particulate matter (PM) concentrations and increased market penetration of residential air conditioning. The paper concludes that there have been substantial decreases in population exposures to PM in all particle size ranges during this period, primarily in the locations having the worst initial air quality. Epidemiological studies designed to study long-term or chronic health effects based on spatial contrasts must recognize these differential rates of air quality improvement in order to represent long-term exposures realistically.

INTRODUCTION

The U.S. Environmental Protection Agency (EPA) is considering revisions to the ambient air quality standard for particulate matter (PM), with special emphasis on fine particles (aerodynamic diameters < 2.5 um). If the standards are tightened, further reductions in emissions will be required. A previous paper[1] examined trends in emissions for fine and coarse particles; this companion paper extends the analysis to ambient air quality.

EPA has included analyses of long-term trends in ambient TSP and PM_{10} in their annual "National Air Quality and Emissions Trends" reports. However, the TSP trends have now been supplanted by PM_{10} trends, which begin only in the mid-1980s. The 1988 report[2] shows a long-term TSP trend from 1960-88, but the monitoring stations used vary with the period of analysis. The overall trend was downward, at an overall rate of about 2.5% per year. No attempts appear to have been made to analyze long-term trends in fine particle concentrations.

Measurement of Ambient PM Concentrations

Perhaps the earliest sampling device for estimating PM mass involved the determination of "smokeshade", the darkness of filter paper through which ambient air has been drawn. This methodology has been implemented in various ways, including "British smoke", which is calibrated to read in units of ug/m^3, and coefficient of haze (COH), which is still used in some urban locations in the U.S. These devices generally only sample particles of 5 um and smaller and are most sensitive to the carbon content of the aerosol; the relationship with mass tends to be site-specific. Strong statistical associations have been shown between various smoke indices and health effects.[3,25] A few early attempts were made to estimate particle sizes using optical characterization;[4,5] resolution was only possible down to about 0.2 um and the air sampler used appeared to be incapable of collecting particles larger than about 5-10 um.

Beginning about 1953, the high-volume (hi-vol) sampler for "total suspended particulate matter" (TSP) came into widespread use in the U.S., where it continues. The upper particle size limit for this device is from 30 to 50 um, depending on wind conditions.[6] Glass-fiber filters have usually been used to collect the particles, and the resulting artifacts due to chemical reactions on the filters present a major problem in the accurate determination of sulfate and nitrate contents and total mass.[7] Nevertheless, the longest continuous air sampling records in the U.S. are based on TSP (beginning in 1953), and numerous epidemiological studies have drawn on portions of this data base.[3,8]

In order to emphasize particles thought to be more harmful to health, EPA operated a prototype "inhalable" particle (IP) network nationwide from 1979-81 limited to particles nominally less than 15 um;[9] these data are referred to as the "Inhalable Particle Network" (IPN). This initial size cut was further reduced when PM_{10} sampling came into widespread use in the

late 1980s in response to changes in the National Ambient Air Quality Standards (NAAQS). Although some investigators have assumed that $PM_{10} = PM_{15}$,[10] side-by-side sampling indicates the difference depends on the concentration of coarse particles present.[11] Typically, PM_{10} mass is about 10% less than PM_{15} mass.[12,13] The most common type of PM_{10} sampler is essentially a hi-vol equipped with a circular inlet designed to admit mainly particles less than about 10 um in aerodynamic diameter.[6] The EPA specification requires use of low alkalinity filters to reduce artifact problems; nevertheless, there are also problems with accurate nitrate collection with PM_{10} samplers.[7] Given the excess SO_4^{2-} and NO_3^- on glass-fiber filters and the loss of NO_3^- from Teflon filters, it appears that a substantial portion of the differences between TSP and PM_{10} or PM_{15} may be due to filter artifacts.

An alternative device is the low-volume dichotomous sampler, which partitions the airstream into two parts such that fine particles ($PM_{2.5}$) and "coarse" particles (from 2.5 to 10 or 15 um) are collected separately on small quartz or Teflon filters. The diversion of the air stream separates the particles inertially, a process that is also known as "virtual impaction." PM_{10} or PM_{15} concentrations are determined from the sum of the two separate particle mass collections. There may be overlap between the two size cuts (fine particles also appear in the "coarse" fraction and vice versa) and that the precision of determination of coarse particles is worse than for fine particles.[11] It has also been noted that coarse particles can be lost from the surface of the filter during shipment.[14] Finally, PM_{10} as determined from the sum of coarse and fine fractions is expected to be inherently less precise than when it is determined directly. Comparisons between the two types of PM_{10} (or PM_{15}) determinations have also shown bias as well; the sums of the two separate size cuts were about 30% less than the direct determination of PM_{15}, averaged over 6 cities and 5 years.[14]

The dichotomous sampler provides no detailed information on the actual distributions of particle sizes. Such distributions may be obtained from cascade impactors or by various methods of particle counting, in which number distributions must be converted into mass distributions. This involves assumptions about particle shape and density. Multi-stage cascade impactors sort the particles in the airstream inertially and sequentially, by subjecting them to bends of increasingly tighter radii such that particles are centrifuged out in decreasing order of size where they impact on separate collectors. The smallest particles are then collected on a final filter. One of the main problems with this type of device is particle "bounce" from one stage to another; hence the development of the virtual impactor that eliminated the sequential solid collection surfaces. A modified cascade impactor was used in six U.S. cities for three years and determined that the particles sampled there were mostly of submicron size.[15-17]

Sources of Uncertainty in Long-Term Trend Analysis

The goal of this analysis is to describe long-term trends in U.S. population exposures to airborne PM of various size classifications. Outdoor air quality is emphasized, as modified by the additional factors that influence actual exposures. Ambient air quality can vary substantially in both time and space, but these variations and the uncertainties of measurement error are reduced by comparing averages over months to years. Because of their lower deposition rates, smaller particles are expected to exhibit smoother spatial distributions, and this in turn may also imply less short-term temporal variability. However, smaller masses are inherently more difficult to measure accurately. Seasonal differences in air quality are also expected, because of differences in emission rates, atmospheric properties, and rates of chemical reactions. Outdoor exposure will also vary by season and climatic conditions. Thus, estimating a valid long-term trend requires accounting for all of these sources of variability, in addition to the various biases that might have been introduced by using different types of measurement devices during different time periods. Reductions in filter artifacts over time might be a source of bias in trend analyses, for example.

DATA AND METHODS USED

The most pressing question for ambient PM trends is probably whether there have been shifts in particle size distributions over time, which may depend partly on season and location. PM concentrations also vary spatially in any given year and location; to avoid confounding temporal with spatial trends, recent (ca. 1980-90) data were included for each location for which earlier

(1960-70) data could be obtained. The original references should be consulted for details on the sampling and analysis protocols involved for each of the studies used in these comparisons.

Total Suspended Particles

Lipfert[18] compiled TSP data for major U.S. cities, averaged over 3 periods: 1953-57 ("1955"), 1957-61 ("1959"), and 1969-71 ("1970"). A subsequent report[19] compiled 1980 TSP averages across Standard Metropolitan Statistical Areas (SMSAs), often comprising more than one of the cities used earlier. The 1980 data had an average of 10 monitoring sites per SMSA. In order to examine trends, the earlier city data were aggregated geographically to correspond with the 1980 SMSAs. There are 81 SMSAs with data for all four time periods.

Inhalable Particles

PM_{10} is the current IP measure of choice, but only limited trend data are available, as discussed above. The earliest IP network data (ca. 1980) were measured as PM_{15}, and the variable relationship between PM_{10} and PM_{15} makes comparison difficult, especially when both arithmetic and geometric means are reported (as has been the case). IP trends are thus not formally considered in this paper.

Fine Particles

$PM_{2.5}$ data were obtained from various publications in the literature and from the data presented in the revised EPA Criteria Document for PM,[20] based mainly on dichotomous sampling. There are some minor variations among these data in the sampler design size cuts, from about 2 to 3.5 um. However, intercomparison tests[11] indicate that FP concentrations are not very sensitive to the upper size cut. Indirect estimates of $PM_{2.5}$ were obtained for earlier time periods from various particle size distributions, using 2.5 um as the upper size cut-off. These data sources include cascade impactor data and particle count data. The latter were converted to mass assuming spherical shape and a density of unity.

RESULTS

Trends in Total Suspended Particle Concentrations

The overall TSP trends are presented in Figure 1, using the 1953-57 city averages as a point of reference. The highest annual average TSP in this dataset was in Detroit (340 ug/m^3). Each period is represented by an approximate best-fit line for the observations that depart from the 1:1 line. All of these data indicate that the improvement in TSP air quality is greatest for the cities with the worst initial air quality; changes have been much less drastic in the cleaner locations. The mean values (ug/m^3) for all observations for these five periods were 149, 113, 105, 86, and 68, for an average decrease of about 3% per year.

By way of regional comparisons, New York State[21] showed that statewide composite TSP dropped from 96 to 32 ug/m^3 since 1964, for an average decrease of about 3.7% per year. New York State also showed a substantial recent drop in the statewide composite average PM_{10}, from 32 ug/m^3 to 21 ug/m^3 in 1993. This finding is consistent with that of the revised PM CD,[20] which noted continuing reductions in PM_{10} since monitoring began.

Earlier analyses[22-24] also showed decreases in specific constituents of TSP, such as benzo(a)pyrene and metals. Data on COH trends are quite limited, but data from New York City[25] indicate declines beginning in about the late 1960s.

Trends in Fine Particle Concentrations

Because of the lack of suitable data, considerably more effort is required to deduce long-term trends in $PM_{2.5}$. The apparent overall trend in all available measurements and the trends in specific locations were considered. Figure 2 shows the trend in all of the available $PM_{2.5}$ data, from 1933 to 1990. Certain subgroupings are necessary: the oldest data were taken in winter in urban areas and probably exceed their respective annual averages. Many of the research campaign data from the late 1970s and early 1980s were taken in the summer and are also likely to exceed their respective annual averages. Southern California and the Midwestern U.S. are two regions suspected of exhibiting higher $PM_{2.5}$ levels than the rest of the country; these data are identified to preclude confusing spatial gradients with temporal trends. The estimated trend

line shows a decrease of about 4.6% per year.

Figure 3 limits the data display to annual averages; the corresponding trends in TSP are also shown for reference. Two different TSP trend lines are shown for reference: the trend for the 10 cities with the highest TSP concentrations in 1955, and the trend for 81 SMSAs having data in all time periods. The TSP slopes are about -3.2% per year; the $PM_{2.5}$ data appear to decrease somewhat faster than this for the range shown. When a linear scale is used (not shown), there appears to be nearly constant difference between TSP and $PM_{2.5}$ of about 40 ug/m^3, about half of which could be filter artifact. Note that the $PM_{2.5}$ values at Midwestern sites appear to be consistently higher than in other regions, by about 5-10 ug/m^3.

Figure 4 shows $PM_{2.5}$ trend data for selected locations for which enough data were available. Best-fit trend lines are shown for Steubenville (-5.1% per year) and St. Louis (-7.8% per year). The trend lines for New York City and Philadelphia are estimated but are also consistent with these general levels of decrease. Note that different sources of data are used in each of the plots in Figure 4, yet they all indicate similar decreases, of about 5% per year. This suggests that the overall impression of a substantial decline in fine particle concentrations over time is not solely dependent on a few early measurements. Although the extrapolations to years before about 1970 must be considered speculative, trends defined by all of the available data suggest that fine particle concentrations in major and industrial cities ca. 1950 and earlier may have approached 100 ug/m^3, which is consistent with the early TSP measurements.

Ambient Sulfate Aerosol Trends

Longer-term SO_4^{2-} concentration trends are problematic because of artifact formation on the glass-fiber filters used for most of the earlier measurements. Because SO_2 (the source of such artifacts) was also higher in many of the locations for the earlier period, it is possible that some of the indicated changes in $SO_4^{=}$ concentration may be due to changes in artifacts. The local $SO_4^{=}$ ratios from 1970 to 1980 range from about 0.4 to about 2.0, with even more variability in the earlier data. Part of this variability is due to differences by region; sulfur oxides decreased in major Northeastern cities as cleaner fuels came into use, but they may have increased in parts of the South due to the influx of industry and population. However, the overall trends in ambient data are reasonably consistent with the SO_2 emission rates, which show relatively minor differences between 1960 and 1980. New York State also showed only modest SO_4^{2-} decreases from 1964-84 (and an increase from 1984-89) in statewide composite SO_4^{2-} levels based on high-volume sampling with glass-fiber filters. However, based on the Teflon filters used in IP sampling, SO_4^{2-} decreased from about 7 ug/m^3 to about 5 ug/m^3 from 1986 to 1993 (about 4.8% per year).

Trends in Exposures to Ambient Air Pollution

Exposure to outdoor air is governed by individual activity patterns and structural air exchange rates. Information on these trends is generally not available, but one might speculate that people now spend more time indoors than at the middle of the century (because of the influence of home entertainment) and that buildings have become tighter because of the emphasis on energy conservation that began in the mid-1970s. Use of residential air conditioning has also increased dramatically since about the mid-1960s, as shown in Figure 5. The increase is most pronounced in the South (as expected), where central air conditioning is now more prevalent than room units. An offsetting factor affecting these exposure trends in some locations may be the shift from winter to summer peaks in PM concentrations in some northeastern locations.

Quantitative use of this information is beyond the scope of this paper, but it follows that less outdoor air pollution is experienced indoors when residential air conditioning is operating. Thus the trends shown in Figure 5 would serve to reinforce then trend towards reduced exposure to air pollution.

CONCLUSIONS

This analysis has shown that the U.S. has benefited from a substantial reduction in airborne particle loadings since about the middle of the century. These reductions appear to have occurred in all particle size classifications, with an overall decreasing trend of about 3-5% per year, which is consistent with trend in national PM emissions.[1] The downward trends in TSP

and IP are generally well known, and this finding of parallel trends in fine particles suggest that particle size distributions in urban areas may have been relatively steady during this period of greatly improving air quality. The concurrent trend towards increasing market penetration of residential air conditioning would appear to reinforce the trend towards lower exposures to outdoor air pollution.

It follows that long-term epidemiological studies must consider the fact that ambient exposures to all particle size fractions were likely to have been substantially higher in previous years than they are currently. Studies that are intended to examine any roles that air pollution may have had in the development of chronic disease patterns should recognize these trends in estimating the appropriate long-term or cumulative exposures.

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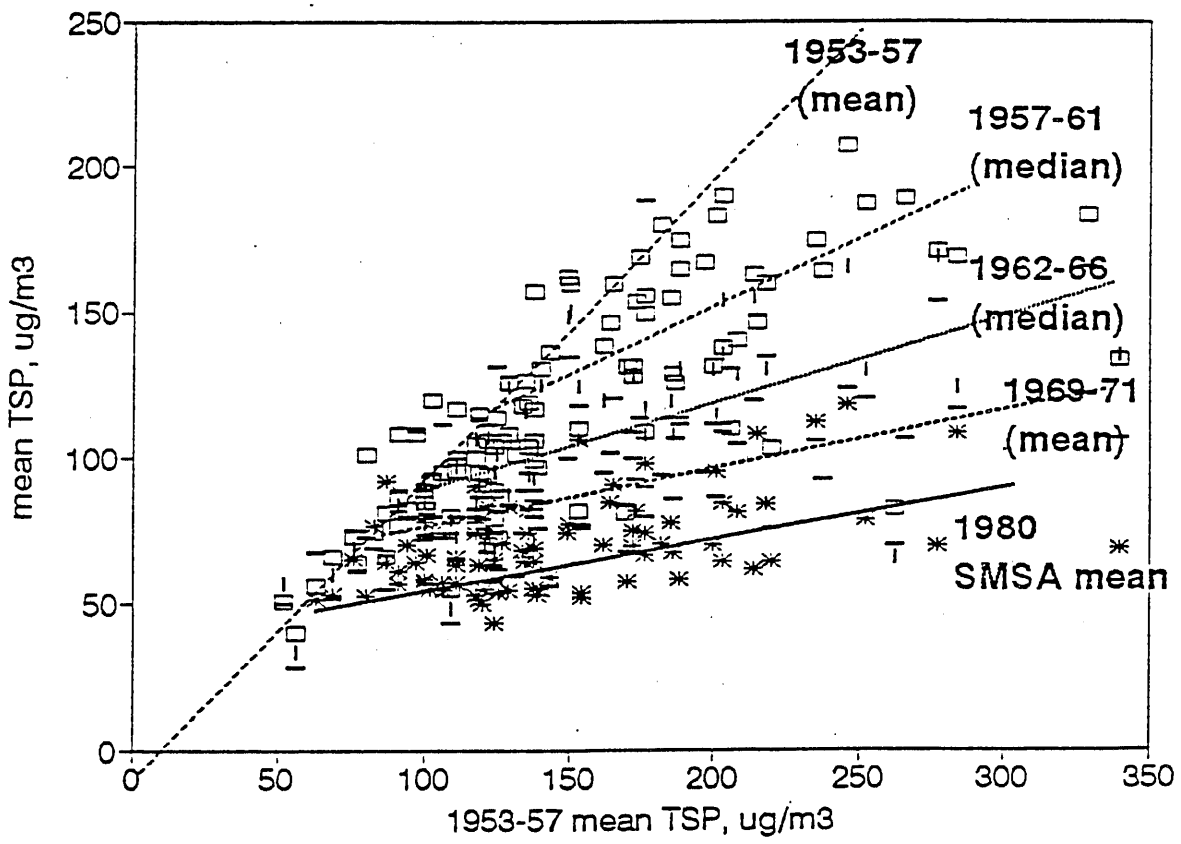

Figure 1. Trends in urban TSP concentrations. Basic data from U.S. EPA sources, as analyzed by various authors.

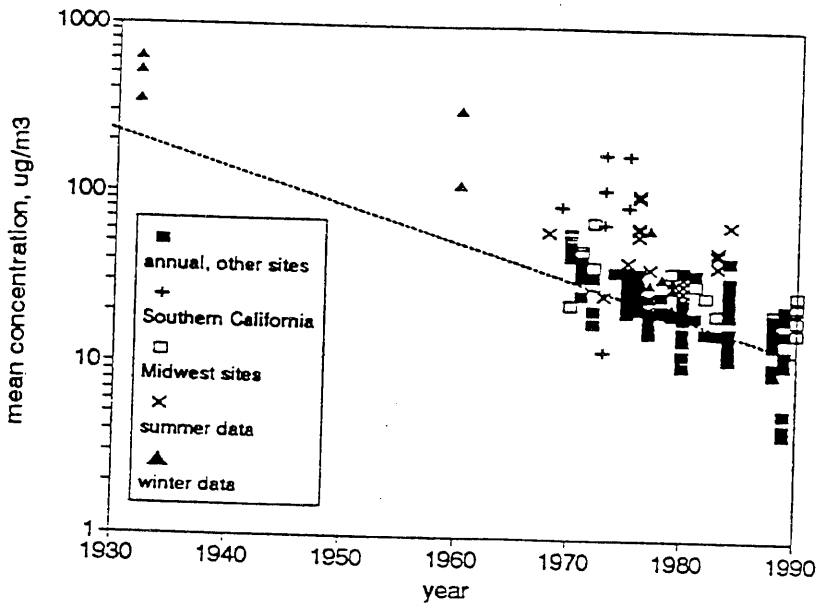

Figure 2. Trends in urban fine particle concentrations for various locations and time periods. Data from various sources.

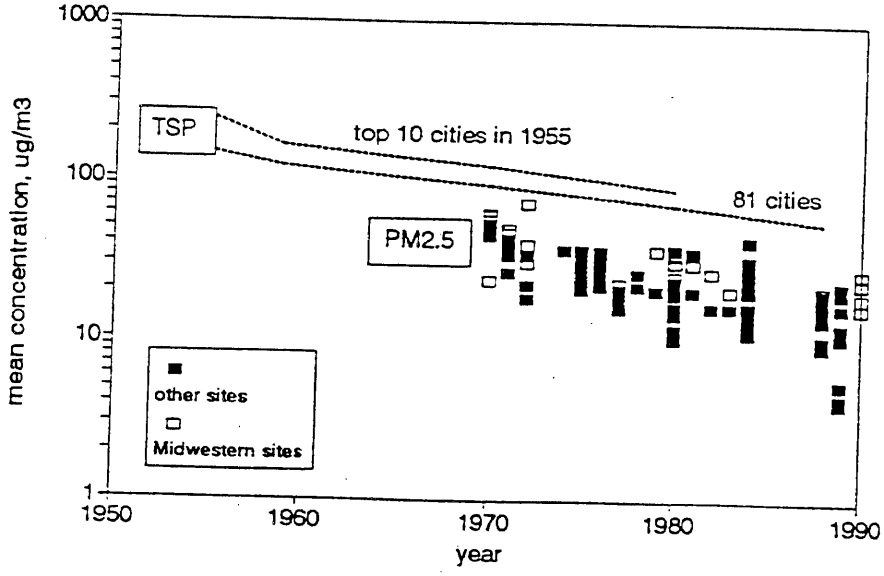

Figure 3. Trends in annual average urban fine particle concentrations. Data from various sources.

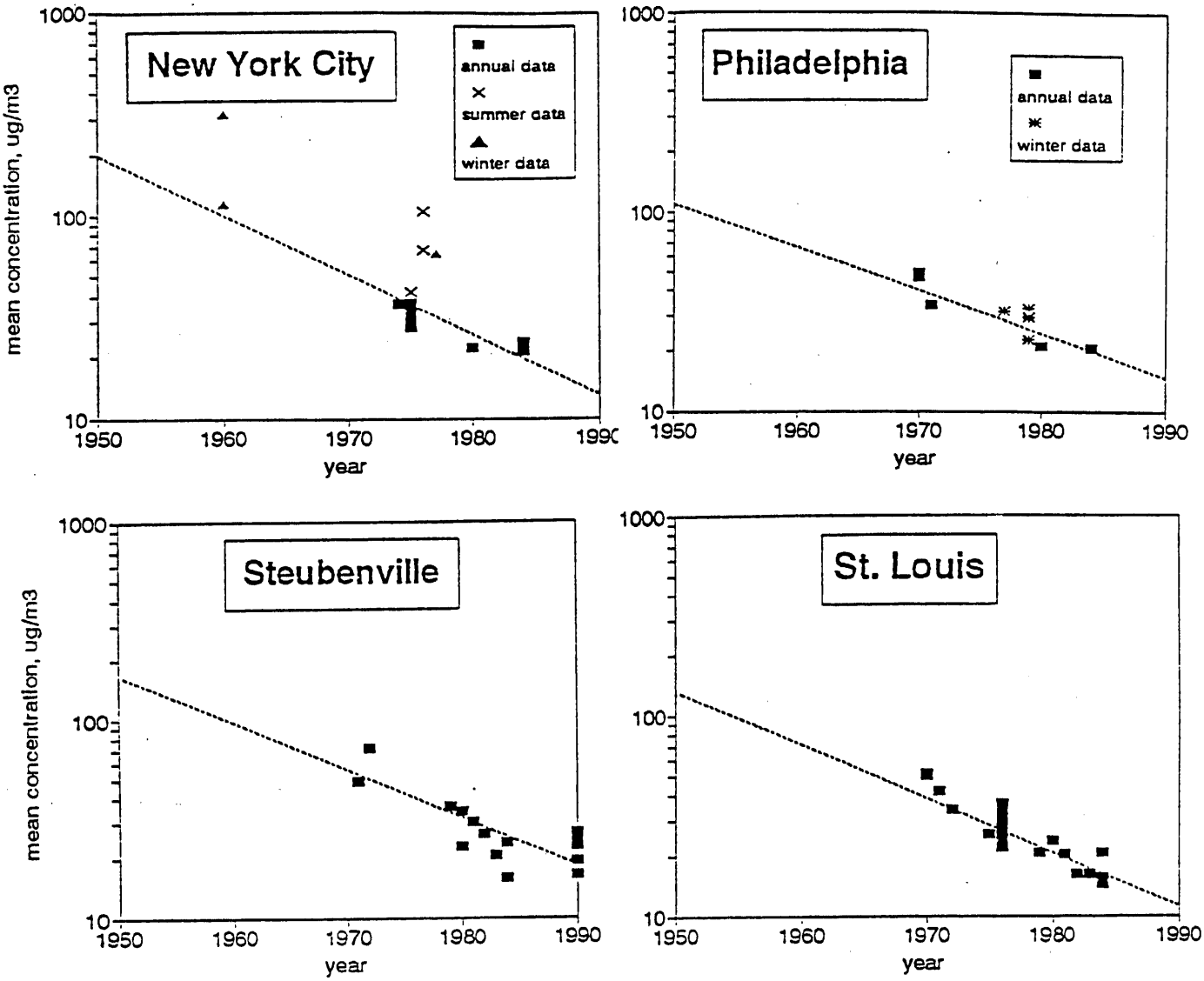

Figure 4. Trends in fine particle concentrations in various urban areas. (a) New York City. (b) Philadelphia. (c) Steubenville, OH. (d) St. Louis. Trend lines are approximate.

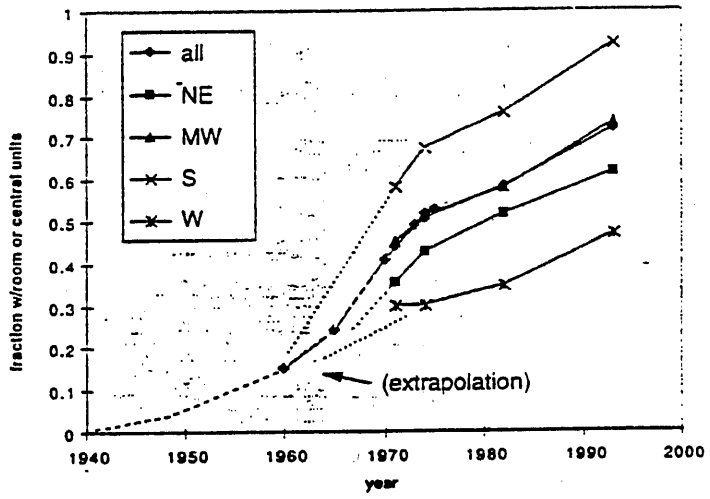

Figure 5. Trends in use of residential air conditioning. Data source: Statistical Abstract of the United States (various years). Legend refers to Census regions.

The Effects of Exposure Error on Environmental Epidemiology

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Abstract - This paper outlines the important concepts of uncertainties in the independent variables that have been used to characterize exposure in environmental epidemiology studies and some of their ramifications, with special attention to airborne particles. Sources and typical magnitudes of such errors are discussed and it is shown that these errors may be exerting profound influences on the results of epidemiological studies that are being considered as the basis for further regulation of air pollution. An important finding in this regard is that the coarse particle mass obtained from dichotomous samplers typically has much more uncertainty than the fine particle mass, which makes comparisons of these two quantities problematic.

INTRODUCTION

The types of regression analyses that have been used to explore statistical relationships between ambient air quality and various health outcomes assume that the independent variables used have been measured without error. This assumption extends well beyond the actual instruments used; if a causal interpretation of such relationships is to be inferred, then it is also inherently assumed that the ambient air quality measures used in the study also apply to each affected individual (i.e., define his/her "personal exposure") and, moreover, constitute valid surrogates for the pollutant doses received by the target organs of those individuals. This chain of linkages inherently implies substantial uncertainties, especially since personal exposures have been shown to differ markedly from ambient measures and since the target organs are unknown for some pollutants, notably particulate matter (PM). We refer to all of these exposure uncertainties collectively as "measurement error" or "exposure error." This paper is intended to briefly lay out what is known about such errors, some of their implications, and to suggest what is needed to close the resulting gaps in understanding. Note that the exposure error issue does not question the existence of the observed linkages between environment and health, but seeks to further describe these relationships without the distortions that may have resulted from uncertainties in the actual exposures.

SOURCES OF ERROR

Sources of exposure error that pertain to this inquiry include:

1. Instrumental error. Measurement systems are not always repeatable and vary in their conformity with standards. Coarse particle measurements are among the least reliable.
2. Spatial variability in the ambient. Any epidemiological study must rely on a finite number of air monitors in a given city. Concentrations of air pollutants vary considerably spatially (including vertically), because of the local effects of pollutant sources and sinks within the city.
3. Temporal variability. It is not always clear which pollutant averaging time should be used; peak concentrations tend to vary more in space than averages. Studies that seek to describe chronic responses should use some measure of long-term, cumulative exposures.
4. Personal exposures vs. ambient air quality. Different pollutants have been shown to vary considerably in this regard, depending on activity patterns and the balance between sources and sinks in indoor environments and on rates of penetration of outdoor air.
5. Other factors. Other factors include human heterogeneity with respect to breathing rates and metabolic uptake of inhaled pollutants that control doses to target organs.

Table 1 is a subjective assessment that compares the air pollutants of interest in this regard. Tradeoffs are involved, for example, because some of the most accurately measured pollutants tend to vary more spatially, and vice versa.

These concepts are also extended to ambient temperature, which is a common confounder in many studies. Airport data are usually used, but virtually no one is actually exposed to those measured levels. Heat-wave victims, for example, are often found to have been exposed to much higher temperatures.

TABLE 1
SUBJECTIVE JUDGMENTS ABOUT EXPOSURES TO DIFFERENT POLLUTANTS

species	instrument error	spatial variability	personal exposures	human variability
TSP	overestimate	fair	unknown	unknown
PM_{10}	underestimate	fair	variable	unknown
$PM_{2.5}$	random	small	> ambient	high (smoking)
CP	underestimate	fair (?)	unknown	unknown
SO_4^{2-}	(depends on filter)	small	unbiased	unknown
H^+	small	high	< ambient	high
SO_2	nil	high	<< ambient	high
O_3	nil	high (urban)	< ambient	high
NO_2	nil	fair (?)	< or > ambient	high (smoking)
CO	nil	high	< or > ambient	high (smoking)
temperature	nil	small	< or > ambient	high

The entry "smoking" refers to the heterogeneity that is expected when the population of interest includes both smokers and non-smokers.

EFFECTS OF MEASUREMENT ERRORS

The most commonly considered exposure error involves a bivariate situation with normally distributed errors (no bias). In such cases (which are the exception rather than the rule here), the slope of a regression will be biased towards the null, the goodness of fit will be impaired, and the x-intercept will be shifted to the left. As a result, if the true relationship has a positive x-intercept (such as a "hockey-stick" function), exposure error may make the function appear to be linear. These concepts also apply to logistic regression functions,[1] which become flatter as a result of measurement error. Such errors may have profound effects on the interpretation of the perceived relationships between exposure and health.

Multiple exposure errors add considerable complications when several "independent" variables are actually correlated with one another, thus qualifying as confounders. In such cases, the error in the confounder may be more critical than the error in the variable(s) of primary interest. If two correlated independent pollutants in a joint regression have equal underlying toxicity, the one with less measurement error will tend to prevail.[2] Such a situation is termed "differential" exposure error. Measurement uncertainties may also obscure the true degrees of collinearity.

A further outcome of measurement error may be masking of non-linearities in the true dose-response functions, including thresholds and curvature.[3] It has been shown that such curvature may be biased towards downward concavity.[4]

The underlying concept here is that the health outcomes of individuals will be controlled by their individual exposures, as opposed to some surrogate or community mean value. Although the epidemiological data base involving personal exposures is meager, this concept has been verified experimentally by studies involving severe indoor PM exposures in Beijing.[5] Use of the community mean exposure in epidemiology invokes the "ecological fallacy", in which the exposed and affected portions of a population do not necessarily coincide.

EXAMPLES OF EXPOSURE ERROR

Coarse vs. Fine Particles. The most common classification of aerosols by particle size involves the dichotomous virtual impactor. In its current configuration, this is a low-flow device with an inlet cut-point of 10 um that inertially separates the sample further into particles < 2.5 um (FP) and those between 2.5 and 10 um (CP). Since only 10% of the flow is used for the latter, extremely precise weighing of filters is required. In addition, there have been problems with loss of coarse particles from the filters during shipment to the analytical laboratory.[6] Thus, the basic design of the sampler favors greater precision (repeatability) and accuracy (conformance to a standard) for the fine fraction; this has been observed in field operations. Camp[7] reported precisions of +/- 5% and +/- 16% for fine and coarse fractions and accuracies of +/- 15% and +/- 44%, respectively, in side-by-side comparisons of different sampler designs. Figure 1 compares correlations between fine and coarse fractions obtained from various data sources; here, the mean magnitude of the fine or coarse fraction (whichever is smaller) appears to control the correlation, which in turn implies that measurement error may be controlling the apparent relationships rather than the characteristics of the particles. In addition, data reported by Watson *et al.*[8] for $PM_{2.5}$ and PM_{10} showed that the most important factor controlling temporal correlations between samplers is not the separation distance (up to 180 km) but the mean magnitude of the concentration (Figure 2). This implies that measurement error is also a problem with fine particles at low concentrations.

Figure 1 implies that FP and CP may actually be well correlated, but that at low mean concentrations, say < 15 ug/m^3, measurement error obscures this fact. Similarly, if FP and CP were entered jointly into a regression for health outcomes, one would expect FP to dominate by virtue of lower measurement error in most instances, even if the underlying toxicities of FP and CP were similar.

Personal Exposure Data. Personal exposure data are very limited, since it is difficult to persuade subjects to tolerate the inconvenience for long periods. Personal exposures to PM_{10} were obtained by Lioy *et al.*[9] for 14 people for 14 days. Although the mean of the 14 subjects tracked the mean outdoor ambient levels quite well, the variability among individuals exceeded what would have been expected just due to randomness (correlations from about 0.15 to about 0.9 (Figure 3); note the lack of dependence of individual correlation on mean personal exposure. The variation in personal exposures greatly exceeded the spatial variation among 4 outdoor ambient samplers, suggesting that these individual variations may be the dominant source of variance. This wide variability in the relationships between ambient air and personal exposures makes it problematic to estimate the exposures of those specific individuals who may have been affected by air pollution on a given day.

Personal exposures to PM_5, SO_2, and NO_2 were measured simultaneously, along with similar measurements at fixed locations, by Silverman et al.[10] and in subsequent experiments using the same technology (personal communication, B. Urch, April 1996). These data allow personal pollutant exposure collinearities to be compared with those obtained from fixed stations; the personal data were less collinear than the ambient. These data also showed that SO_2 and NO_2 had higher temporal correlations between fixed stations and personal exposures than did PM_5 (averages over individuals of 0.3, 0.4 vs. 0.1), even though the SO_2 was greatly attenuated indoors. This finding is consistent with the earlier report[10] that changes in lung function during the day correlated only with personal NO_2 measurements, which in turn suggests that personal exposures should be considered more carefully as candidate causal agents in observational epidemiology.

CORRECTING FOR EXPOSURE ERROR

The above examples show that exposure error may constitute a serious problem in environmental epidemiology, especially for PM. In the classic bivariate case with normally distributed errors, a correlation of 0.1 between true and surrogate exposure measures would require adjusting the observed slope upward by a factor of 100 ($1/R^2$), i.e., to a nearly vertical line. Since such a situation seems to be at variance with observations, some alternative explanations should be considered:

1. The simple theory (normally distributed errors) does not apply to the case at hand.
2. Some agent other than PM may actually be responsible for the observed health effects, and that agent has a higher correlation than PM between fixed and personal measurements.
3. The personal exposure measurements may not be representative of the affected subpopulation, which constitutes a tiny minority of the general public. Those affected could either have had much higher correlations than average, much higher personal exposures than average, or both.

Methods for correcting for exposure error require knowledge of the errors, which could be obtained by sampling a subset of the cohort being studied. The personal exposure data described above could constitute such subset sampling, but no assurance can be given that these small samples are in fact representative of the victims of air pollution, who remain unknown in these observational studies. Also, one of the methods requires that all of the covariates used in the health effects model be included in the exposure model that is developed for "correction" purposes. This means that weather data must be collected simultaneously with personal exposures; such data have not been reported. The possibility that errors in personal exposure to heat and cold may be important must also be considered.

Lacking the means to make corrections, we used probabilistic simulations of synthetic epidemiological data to further explore possible ramifications of exposure error. Using relationships from the data reported by Lioy et al.,[9] we found that a true PM_{10} threshold of up to 150 ug/m^3 in personal could be consistent with the types of linear (no-threshold) models that have been reported based on data from fixed ambient monitors (Figure 4). A true threshold higher than the observed mean can result from the tendency of personal PM exposures to exceed ambient levels and the expansion of the few observed personal exposures to hundreds or thousands using probability distributions. Other simulations showed that the (non-normal) distribution of errors can be important and that the true slope may not always exceed the observed slope with non-normal errors.

Perturbing actual epidemiological data by adding error has demonstrated that additional error in one of a pair of collinear variables will cause the other one to appear more important, sometimes dramatically so. However, it is difficult to make a variable with an observed weak effect (or no effect) appear to be stronger by adding error to the system. If the variables that we are forced to work with (from fixed ambient monitors) already contain a lot of exposure error, no amount of analysis of this type can provide a remedy since the error cannot be removed. In such situations (which may include most of the PM studies), even sophisticated statistical analysis cannot impart real meaning to the data.

CONCLUSIONS

From these analyses, we conclude:

1. All PM measurements are subject to substantial errors and uncertainties, especially at low concentrations. In particular, relationships between fine and coarse particles appear to have been attenuated by measurement error.

2. Personal exposures to all air pollutants and to temperature differ substantially from the fixed-monitor data used in epidemiology. These differences result from indoor pollution sources and sinks, personal activities, structural and heating/cooling system characteristics. They vary in both time and space (among individuals).

3. These disconnects between actual and surrogate exposures can have dramatic effects on the epidemiology:
   a. slopes and thresholds may be biased low.
   b. goodness of fit is reduced.
   c. when differential error exists among collinear variables, the results of joint regressions may be misleading in that the variables with the least measurement

error may be favored.
d. the actual degree of collinearity will be obscured.
e. the shape of the dose-response functions will be obscured.

4. It is inappropriate to try to estimate health risks from specific agents based on the types of epidemiological studies considered above.

As a result, the findings of the extant observational epidemiology studies that used data from fixed monitors should not be taken at face value. While the existence of the observed effects is not in question, it cannot now be determined which agents are responsible for the observed effects or at what concentration levels.

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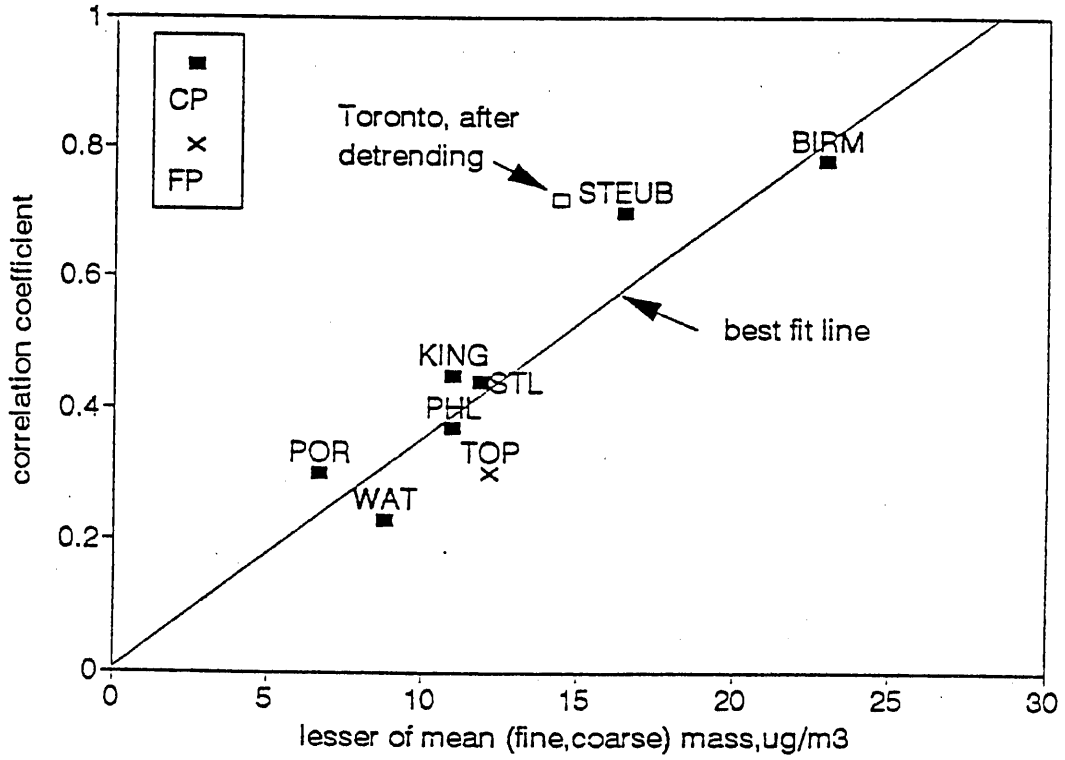
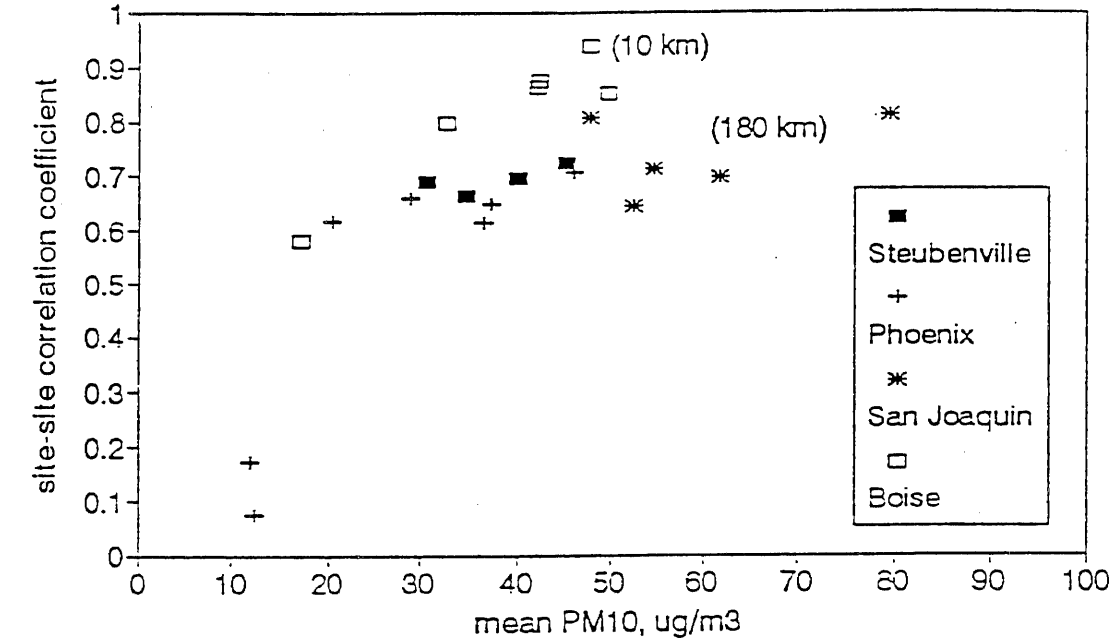


Figure 1. Correlations between fine and coarse fractions of PM_{10} vs. the lesser of the two mean masses, from various sources. Labels identify cities. Seasonal trends were removed from the data from Toronto (only) were removed before calculating the correlation.



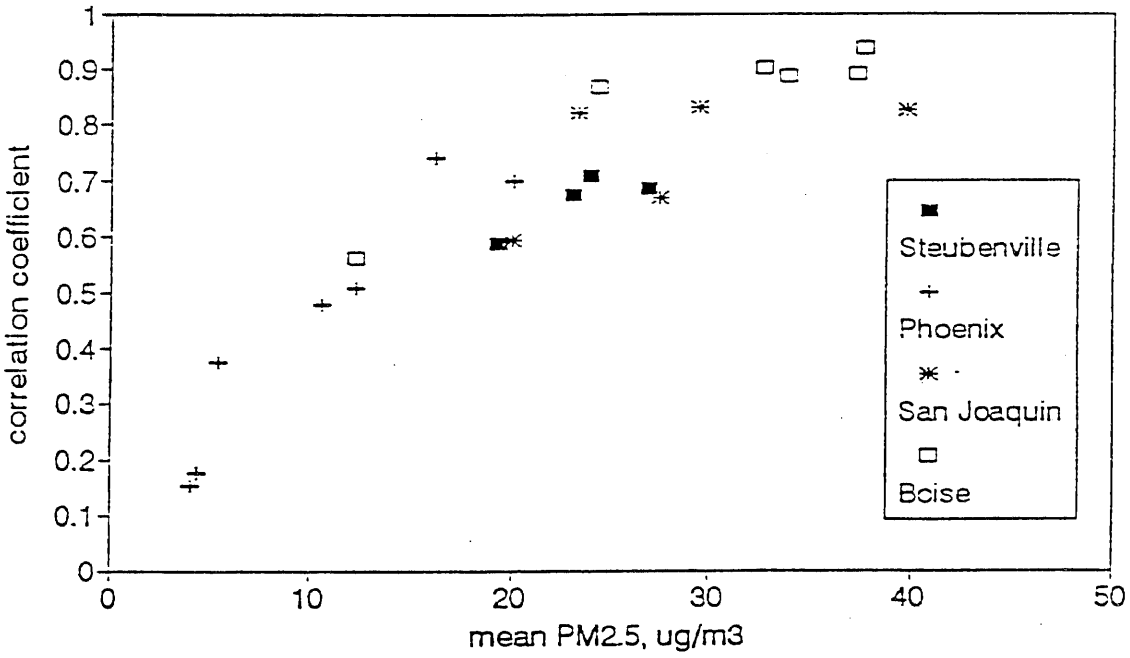


Figure 2. Plots of correlations between samplers from four geographic areas, as reported by Watson *et al.*[8] (a) PM_{10}; distance notations refer to the maximum separation among samplers in a given area. (b) $PM_{2.5}$.

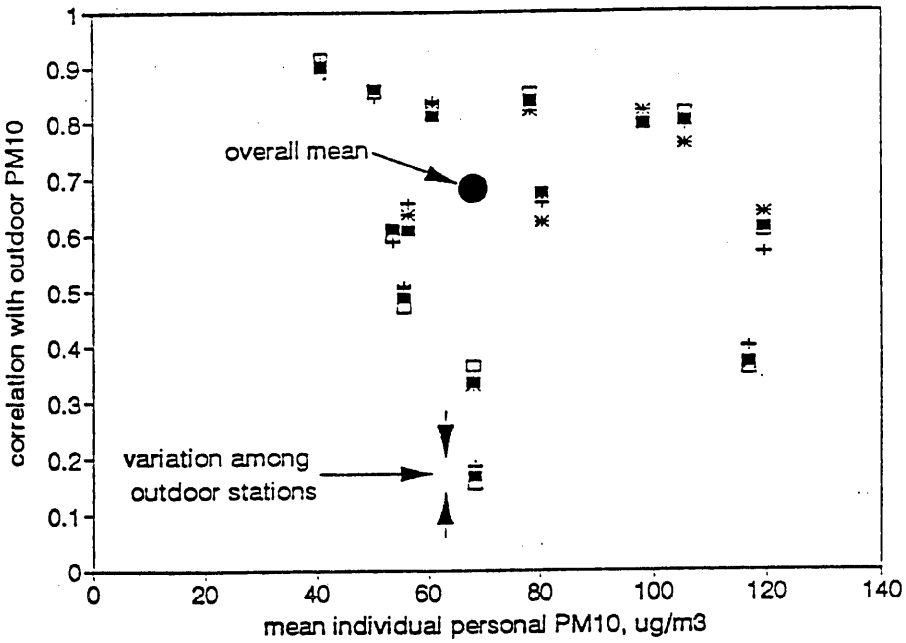


Figure 3. Distribution of individual correlations (n=14) between personal and ambient PM_{10} exposures in Phillipsburg, NJ.[9]

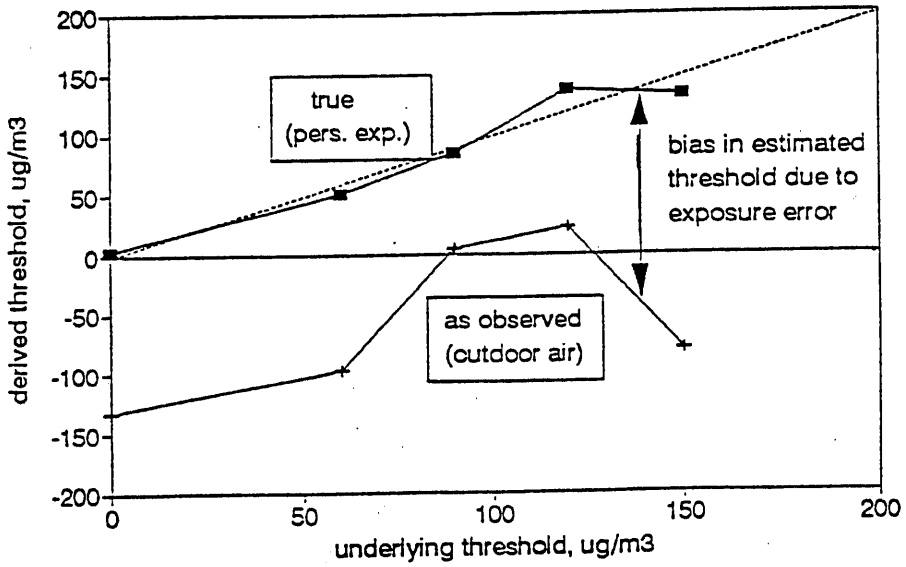


Figure 4. Thresholds derived from simulated personal exposure data based on the experimental data of Lioy *et al.*[9]

PM_1, $PM_{2.5}$, and PM_{10} Aerosol Chemistry vs. Meteorology for Phoenix, Arizona

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