Epidemiology Investigations of the Health Effects of Particulate Air Pollution: Strengths and Limitations

C. Arden Pope, III
Brigham Young University
Provo, Utah 84602

Draft Copy

May 24, 1996

This paper was presented at the
2nd Colloquium on Particulate Air Pollution and Health Program Park City, Utah,
May 1-3, 1996

Abstract

Many epidemiological studies have investigated health effects of particulate air pollution. This paper provides a simple framework to catagorize the basic study designs of most of the currently available studies of the health effects of particulate air pollution and briefly discusses the common methods of statistical analysis. Within this framework it outlines basic strengths and limitations associated with currently available epidemiological evidence. Both strengths and limitations of the epidemiological studies stem largely from the use of people who are living in uncontrolled environments, and who are exposed to complex mixtures of particulate air pollution. Inherent to these studies are at least four basic limitations including: 1) limited information about biological mechanisms, 2) relatively meager information regarding linkages between ambient and personal exposures, 3) difficulty of disentangling independent effects or potential interactions between highly correlated risk factors, and 4) inability to fully explore the relative health impacts of various constituents of particulate pollution. Associations of cardiopulmonary health outcomes with particulate air pollution that have been observed in the epidemiological studies provide only one important part of the full picture. A more complete understanding of the health effects of particulate air pollution will require important contributions from toxicology, exposure assessment, and other disciplines. Nevertheless, the pattern of cardiopulmonary health effects associated with particulate air pollution that has been observed by the epidemiological studies is currently the strongest evidence of the potential health effects of this pollution.
Key Words: Public Health, Air Pollution, Particulate Pollution, Epidemiology

Introduction

Many epidemiological studies have investigated the health effects of particulate air pollution. There have been several recent reviews of these studies.[1-7] Although these studies have often been well-conceived and conducted, the overall course of investigative efforts has been somewhat haphazard without overall design or strategy. Various researchers with differing training, interests, and research skills have conducted a wide variety of studies. These studies have often been highly opportunistic, taking advantage pollution events, natural experiments, and available health, pollution, and weather data.

In an attempt to evaluate the strengths and limitations of the available epidemiological evidence, it is useful to characterize and classify the currently available studies. Unique data limitations coupled with recent advances in bio-statistical and econometric analytic techniques seem to have rendered traditional categorization inadequate to represent recent epidemiological studies on the health effects of air pollution. This paper will briefly provide a framework to catagorize the basic study designs of most of the currently available studies of the health effects of particulate air pollution. It will briefly discuss the methods of statistical analysis that have been used. It will then try to outline the strengths and limitations associated with the currently available epidemiological evidence.

Basic Study Designs

Currently available studies typically fall within two broad classifications: 1) acute exposure studies, and 2) chronic exposure studies (See Figure 1). The acute exposure studies use short-term temporal changes in pollution as its source of exposure variability. These studies evaluate short-term changes in health endpoints associated with short-term changes in pollution. These studies may be as simple as observing changes in health over a pollution episode that lasts for 1 or more days, or they may be highly formal daily time-series studies. Because these studies typically

evaluate only short-term temporal relationships (usually 1-5 days), the observed pollution effects are typically interpreted as the health effects of acute exposure.

Available chronic exposure studies primarily use spatial differences in pollution as their source of exposure variability. Chronic exposure studies, therefore, compare various health outcomes across communities or neighborhoods with different levels of pollution. These studies are principally cross-sectional in design and use longer-term pollution data (usually 1 year or more). These studies are often interpreted as evaluating the chronic and/or cumulative effects of exposure.

Nearly all of the currently published acute and chronic exposure studies can also be subdivided as population-based studies or cohort-based studies. The population-based studies are often referred to as ecological studies where the units of comparison are entire populations of communities or neighborhoods. The cohort-based studies include studies descriptively referred to as panel studies or sample-based studies. Although, central-site community-based monitoring is typically used to estimate pollution exposure in the cohort-based studies, the units of comparison for health outcomes and co-risk factors are individuals enrolled in a well-defined cohort, panel, or sample.

These studies can be further subdivided by the specific health outcomes evaluated. Bates[7] has suggested that an appraisal of the strength of the overall epidemiological evidence of health effects of air pollution requires an evaluation of coherency. He has pointed out that the adverse health effects of pollution should be observable across a range of related health outcomes. Cardiopulmonary health outcomes that have been evaluated include mortality, hospitalizations or health care visits for respiratory and/or cardiovascular disease, respiratory symptoms, measures of lung function, and restricted activity due to illness.

Table I presents a tabulation of selected published studies on the health effects of particulate air pollution separated by basic study design and health outcomes. For the health outcomes such as mortality and hospitalization, nearly all of the acute and chronic exposure studies are population-based. This is because these outcomes reflect relatively rare events. In order to make any statistical inferences, a cohort-based acute exposure mortality study would require a significant number of deaths per day for a substantial period of time. Such a study would require a cohort as large as the population of some entire communities that have been studied.

Cohort-based chronic exposure studies provide some of the most compelling evidence of the health effects of air pollution but they involve collecting large amounts of information on a large number of people and following them for long periods of time. Because they are very costly and time-consuming only a few have been conducted. The two large cohort-based chronic exposure mortality studies that have been completed, followed well-defined cohorts of individuals living in different communities over time. Although daily changes in mortality and pollution were not and could not be evaluated, individual survival times were associated with average long-term exposure. These cohort studies differed fundamentally from the population-based (purely ecologic) cross-sectional studies in using a prospective cohort design that allowed for direct control for individual differences in other risk factors including age, sex, race, exposure to cigarette smoke, occupational exposure, education, body mass index, and alcohol use.

Studies of lung function or respiratory symptoms require cohort-based study designs. When these are time-series studies, they are often referred to as panel studies; when they are cross-sectional studies, they are typically sample-based studies. Monitoring or measuring health

outcomes such as common symptoms or lung function for a large population would be prohibitive, so only cohort-based have been conducted.

A summary of the estimated health effects associated with particulate air pollution is presented in Table II. When the epidemiological evidence is presented together as in Table II, a fairly consistent and coherent pattern emerges that suggests adverse cardiopulmonary health effects associated with particulate air pollution. Table II helps illustrate that, due to data, study design, and other limitations, not all of the pieces of the puzzle regarding the health effects of particulate air pollution can be put into place. In fact this is only a small part of the puzzle, because it does not include many other potential avenues of investigation including toxicological approaches. Nevertheless, the epidemiological portion of the puzzle is filled in enough to provide evidence of a relationship between particulate air pollution and cardiopulmonary disease.

Methods of statistical modeling

Statistical approaches to analyzing epidemiological data can be extremely useful, but no amount of statistical sophistication can compensate for sloppy study design or poor data collection. Some of the most compelling evidence of health effects of particulate air pollution requires only very simple statistical analysis--such as early studies that compared cardiopulmonary mortality before, during and after major pollution episodes. Most recent studies have employed some basic straightforward comparative statistical approaches to presenting the data; they have also begun to employ increasingly advanced biostatistical and econometric modeling techniques to analyze the data.

The most commonly used set of statistical modeling techniques that have been used is multivariate regression modeling. There are at least two primary reasons that multivariate regression models are so useful to analyze epidemiological data on the health effects of air pollution: 1) they allow for the estimation of the health-particulate associations while controlling for at least some other risk factors, and 2) they can, when used appropriately, add additional rigor to the analysis by providing a way to conduct formal hypothesis testing and more formally make statistical inferences.

A detailed discussion of these analytic techniques is beyond the scope of this paper. Pope and Schwartz give a more detailed discussion of these analytic methods for time-series data.[66] In general, however, the specific type of regression model to be used is dependent on the objectives of the study, the questions being asked, the study design, and the type of data that has been generated. A basic understanding of the process that generates different types of data to be analyzed is also essential. The four most common types of health data generated in the epidemiological studies include continuous, binary, count, and survival data, and they have typically been modeled using Gaussian, Logistic, Poisson, and proportional hazard regression models, respectively. Table III presents the type of data generated and typical statistical modeling methods commonly used for the different basic study designs.

The regression models that have typically been used are part of a family of models often referred to as Generalized Liner Models (GLM).[67] In these models the right hand side of the regression equation is a linear function of some set of covariates. This imposed linearity has been criticized, but it is not as restrictive as it may first appear. For example, binary indicator variables can be used as covariates. A series of indicator or dummy variables for different ranges of values for a certain variable allows for a non-linear "stair-step" relationship to be estimated. Also, various non-linear functional transformations of the covariates can be performed and used to allow for nonlinearity. An alternative to general linear models that has been used recently is the

generalized additive model (GAM).[68] The models can be estimated as nonlinear additive regression models where some or all of the terms on the right hand side of the regression equation are estimated as nonparametric functions (or smooths).

The uses of these statistical modeling techniques have been viewed suspiciously by some. Certainly they can be and have been misused. Some of the most common mistakes associated with multiple regression are: 1) Selecting an inadequate statistical model or estimation technic that results in biased effect estimates or standard errors; 2) imposing linearity when the relationship is not approximately linear; 3) inappropriate or inadequate evaluation of lag structure in time-series models; 4) Searching (or fishing) across models for preferred outcomes or for statistically significant correlations; 5) Over- or under-controlling for other factors; 6) Over-stratifying the data; 7) Over- or under-filtering or smoothing the data; 8) making premature judgements about causality based on associations observed in a regression model or conversely suggesting that the association is "only statistical," implying that they are not meaningful.

Primary Strengths and Limitations of the Epidemiology

An understanding of the basic study designs and analytic approaches used in the available epidemiological studies, helps elucidate their overall strengths and limitations. The fundamental strength of the currently available epidemiological evidence is its ability to evaluate health outcomes with real people, who are living in uncontrolled environments, and who are exposed to typical pollution. There are now many studies of assorted study designs, conducted by various researchers, in numerous study areas. Several recent reviews have concluded that the findings from many differing study designs, data sets, and analytic techniques make it unlikely that the overall PM effects observed could be due to systematic methodologic or analytic bias.[1-7] The reasonably consistent and coherent pattern of cardiopulmonary health effects associated with particulate air pollution that has been observed by the epidemiological studies currently is the strongest evidence of the potential health effects of this pollution.

Inherent in the use of observational studies on real people, living in uncontrolled environments, exposed to complex particulate air pollution are at least four basic limitations. The first deals with limited information about the biological mechanisms involved. The results of epidemiologic studies of the health effects of particulate air pollution seem to provide a pattern that points toward biological significance. Biological plausibility is enhanced by the observation of a coherent cascade of cardiopulmonary health effects and by the fact that non-cardiopulmonary health endpoints are not typically associated with particulate pollution. However, the epidemiological evidence is clearly limited on this subject. For example, both the acute and chronic exposure studies observed significant health affects but the linkages between the acute and chronic effects in terms of biological mechanisms remain unclear.

A second basic limitation relates to the relatively meager information regarding linkages between ambient and personal exposures. The epidemiological studies are unable to deal well with personal exposures. Accurate measures of personal exposure to air pollutants and other risk factors would be ideal for many research purposes. For population-based -studies or for studies of large cohorts, personal exposure monitoring is impractical. Exposures to air pollution are, therefore, typically estimated using ambient air pollution data. Such an approach is not without merit because public policy and pollution abatement strategies typically (and often necessarily) focus on ambient concentrations of air pollutants. Nonetheless, if the goal is to measure the health effects directly associated with personal exposures, currently available epidemiological studies do not deliver.

A third basic limitation of the epidemiological studies involves the difficulty of disentangling independent effects or potential interactions between highly correlated risk factors. The difficulty of disentangling independent effects or interactions exists largely because alternative risk factors may be correlated with air pollution resulting in potential confounding. Confounding may result when another risk factor that is correlated with both exposure and disease is not adequately controlled for in the analysis, resulting in spurious correlations. Although any single epidemiology study is highly limited in its ability to deal with all potential confounders, the broader body of epidemiological evidence provides some important information.

Cigarette smoking, for example, contributes to baseline or underlying respiratory disease rates in a population, but it is not likely serving as a common confounder across the epidemiologic studies of PM air pollution. Cigarette smoking would not be a confounder in the acute exposure studies for several reasons: 1) Most of the lung function, respiratory symptoms, and school absences studies were conducted among nonsmoking children. 2) The largest association between respiratory hospitalizations and pollution was often with nonsmoking children. 3) Cigarette smoking does not change day-to-day, week-to-week, or month-to-month in positive correlation with air pollution. Furthermore, in recent cohort-based chronic exposure studies, the estimated pollution effects were observed after analytically controlling for cigarette smoking or restricting the analysis to never smokers.

As with cigarette smoking, socioeconomic status in a population does not change day-to-day in correlation with air pollution. Therefore, socioeconomic variables are not likely confounders in the short-term time-series studies looking at lung function, respiratory symptoms, school absences, outpatient visits, and mortality. Furthermore, recent cohort-based chronic exposure studies have controlled for various socioeconomic variables including sex, race and education levels.

In the acute exposure studies, confounding due to temporal correlations between pollution, weather, and seasonal variables is a concern. However, independent pollution effects are typically observed even after using various approaches to control for weather variables in the regression model, and the estimated pollution effects are reasonably consistent for areas with very different climates and weather conditions. Furthermore, daily, seasonal, or annual changes in weather are not potential confounders in the chronic exposure mortality and morbidity studies.

The potential for confounding by co-pollutants that are correlated with particulate pollution remains one of the most important limitations of the current epidemiology. Two basic approaches to evaluating the potential of confounding by co-pollutants have been used. One approach is to try to analytically control for co-pollutants by including them in regression models and using statistical criteria such as significance levels or coefficient size and stability to evaluate the impact. Unfortunately, there are often strong correlations between the various pollutants making analytic control techniques replete with statistical problems. Attempts to separate effects of a single pollutant are rarely conclusive for any single data set. Fortunately, across various study areas, there is substantial variability in the levels of co-pollutants and the degree of co-linearity of these co-pollutants with PM. Therefore, a second and more compelling approach to evaluate for confounding by co-pollutants is to compare the estimated PM effects in areas with different potential for confounding by the co-pollutants. If the estimated PM effects are due to confounding by co-pollutants, then estimated PM effects would be larger in areas with higher potential for positive confounding by co-pollutants. Analyses of this type have been conducted that provide little or no evidence of confounding by O_3, or SO_2.[69] The potential for confounding by other measured or unmeasured pollutants remains unclear.

A fourth basic limitation of the epidemiological studies is the inability to fully explore the relative health impacts of various constituents of particulate pollution. Various measures or estimates of PM mass may be serving only as proxy variables for a primary toxic component or characteristic of PM, such as combustion-source particles, sulfates, ultra fine particles, or particulate acidity. Various physiologic and toxicologic considerations suggest that combustion-source particulate pollution may be a larger health concern than naturally occurring particles.[70] Their size is such that they can be breathed most deeply in the lungs and they include sulfates, nitrates, acids, transitional metals, and carbon particles with various chemicals adsorbed onto their surfaces. Also, relative to coarse particles, indoor and personal exposure to combustion-source fine particles are much better represented by central site ambient monitors. Long-term transport and large-scale mixing of combustion products result in concentrations of combustion related particles that are relatively uniform within communities.[71] Penetration of fine combustion-source particles also results in measured indoor and personal exposures to sulfate and fine particles being strongly correlated with and similar to measured outdoor concentrations.[72-74]

Much of the epidemiological evidence is also consistent with the expectation that combustion-source air pollution may be a larger health risk than naturally occurring particles. Evaluations of the acute and chronic exposure studies suggest that respiratory morbidity and cardiopulmonary mortality are most consistently associated with proxy measures of combustion-source particulate air pollution such as fine particles or often sulfate particles.[69] Other pollution measures are more commonly associated with cardiopulmonary health endpoints when they are also highly correlated with fine particles.

While the epidemiology suggests that combustion-source particulate pollution has a larger impact on cardiopulmonary health than comparable exposure to non-combustion related particles, it has substantial limitations with regards to characteristics or constituents of particulate pollution that are most likely responsible for the observed health effects. These limitations are largely due to PM measures being based mostly on mass, size cuts, sulfate concentrations, or acidity. Real-world urban particulate pollution is a complex mixture. The currently available epidemiological data cannot reveal if the relative importance of combustion-source particles is due to the relative small size of these particles, their chemical composition, or both.

Conclusion

Both the strengths and limitations of the epidemiological studies stem largely from the use of people who are living in uncontrolled environments, and who are exposed to complex mixtures of particulate air pollution. Inherent to these studies are at least four basic limitations including: 1) limited information about biological mechanisms, 2) relatively meager information regarding linkages between ambient and personal exposures, 3) difficulty of disentangling independent effects or potential interactions between highly correlated risk factors, and 4) inability to fully explore the relatively health impacts of various constituents of particulate pollution. The pattern of cardiopulmonary health outcomes associated with particulate air pollution that has come from the epidemiological studies, therefore, is only one important part of the full picture. A more complete understanding of the health effects of particulate air pollution will require important contributions from toxicology, exposure assessment, and other disciplines. Nevertheless, the pattern of cardiopulmonary health effects associated with particulate air pollution that has been observed by the epidemiological studies is currently the strongest evidence of the potential health effects of this pollution.

REFERENCES

1. Lipfert, F.W.: Air Pollution and Community Health: A Critical Review and Data Sourcebook. Van Nostrand Reinhold, New York, NY (1994).
2. Ostro, B.: The Association of Air Pollution and Mortality: Examining the Case for Inference. Arch. Environ. Health 48:336-342 (1993).
3. Dockery, D.W.; Pope, C.A. III: Acute Respiratory Effects of Particulate Air Pollution. Annu. Rev. Public Health. 15:107-132 (1994).
4. Pope, C.A. III; Dockery, D.W.; Schwartz, J.: Review of Epidemiological Evidence of Health Effects of Particulate Air Pollution. Inhalation Toxicology 7:1-18 (1995).
5. Pope, C.A. III; Bates, D.V.; Raizenne, M.E.: Health Effects of Particulate Air Pollution: Time for Reassessment? Environ. Health Persp. 103:472-480 (1995).
6. Schwartz, J.: Air Pollution and Daily Mortality: A Review and Meta Analysis. Environ. Res. 64:36-52 (1994).
7. Bates, D.V.: Health Indices of the Adverse Effects of Air Pollution: The Question of Coherence. Environ. Res. 59:336-349 (1992).
8. Logan, W.P.D.: Mortality in London Fog Incident. Lancet 1:336-338 (1953).
9. Ostro, B.D.: A Search for a Threshold in the Relationship of Air Pollution to Mortality: A Reanalysis of Data on London Winters. Environ Health Perspect 58:397-399 (1984).
10. Fairley, D.: The Relationship of Daily Mortality to Suspended Particulates in Santa Clara County, 1980-1986. Environ. Health Perspect. 89:159-168 (1990).
11. Schwartz, J.; Dockery, D.W.: Increased Mortality in Philadelphia Associated with Daily Air Pollution Concentrations. Am. Rev. Respir. Dis. 145:600-604 (1992).
12. Schwartz, J.; Dockery, D.W.: Particulate Air Pollution and Daily Mortality in Steubenville, Ohio. Am. J. Epidemiol. 135:12-19 (1992).
13. Pope, C.A. III; Schwartz, J.; Ransom, M.R.: Daily Mortality and PM_{10} Pollution in Utah Valley. Arch. Environ. Health 47:211-217 (1992).
14. Pope, C.A. III; Kalkstein, L.S.: Synoptic Weather Modeling and Estimates of the Exposure-Response Relationship Between Daily Mortality and Particulate Air Pollution. Environ. Health Perspect. 104:414-420 (1996).
15. Dockery, D.W.; Schwartz, J.; Spengler, J.D.: Air Pollution and Daily Mortality: Associations With Particulates and Acid Aerosols. Environ. Res. 59:362-373 (1992).
16. Schwartz, J.: Particulate Air Pollution and Daily Mortality in Detroit. Environ. Res. 56:204-213 (1991).
17. Schwartz, J.: Air Pollution and Daily Mortality in Birmingham, AL. Am. J. Epidemiol. 137:1136-1147 (1993).
18. Saldiva, P.H.N.; Pope, C.A. III; Schwartz, J.; et al.: Air Pollution and Mortality in Elderly People: A Time Series Study in Sao Paulo, Brazil. Arch. Environ. Health 50:159-163 (1995).
19. Kinney, P.L.; Ito, K.; Thurston, G.D.: A Sensitivity Analysis of Mortality/PM_{10} Associations in Los Angeles. Inhalation Toxicol. 7:59-69 (1995).
20. Ito, K.; Thurston G.D.: Daily PM10/Mortality Associations: An Investigation of At-Risk Subpopulations. J. Exposure Analysis and Environ. Epidem. 6:79-96 (1996).
21. Samet, J.M.; Speizer, F.E.; Bishop, Y.; et al.: The Relationship Between Air Pollution and Emergency Room Visits in an Industrial Community. J Air Pollut Control Assoc 31:236-240 (1981).

22. Bates, D.V.; Sitzo, R.: Air Pollution and Hospital Admissions in Southern Ontario: The Acid Summer Haze Effect. Environ Res 43:317-331 (1987).
23. Pope, C.A. III: Respiratory Disease Associated with Community Air Pollution and a Steel Mill, Utah Valley. Am. J. Pub. Health 79:623-628 (1989).
24. Pope, C.A. III: Respiratory Hospital Admissions Associated with PM_{10} Pollution in Utah, Salt Lake, and Cache Valleys. Arch. Environ. Health 46:90-97 (1991).
25. Thurston, G.D.; Ito, K.; Kinney, P.L.; Lippmann, M.: A Multi-Year Study of Air Pollution and Respiratory Hospital Admissions in Three New York State Metropolitan Areas: Results for 1988 and 1989 Summers. J. Expos. Anal. Environ. Epidem. 2:429-450 (1992).
26. Thurston, G.D.; Ito, K.; Hayes, C.G.; et al.: Respiratory Hospital Admissions and Summertime Haze Air Pollution in Toronto, Ontario: Consideration of the Role of Acid Aerosols. Environmental Research 65:271-290 (1994).
27. Schwartz, J.: PM_{10}, Ozone, and Hospital Admissions for the Elderly in Minneapolis-St.Paul. Arch. Environ. Health 49:366-374 (1994).
28. Schwartz, J.: Air Pollution and Hospital Admissions for the Elderly in Detroit, Michigan. Am. J. Respir. Crit. Care Med. 150:648-655 (1994).
29. Schwartz, J.: Air Pollution and Hospital Admissions for the Elderly in Birmingham, Al. Am. J. Epidem. 139:589-598 (1994).
30. Burnett, R.T.; Dales, R.E.; Raizenne, M.E., et al.: Effects of Low Ambient Levels of Ozone and Sulfates on the Frequency of Respiratory Admissions to Ontario Hospitals. Environ. Res. 65:172-194 (1994).
31. Burnett, R.T.; Dales, R.E.; Krewski, D.; et al.: Associations Between Ambient Particulate Sulfate and Admissions to Ontario Hospitals for Cardiac and Respiratory Diseases. Am. J. Epidemiol. 1995 (in press).
32. Ransom, M.R.; Pope, C.A. III: Elementary School Absences and PM_{10} Pollution in Utah Valley. Environ. Res. 58:204-219 (1992).
33. Dockery, D.W.; Ware, J.H.; Ferris, B.G. Jr.; et al.: Change in Pulmonary Function in Children Associated with Air Pollution Episodes. J. Air. Pollut. Control. Assoc. 32:937-942 (1982).
34. Pope, C.A. III; Dockery, D.W.; Spengler, J.D.; Raizenne, M.E.: Respiratory Health and PM_{10} Pollution: A Daily Time Series Analysis. Am. Rev. Respir. Dis. 144:668-674 (1991).
35. Pope, C.A. III; Dockery, D.W.: Acute Health Effects of PM_{10} Pollution on Symptomatic and Asymptomatic Children. Am. Rev. Respir. Dis. 145:1123-1128 (1992).
36. Hoek, G.; Brunekreef, B.: Acute Effects of a Winter Air Pollution Episode on Pulmonary Function and Respiratory Symptoms of Children. Arch. Environ. Health 48:328-335 (1993).
37. Koenig, J.Q.; Larson, T.V.; Hanley, Q.S.; et al.: Pulmonary Function Changes in Children Associated With Fine Particulate Matter. Environ Res 63:26-38 (1993).
38. Whittemore, A.S.; Korn, E.L.: Asthma and Air Pollution in the Los Angeles Area. Am. J. Pub. Health 70:687-696 (1980).
39. Braun-Fahrlander, C.; Ackermann-Liebrich, U.; Schwartz, J.; et al.: Air Pollution and Respiratory Symptoms in Preschool Children. Am. Rev. Respir. Dis. 145:42-47 (1992).
40. Ostro, B.D.; Lipsett, M.J.; Wiener, M.B.; Selner, J.C.: Asthmatic Response to Airborne Acid Aerosols. Am. J. Pub. Health 81:694-702 (1991).

41. Schwartz, J.; Spix, C.; Wichmann, H.E.; Malin, E.: Air Pollution and Acute Respiratory Illness in Five German Communities. Environ Res 56:1-14 (1991).
42. Schwartz, J.; Dockery, D.W.; Neas, L.M.; et al.: Acute Effects of Summer Air Pollution on Respiratory Symptom Reporting in Children. Am. J. Respir. Crit. Care. Med. 150:1234-1242 (1994).
43. Ostro, B.D.: The Effects of Air Pollution on Work Loss and Morbidity. J. Environ. Econ. Manage. 10:371-382 (1983).
44. Ostro, B.D.: Air Pollution and Morbidity Revisited: A Specification Test. J. Environ. Econ. Manage. 14:87-98 (1987).
45. Ostro, B.D.: Associations Between Morbidity and Alternative Measures of Particulate Matter. Risk Analysis 10:421-427 (1990).
46. Ostro, B.D.; Rothschild, S.: Air Pollution and Acute Respiratory Morbidity: An Observational Study of Multiple Pollutants. Environ Res 50:238-247 (1989).
47. Martin, A.E.: Mortality and Morbidity Statistics and Air Pollution. Proc. Roy. Soc. Med. 57:969-975 (1964).
48. Lave, L.B.; Seskin, E.P.: Air Pollution and Human Health. Science 169:723-733 (1970).
49. Chappie, M.; Lave, L.: The Health Effects of Air Pollution: A Reanalysis. J. Urban Econ. 12:346-376 (1982).
50. Lipfert, F.W.: Air Pollution and Mortality: Specification Searches Using SMSA-Based Data. J. Environ. Econ. Manage. 11:208-243 (1984).
51. Evans, J.S.; Tosteson,T.; Kinney, P.L.: Cross-Sectional Mortality Studies and Air Pollution Risk Assessment. Environ. Int. 10:55-83 (1984).
52. Ozkaynak, H.; Thurston, G.D.: Associations Between 1980 U.S. Mortality Rates and Alternative Measures of Airborne Particle Concentration. Risk Analysis 7:49-61 (1987).
53. Lipfert, F.W.; Malone, R.G.; Daum, M.L.; et al.: A Statistical Study of the Macroepidemiology of Air Pollution and Total Mortality; A report prepared for the Office of Environmental Analysis United States Department of Energy, 1988.
54. Archer, V.E.: Air Pollution and Fatal Lung Disease in Three Utah Counties. Arch Environ Health 45:325-334 (1990).
55. Bobak, B.; Leon, D.A.: Air Pollution and Infant Mortality in the Czech Republic, 1986-1988. Lancet 340:1010-1014 (1992).
56. Dockery, D.W.; Pope, C.A. III; Xu, X.: et al.: Mortality Risks of Air Pollution: A Prospective Cohort Study. N. Engl. J. Med. 329:1753-1759 (1993).
57. Pope, C.A. III; Thun, M.J.; Namboodiri, M.M.; et al.: Particulate Air Pollution as a Predictor of Mortality in a Prospective Study of U.S. Adults. Am. J. Respir. Dis. Critical Care Med. 151:669-674 (1995).
58. Holland, W.W.; Reid, D.D.: The Urban Factor in Chronic Bronchitis. Lancet 1:445-448 (1965).
59. Dockery, D.W.; Speizer, F.E.; Stram, D.O.; et al.: Effects of Inhalable Particles on Respiratory Health of Children. Am. Rev. Respir. Dis. 139:587-594 (1989).
60. Schwartz, J.: Lung Function and Chronic Exposure to Air Pollution: A Cross-Sectional Analysis of NHANES II. Environ. Res. 50:309-321 (1989).
61. Chestnut, L.G.; Schwartz, J.; Savitz, D.A.; Burchfiel, C.M.: Pulmonary Function and Ambient Particulate Matter: Epidemiological Evidence from NHANES I. Arch. Environ. Health 46:135-144 (1991).

62. Euler, G.L.; Abbey, D.E.; Magie, A.R.; Hodgkin, J.E.: Chronic Obstructive Pulmonary Disease Symptom Effects of Long-Term Cumulative Exposure to Ambient Levels of Total Suspended Particulates and Sulfur Dioxide in California Seventh-Day Adventist Residents. Arch. Environ. Health 42:213-222 (1987).
63. Portney, P.R.; Mullahy, J.: Urban Air Quality and Chronic Respiratory Disease. Regional. Sci. Urban Econ. 20:407-418 (1990).
64. Vedal, S.; Manna, B.: Adverse Respiratory Health Effects of Ambient Inhalable Particle Exposure. Paper 91-171.3, Air & Waste Management Association, 1991.
65. Schwartz, J.: Particulate Air Pollution and Chronic Respiratory Disease. Environ. Res. 62:7-13 (1993).
66. Pope, C.A., III; Schwartz, J.: Time Series for the Analysis of Pulmonary Health. Am. J. Respir. Dis. Critical Care Med. 1996, in press.
67. McCullagh, P.; Nelder, J.A.: Generalized Linear Models. Chapman and Hall, London (1983).
68. Hastie, T.; Tibshirani, R.: Generalized Additive Models. Chapman and Hall, London (1990).
69. Pope, C.A., III.: Combustion-source particulate air pollution and human health: causal associations or confounding? In Particulate Matter: Health and Requlatory Issues. Air & Waste Management Association, Pittsburgh, PA, 1995.
70. Seaton, A.; MacNee, W.; Donaldson, K.; Godden, D.: Particulate Air Pollution and Acute Health Effects. Lancet 345:176-178 (1995).
71. Wilson, R.; Colome, S.D.; Spengler, J.D.; Wilson, D.G.: Health Effects of Fossil Fuel Burning. Ballinger, Cambridge, MA (1980).
72. Dockery, D.W.; Spengler, J.D.: Indoor-Outdoor Relationships of Respirable Sulfates and Particulates. Atmos. Environ. 15:335-343 (1981).
73. Suh, H.H.; Spengler, J.D.; Koutrakis, P.: Personal Exposures to Acid Aerosols and Ammonia. Environ. Sci. Tech. 26:2507-17 (1992).
74. Wallace, L.A.; Pellizzari, E.; Sheldon, L., et al.: The TEAM Study of Inhalable Particles (PM_{10}): Study Design, Sampler Performance, and Preliminary Results. Paper 91-171.3, 84th annual meeting of the Air & Waste Management Association, June 16-21, 1991.

Figure 1: Basic Study Designs of Currently Published Studies of Health Effects of Particulate Air Pollution

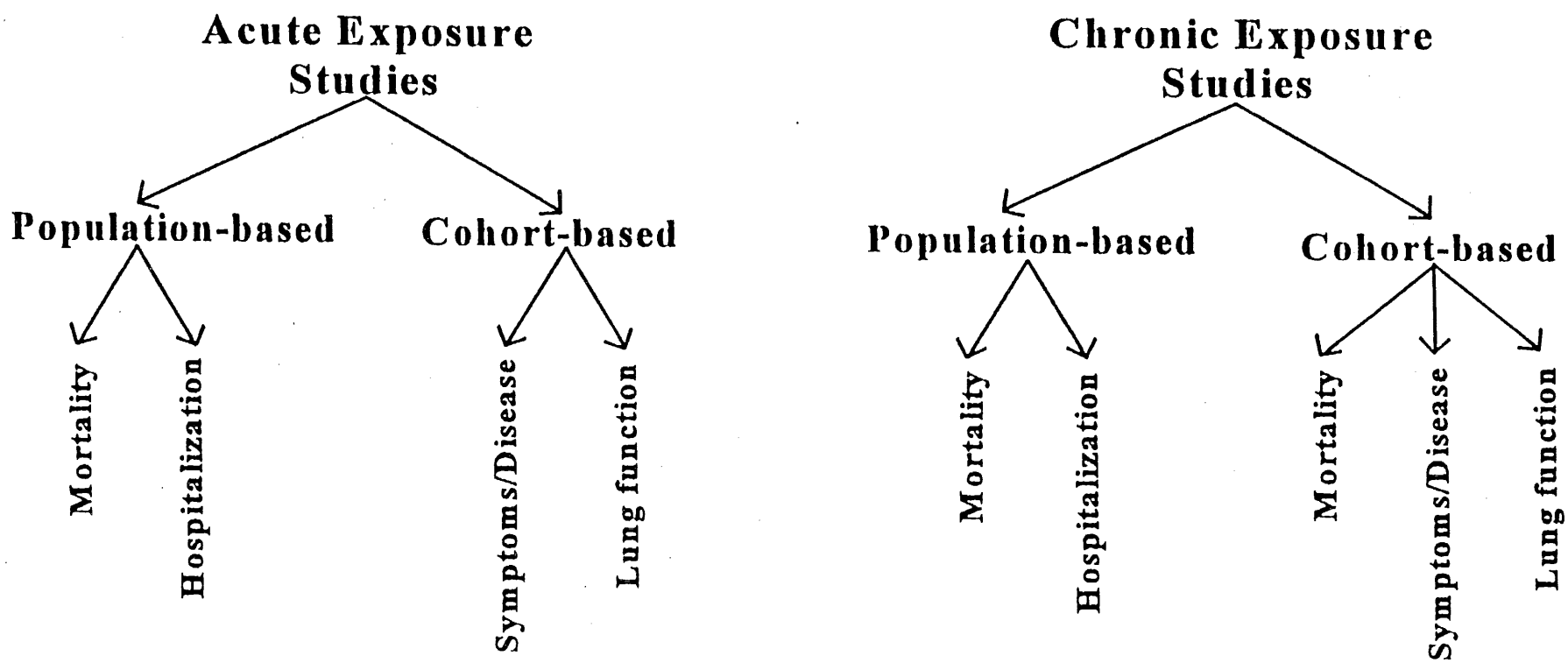


Table I. Authors and dates of selected studies for basic study designs of studies of health effects of particulate air pollution.

Health Endpoints	Acute Exposure		Chronic Exposure	
	Population-Based	Cohort-Based	Population-Based	Cohort- or Sample-Based
Mortality	Logan 1953[8] Ostro 1984[9] Fairley 1990[10] Schwartz & Dockery 1992[11-12] Pope et al 1992, 1996[13-14] Dockery et al 1992[15] Schwartz 1991, 1993[16-17] Saldiva et al 1995[18] Kinney et al 1995[19] Ito & Thurston 1996[20]	None	Martin 1964[47] Lave & Seskin 1970[48] Chappie & Lave 1982[49] Lipfert 1984[50] Evans et al 1984[51] Ozkaynak & Thurston 1987[52] Lipfert et al 1988[53] Archer 1990[54] Bobak & Leon 1992[55]	Dockery et al 1993[56] Pope et al 1995[57]
Hospitalizations, Health Care Visits	Samet et al 1981[21] Bates & Sitzo 1987[22] Pope 1989, 1991[23-24] Thurston et al 1992, 1994[25-26] Schwartz 1994[27-29] Burnett et al 1994, 1995[30-31]	None	A few weak studies. See review by Lipfert 1994[1]	None
Lung Function	None	Dockery et al 1982[33] Pope et al 1991[34] Pope & Dockery 1992[35] Hoek & Brunekreef 1993[36] Koenig et al 1993[37]	None	Holland & Reid 1965[58] Dockery et al 1989[59] Schwartz 1989[60] Chestnut et al 1991[61]
Symptoms, Disease	None	Whittemore & Korn 1980[38] Pope & Dockery 1992[35] Braun-Fahrlander et al 1992[39] Hoek & Brunekreef 1993, 1994[36] Ostro et al 1991[40] Schwartz et al 1991, 1994[41-42]	None	Euler et al 1987[62] Dockery et al 1989[59] Portney & Mullahy 1990[63] Vedal et al 1991[64] Schwartz 1993[65]
Restricted Activity	Ransom & Pope 1992[32]	Ostro 1983, 1987, 1990[43-45] Ostro & Rothschild 1989[46]	None	None

Table II. Approximate range of estimated effects measure as percent change in health endpoint per 10 μg/m³ increase in PM10 for the different basic study designs.

Health Endpoints	Acute Exposure		Chronic Exposure	
	Population-Based	Cohort-Based	Population-Based	Cohort- or Sample-Based
Mortality	Total: 0.5 - 1.5% Respiratory: 1.5 - 4.0% Cardiovascular: 0.5 - 2.0%		Total: 0 - 5%	Total: 3 - 6% Cardiopulmonary: 5 - 9% Lung cancer: 0 - 9%
Hospitalizations, Health Care Visits	Respiratory Hospital Admissions: 0.5 - 4.0% Respiratory emergency Visits: 0.5 - 3.5%			
Lung Function		Forced expired volume: 0.05 - 0.35% Peak expiratory flow: 0.04 - 0.25%		Decrease in lung function: 0 - 2%
Symptoms, Disease		Lower respiratory: 0 - 15% Upper respiratory: 0 - 7% Cough: 0 - 25% Asthmatic attacks: 1 - 12%		Emphysema, Chronic bronchitis or Chronic cough 10 - 25%
Restricted Activity	Grade school absences: 1.0 - 4.0 %	Restricted activity days: 1.0 - 5.0%		

Table III. Type of data generated and typical statistical modeling methods used for the different basic study designs.

Health Endpoints	Acute Exposure		Chronic Exposure	
	Population-Based	Cohort-Based	Population-Based	Cohort- or Sample-Based
Mortality	Data: Daily counts. Method: Daily time-series Poisson regression. For large counts, Gaussion regression is often used.		Data: Mortality rates treated as continuous. Method: Cross-sectional Gaussion regression.	Data: Survival Method: Survival analysis including Proportional Hazards regression
Hospitalizations, Health Care Visits	Data: Daily counts. Method: Daily time-series Poisson regression. For large counts, Gaussion regression is often used.			
Lung Function		Data: Continuous Methods: Gaussion regression		Data: Continuous Methods: Cross-sectional Gaussion Regression
Symptoms, Disease		Data: Binary Methods: Time-series Logistic Regression		Data: Binary Methods: Cross-sectional Logistic regression

TITLE The Effects of Building Ventilation Types and Human Activity Patterns on Indoor PM_{10} Levels.

AUTHORS James R. Ramsay Jr. and Dean R. Lillquist

ABSTRACT

Indoor and ambient PM_{10} levels at two Salt Lake hospitals were examined during the months of January through May 1995. In addition to the PM_{10} data, the level of human activity was estimated at each of the six indoor sampler sites at each hospital. At each hospital, indoor air supplied by two different air filtration environments were sampled. At hospital A, bag filtration (BF) and HEPA systems were sampled, and at hospital C, low efficiency (LE) and BF were sampled. The average ambient PM_{10} levels at each hospital were significantly different ($p < 0.05$). At both hospitals the average indoor PM_{10} for each air filtration system was compared to the ambient PM_{10} level. In all but one case the indoor PM_{10} was significantly less than the ambient PM_{10} (hospital A=18.7 $\mu g/m^3/24hr$ and hospital C=26 $\mu g/m^3/24hr$, $p < 0.05$). Within an air filtration system some samplers sites had significantly higher average PM_{10} than did others. The effectiveness of BF versus HEPA and LE versus BF were compared. In both cases the PM_{10} levels were significantly different ($p < 0.05$). The average PM_{10} levels at hospital A in the BF/HEPA comparison were 18 $\mu g/m^3/24hr$ and 11 $\mu g/m^3/24hr$ respectively. In the LE/BF comparison at hospital C the average PM_{10} levels were 18 $\mu g/m^3/24hr$ and 13 $\mu g/m^3/24hr$ respectively. In the LE/BF comparison the difference was driven by a very high PM_{10} level at one sampler site in the LE environment. This site had the highest human activity score of any site at hospital C. We were able to quantify the affect of moderate amounts of human activity and changing air filtration systems on indoor PM_{10} levels by assuming that the PM_{10} level in an unoccupied HEPA filtered patient room represents the minimum possible indoor PM_{10} level. The increase in PM_{10} attributable to a moderate amount of human activity in a HEPA environment was 1.15 $\mu g/m^3/24hr$. By controlling for the amount of human activity and comparing PM_{10} levels between HEPA and BF environments we estimated that a BF increases the infiltration of ambient PM_{10} by 6.5 $\mu g/m^3/24hr$. At Hospital A,this represents 35% of the average ambient PM_{10} level (18.7 $\mu g/m^3/24hr$).

Rocky Mountain Center for Occupational and Environmental Health, Building #512, University of Utah, Salt Lake City, UT 84112

INTRODUCTION

The majority of Americans spend most of their time inside either their homes, 68 - 70%, school/work, 17 - 20%, or in a vehicle ~ 6% (Robinson and Nelson, 1995). Less than 6% of their time is spent outdoors. Major exceptions to these values are outdoor workers (farmers, construction, lawncare, roofers. ...) and children. Outdoor workers are often outdoors for 50% of the day. It is not uncommon for children to be outdoors for more than 8% of a school day and greater than 18% of their time during summer vacation (Johnson et al., 1995). The EPA ambient air quality standards may adequately predict the PM_{10} exposure for these outdoor subpopulations but how well do ambient PM_{10} levels predict the exposure of the "average" American who is inside > 85% of the time?

For the gaseous pollutants ozone (O_3) and carbon monoxide (CO), and very fine particulate (≤ 1 μm), building envelopes are minor barriers and ambient levels can be similar to indoor levels (Nazaroff et al., 1990). In contrast, indoor PM_{10} pollutant levels are often poorly correlated with outdoor levels (Anuszewski et al., 1992). Indoor levels are strongly influenced by many factors. In approximate order of importance these include smoking, cooking, the amount of activity, type of heating ventilation and air conditioning (HVAC) system, and pets (Anuszewski et al., 1992; Clayton et al. 1993; Pellizzari et al., 1993a,b; Thomas et al., 1993). In addition, the physical location of a building in an air shed may place a building in a distinct ambient PM_{10} micro environment (Lillquist et al., 1996).

To control many of the factors that affect indoor PM_{10} levels a three hospital indoor/ambient PM_{10} study in Salt Lake County during the Winter of 1994-1995. Hospitals were selected to avoid many common indoor particulate pollution sources such as smoking, cooking, and pets. In addition, hospitals often have different types of air filtration systems in different patient care units. By using a subset of the three hospital data set (Lillquist et al., 1996), we were able to examine the effect of HVAC system and "clean" occupational activities on indoor PM_{10} levels while avoiding many of the recognized major sources of indoor particulate pollution.

MATERIALS and METHODS

AIR FILTRATION ENVIRONMENTS AND SYSTEMS SAMPLED

Samplers were located at two hospitals, A and C. The relative location of the two hospitals is shown in Figure 1. (Hospital B was not included in this study. At hospital B all of the indoor samplers were located in areas with the same type of air filtration.) At each hospital one sampler was located on the roof near an air intake. Six indoor samplers were located in various units of the hospital. At least two samplers were located in each unit. In addition, samplers were located in at least two units which had different types of air filtration. Table 1 shows the sampler locations and air filtration system for each sampler. In both hospitals, air in the intensive care unit (ICU) was filtered using bag filters (BF). Bag filters remove a minimum of 95% of the total suspended particulate. The other unit, the bone marrow transplant unit (BMTU) at Hospital A, treated the incoming air with a high effciency particulate air filter (HEPA). A HEPA filter removes 99.7% of all 0.3 μm particulate. The air pressures in the

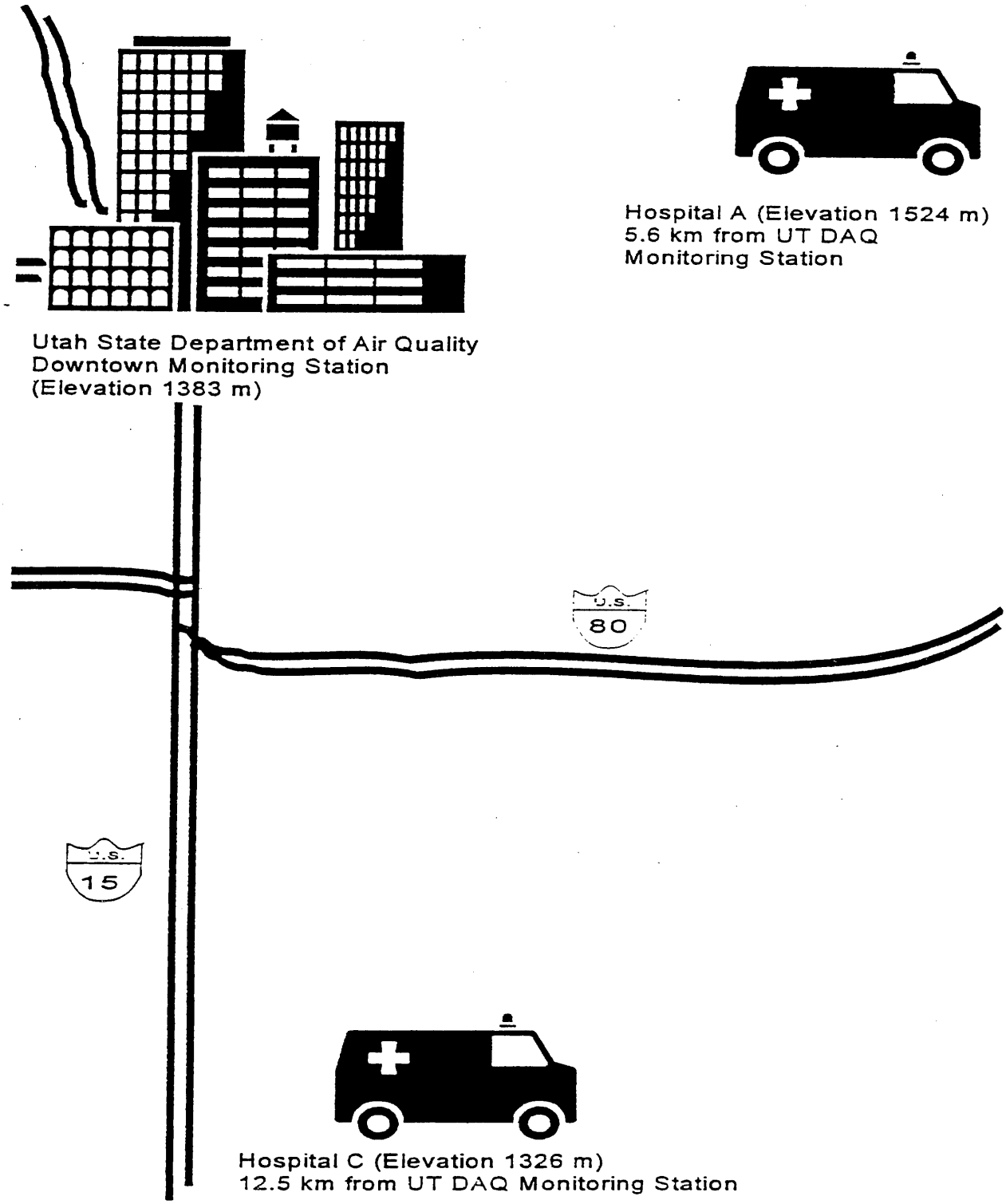


Figure 1. Locations of hospitals A and C relative to Utah Division of Air Quality downtown air monitoring station. The elevation of each hospital and UT DAQ are also shown.

BMTU were controlled. The patient rooms were positive relative to the BMTU nurses station which was positive relative the rest of the hospital. At hospital C the non-ICU units sampled, nursery and maternity, had air handler units equipped with low efficiency filters. The low effciency filters were a 2" thick fiberglass filter. These filters are similar in apperance to home forced air furnace filters. Information on the air filtration system for each sampler site was obtained from the HVAC engineer for each hospital.

DESCRIPTION OF SAMPLER SITES

The location and air filtration environment for each sampler site is shown in Table 1. At both hospitals the ambient roof sampler was located close to the HVAC air intake as far as possible from any exhaust vents. Detailed descriptions of each indoor sampler site are given below.

At Hospital A, the Nursery Room A was a busy neonatal unit. The infants in this room are often critically ill and staffing ratios were very high. The room was busy but kept very quite.

Table 1. Location and air filtration system at each sampler site.

Hospital A		Hospital C	
Sampler Site	**Air Filtration System**	**Sampler Site**	**Air Filtration System**
Roof (ambient)	None	Roof (ambient)	None
Nursery Room A	Bag Filter	Nursery, Well Baby	Low Efficiency
Nursery Room B	Bag Filter	Nursery, At Risk	Low Efficiency
Intensive Care Unit, Main Nurses Station	Bag Filter	Maternity, Ward Kitchen	Low Efficiency
Intensive Care Unit, Respiratory Therapy Island	Bag Filter	Maternity Patient Room	Low Efficiency
BMTU Nurses Station	HEPA	Coronary Care Unit, Nurses Station	Bag Filter
BMTU Patient Room	HEPA	Coronary Care Unit, Nurses Lounge	Bag Filter

The sampler was located on a window sill approximately 1 m from the head of an infant. Nursery Room B was normally about one-half to two-thirds full. The infants in this room were frequently larger and healthier than those in Room A. As a result the staffing ratios were a slightly lower. The sampler was located on a counter approximately 1 - 2 m from the head of the infant. Both nursery rooms were carpeted to reduce noise levels in the units. The ICU was a large and busy unit. One sampler was placed on the main nurses station desk located at the corner of the main entrance and a hall that ran the length of the unit. The nurses station was staffed 24 hrs a day. With the exception of a few isolation beds all of the beds were in a common air environment. The other ICU sampler was located at the respiratory care island in the center of the the south wing of the unit. Also located at this site was a computer used to monitor respiratory care, spare parts, and expendable parts for respirators. The sampler was located on a counter near a pillar. The BMTU was a 4 bed unit. Each bed is located in a separate positive pressure room. The nurses station was also maintained at positive pressure relative to the main hospital. Access to this unit was restricted to staff and relatives of patients. The nurses station sampler for this unit was located on the floor behind the nurses desks. The patient room sampler was normally located on a shelf above the head of the bed. Sampling never occurred in an room occupied by a patient

At Hospital C we placed samplers in two nursery rooms. These rooms were designated the "At Risk Infants Room" and the "Well Baby Room". These names had no relationship to the current uses of the rooms. Only once did we see an infant in the "well baby" nursery. Normally this room was used for storage and for parenting classes. The sampler in this room was kept on an interior window sill near where the lactation classes were done. All of the infants were kept in the "at risk" nursery. Since the seriously "at risk" infants are routinely transported to a hospital with more advanced neonatal care these infants were generally healthy. The census and staffing levels in this room were highly variable. The sampler was located on a shelf approximately 1.5 m above the floor. The maternity kitchen was not used for cooking, but for the storage of drugs, drinks, meals, and for microwave reheating of meals. The sampler was placed on top of the refrigerator. The maternity patient room was carpeted and occupied approximately 33 % of the time. The sampler was located on a small shelf approximately 2 m above the floor. For the last few weeks of the study this sampler was moved to a site in the hall while patient rooms were remodeled. The Coronary Care Unit (CCU) was "C" shaped, with seven to eight beds located along the outside perimeter of the "C". The unit was frequently full, or nearly full. A minimum of three to four staff were present at all times. The nurses station sampler was located on the desk at the end of the "C" furthest from the main entrance. The nurses lounge was a separate room at one end of the "C". The sampler was located on top of the refrigerator.

PM_{10} Sample Collection

PM_{10} samples were collected using Airmetrics Minivol v4.01 samplers. These samplers use an impactor to size fractionate the particulate. Each sampler was calibrated using a Gilabrator bubble calibrator. The flow was set at 5 L/min, the recommended flow for a 10 μm, 50% cut. Schliecher and Schuell Glass 30 filters were used to collect the particulate. These filters have a nominal 1 μm cut point for particle retention. All filters were pre- and post-

conditioned for at least 24 hrs at 25° C ± 5° and 30% ± 5% relative humidity prior to weighing. Filter weights were measured using a Cahn-ATI C-35 microbalance. Data for this study were collected from 6 January to 31 May 1995. These endpoints were selected to ensure that all of the data was collected using the same type and lot of filters. Preweight, postweight, cumulative hours run, starting/stopping times, and miscellaneous comments/observation were recorded for each sample. All of the data and notations were entered in a computer database.

Quality Control and Quality Assurance

Three major sources of concern were, that the air filtration systems were operating normally during the sampling periods, that the samplers were operating properly, and that variation due to weighing and filter handling procedures was minimized. In the first case we relied on hospital staff to inform us if there were any HVAC problems. If an HVAC or filtration system failure was reported to us that involved one of our sampler sites for any part of a sampling day, the PM_{10} data from the affected samplers were excluded from the analysis. Second, sampler performanced was checked daily, monthly and prior to analysis. Samplers were leak tested every time the filter was changed. Monthly sampler flow rates were checked with the Gilabrator. And, sampler run times less than 19 hrs or greater than 30 hrs were not used in the analysis. Third, since the pre- and post-weights were measured 48 hrs apart, variation in filter weights due to other than PM_{10} loading was a major concern. To control for these sources of variation a standard 100 mg weight was used to check the balance at the start of each weighing session. If the weight varied by more than 5 μg the balance was recalibrated, this was rarely required. Filters were always handled with stainless steel forceps. Negative weight samples (preweight > postweight) were dropped from the data set. Negative weights were usually the result of filters that were torn or cut when placed in the filter holder. In addition, three samplers were co-located outdoors at RMCOEH. These samplers were run concurrently for three weeks to check for variation in filter weights due to handling, preseparator variation and other sources of variation.

Human Activity Scoring

The level of human activity at each indoor sampler site was scored from 1 to 4. Each site was ranked based on the number of day shift staff present, an estimate of the swing and night shift staffing levels, an estimate of the average patient census, and the amount of traffic. The ambient roof top samplers were not scored for human activity since there was no daily activity at these sites (with the exception of our changing the filters and batteries on the samplers).

Analysis

For each sampler site the average PM_{10} concentration and the 95% confidence intervals were calculated. The non-independence of the daily PM_{10} levels is not a concern due to the significantly large variation among sites (Lillquist et al., 1996). For each hospital the average PM_{10} levels for each air filtration system were calculated by pooling the daily PM_{10} values from all of the samplers located in a common HVAC filtration system.

RESULTS

Quality Assurance

The average variation among daily weights for the 100 mg tare weight was approximately 1 µg. Average daily variation among the three co-located outdoors at RMCOEH was 7.7 µg. This was well within the acceptable range (~5 - 15 µg) observed by Airmetrics in their repeated field tests of the Minivol samplers.

PM_{10} Levels At Each Sampler Site

The number of days that reliable PM_{10} values were collected from each sampler site ranged from 88 to 103 at Hospital A and from 102 to 107 days at Hospital C (Table 2). The BMTU Patient Room sampler site at Hospital A had the fewest days of data. The excess lost days at this site are due to hospital staff removingthe sampler from the room whenever the room was occupied to avoid the chance of our infecting an immune suppressed patient.

The average PM_{10} concentration at each sampler site is shown in Table 3 and in Figure 2.

Table 2. The number of days that PM_{10} data were analyzed for each sampler site.

Hospital A (average 99 days)		Hospital C (average 105 days)	
Sampler Site	**Number of Days**	**Sampler Site**	**Number of Days**
Roof (ambient)	103	Roof (ambient)	105
Nursery Room A	101	Nursery, Well Baby	102
Nursery Room B	101	Nursery, At Risk	106
Intensive Care Unit Main, Nurses Station	101	Maternity, Ward Kitchen	105
Intensive Care Unit, Respiratory Therapy Island	100	Maternity, Patient Room	104
BMTU Nurses Station	100	Coronary Care Unit, Nurses Station	106
BMTU Patient Room	88	Coronary Care Unit, Nurses Lounge	107

Table 3: Average daily PM_{10} concentrations and 95% confidence intervals at each sampler site.

Hospital A			Hospital C		
Sampler Site	**Daily Average (μg/m³)**	**± 95% Confidence Interval**	**Sampler Site**	**Daily Average (μg/m³)**	**± 95% Confidence Interval**
Roof (ambient)	18.7	2.6	Roof (ambient)	26.0	3.1
Nursery Room A	17.2	0.9	Nursery, Well Baby	14.6	1.0
Nursery Room B	17.9	0.9	Nursery, At Risk	20.6	1.6
Intensive Care Unit Main Nurses Station	21.1	1.3	Maternity, Ward Kitchen	14.1	1.9
Intensive Care Unit Respiratory Therapy Island	16.1	1.1	Maternity Patient Room	14.4	1.0
BMTU Nurses Station	11.4	0.9	Coronary Care Unit-Nurses Station	13.6	1.0
BMTU Patient Room	9.7	1.0	Coronary Care Unit-Nurses Lounge	12.9	1.0

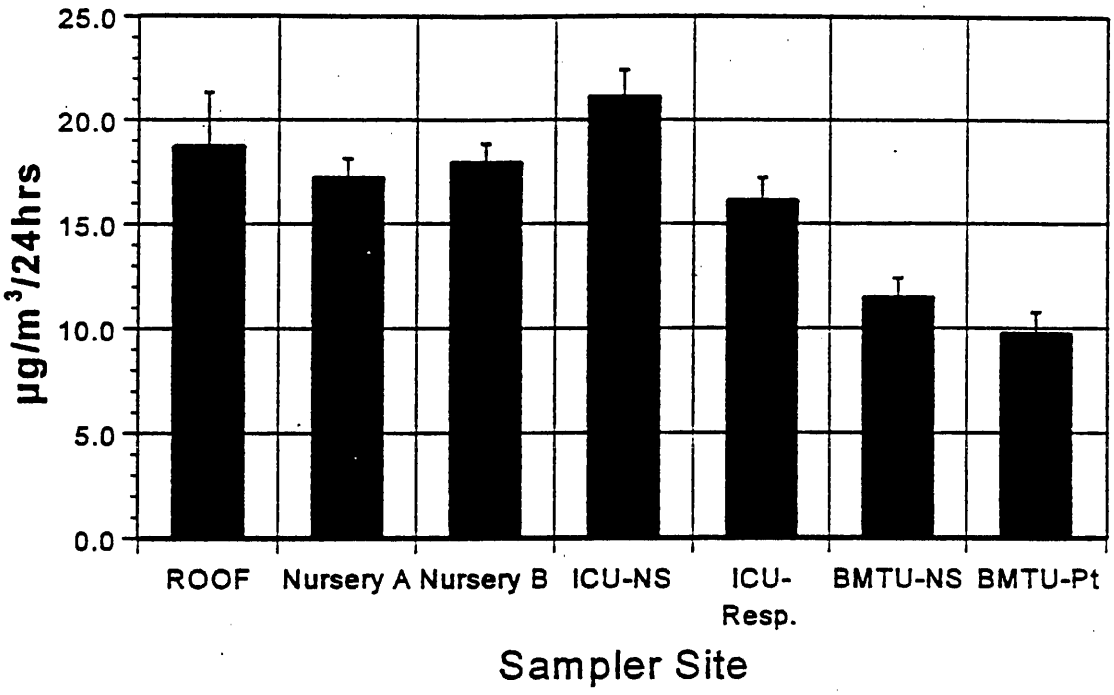
The average ambient concentration at Hospital A was 18.7 μg/m³/24hr. The average ambient concentration at Hospital C was 26.0 μg/m³/24hr. The average ambient PM_{10} levels were significantly different at each hospital ($p < 0.05$). Therefore the absolute PM_{10} values for similar

air filtration systems at the two hospital cannot be directly compared. The distribution of daily PM_{10} levels at each sampler site are slightly skewed. At both hospitals there were more days with low PM_{10} levels than with high PM_{10} levels.

Significant differences in the average daily PM_{10} levels among some sampler sites were observed at both hospitals, both within and between air filtration systems. Within a common air filtration environment two sampler sites were significantly different at $p < 0.05$. These were the ICU Main Nurses Station at Hospital A and the "At Risk Infants" Nursery at Hospital C. The ICU Main Nurses Station sampler site had significantly higher PM_{10} levels than any of the other bag filtration sites in the hospital. At Hospital C the Nursery "At Risk Infants" sampler site had a higher average PM_{10} level than any other low efficiency air filtration site. Finally, the BMTU Nurses Station and BMTU Patient Room average PM_{10} levels were significantly different, $p < 0.10$.

Analysis of the effect of air filtration system on indoor PM_{10} levels was done by pooling the daily PM_{10} levels for all of the sampler sites in a common air filtration environment and calculating the average PM_{10} value and the 95% confidence interval for each air filtration system. The results are shown in Figure 3. At both hospitals all of the air filtration systems reduced the indoor PM_{10} levels relative to ambient PM_{10}. However the Hospital A bag filtration system reduction in PM_{10} levels was not significantly different from ambient, $p < 0.05$. The HEPA filtration system at Hospital A removed significantly more ($p < 0.05$) PM_{10} than did the bag filtration system. This was true even if the ICU Main Nurses Station sampler data was not included in the bag filtration system data pool. At Hospital C the bag filtration system average PM_{10} levels were significantly less ($p < 0.05$) than the low efficiency air filtration system PM_{10} levels. However, this difference is not observed if the "At Risk" Nursery data is removed from the low efficiency air filtration data set.

The human activity scores ranged from a low of 1 at the BMTU Patient Room site to a high of 4 at the Hospital A ICU Main Nurses Station site. The "At Risk" Nursery at Hospital C was the most difficult sampler site to score. Due to the short post delivery maternity stays mandated by many managed care insurers the census in this unit varied greatly, even within any given 24 hour period. The assigned human activity score, 3, may under emphasize the extra activity before and after a high census day. The activity scores for each sampler site are shown in Table 4.



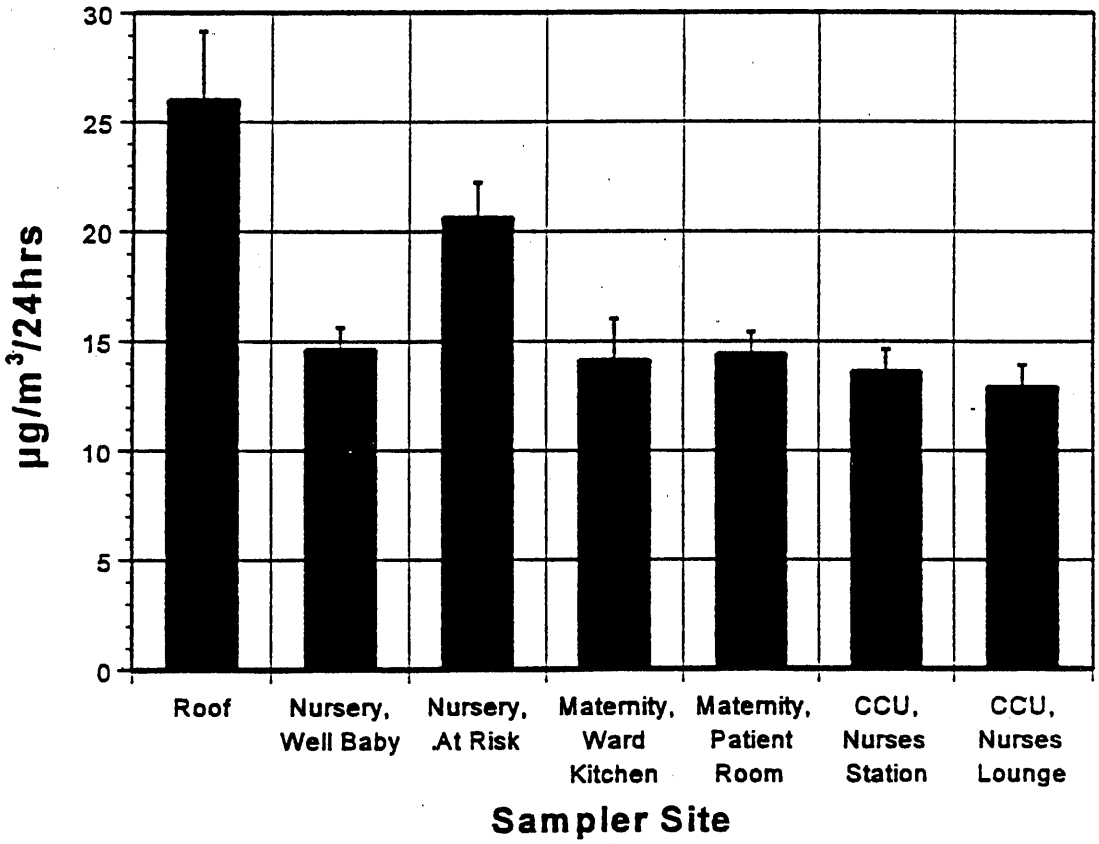


Figure 2. Average daily PM_{10} levels at each sampler site at both hospitals. Top graph isHospital A, bottom graph is Hospital C. Whisker bars are 95% confidence intervals.

DISCUSSION

The average indoor PM_{10} levels were less than the ambient PM_{10} levels at both hospitals included in this study, with one exception. The exception was the Hospital A ICU Main Nurses Station. There was more human activity at this site than at any other sampler site in this study. The correlation between high levels of human activity and high indoor PM_{10} levels was also observed at Hospital C. There the sampler site with both the highest human activity score and average PM_{10} level was the "At Risk" Nursery. The PM_{10} levels at both of these sampler sites, ICU Main Nurses Station and Nursery "At Risk Infants", were significantly higher ($p < 0.05$) than the PM_{10} levels at any of the other sampler site in the same air filtration system. The average PM_{10} at the Main Nurses Station was 5 $\mu g/m^3/24hr$ higher than at the ICU Respiratory Therapy Island sampler site. The ICU Respiratory Therapy Island sampler site recieved approximately 66% as much through-traffic as the Main Nurses Station site. The average PM_{10} level at the ICU Main Nurses Station (21.1 ± 1.3 $\mu g/m^3/24hr$) is greater than the average ambient PM_{10} level (18.7 ± 2.6 $\mu g/m^3/24hr$) at Hospital A. Since the excess PM_{10} at this site cannot be due to infiltration, the large amount of human activity at this site must be

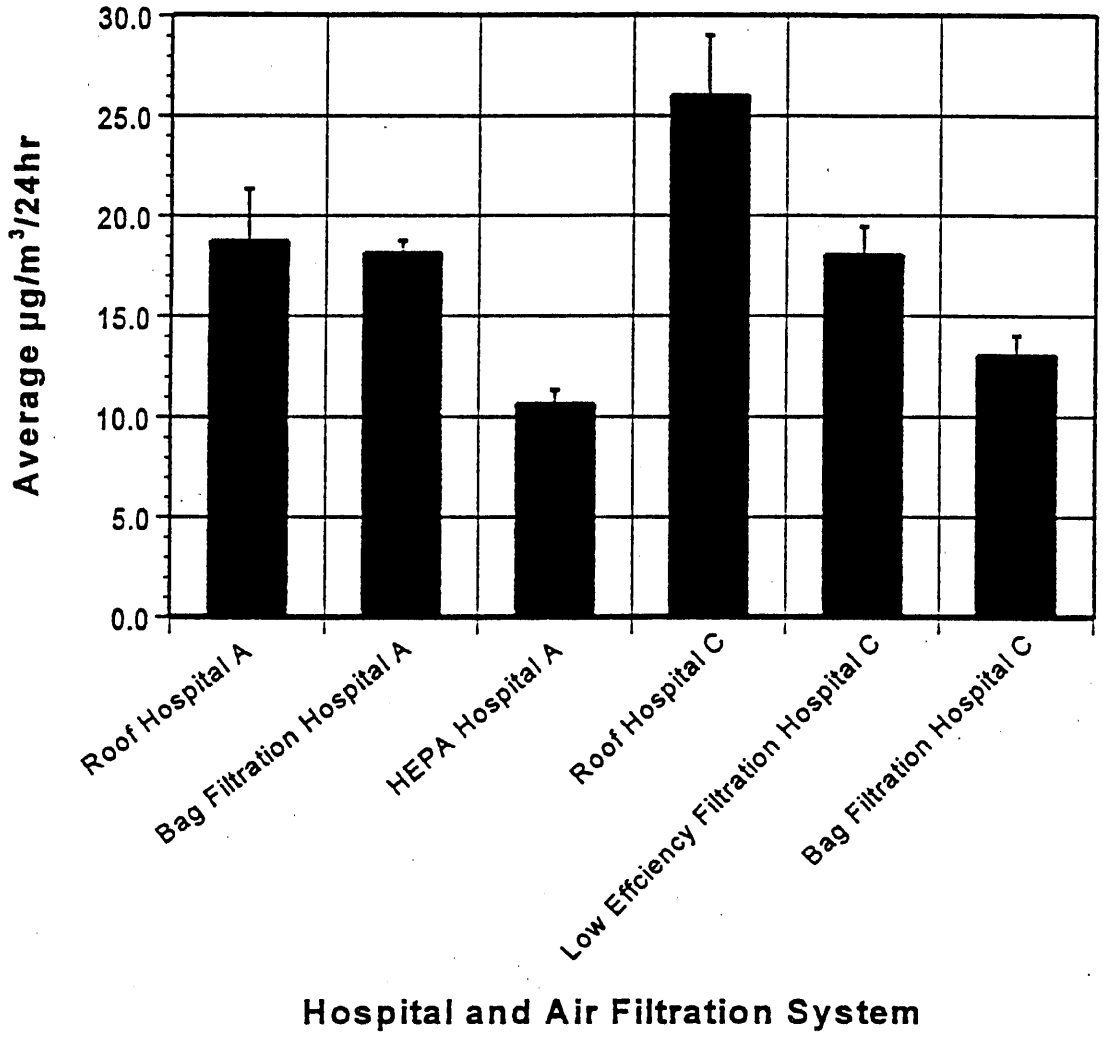


Figure 3. Average PM_{10} levels by air filtration system type. The whisker bars show the 95% confidence intervals.

Table 4. Subjective scoring of human activity patterns at each sampler site. Activity scores range from 1 to 4 and are based on the average patient census, number of hours per day that the site is occupied, and the types of activities being done at the site.

Hospital A		Hospital C	
Sampler Site	**Activity Level**	**Sampler Site**	**Activity Level**
Roof	Not Scored	Roof	Not Scored
Nursery Room A	3	Nursery, Well Baby	1
Nursery Room B	2	Nursery, At Risk Infants*	3
ICU Main Nurses Station	4	Maternity Ward Kitchen	2
ICU Respiratory Therapy Island	3	Maternity Patient Room	2
BMTU Nurses Station	2	CCU Nurses Station	2
BMTU Unoccupied Patient Room	1	CCU Nurses Lounge	2

*The patient census in this nursery was extremely variable, sometimes ranging between 0 to 35 within a 24 hour period.

the major contributor of indoor PM_{10}. Many of the common sources of indoor PM_{10}, such as smoking, cooking, and vacuuming, are either prohibited or severely restricted to specific areas in hospitals. None of these sources of PM_{10} are present in the ICU at Hospital A. The remaining likely sources of the excess PM_{10} are the personal particulate cloud of the individuals passing the sampler (Rodes et al., 1991) and resuspension of settled dust (Thatcher and Layton, 1994).

The increase in PM_{10} attributable to moderate levels of human activity (an activity score of 2) was estimated using the PM_{10} data from the BMTU at Hospital A. The nurses station human activity score was 2. The nurses station was staffed 24 hrs a day by at least two nurses. In addition, during the day shift a pharmacist, doctors, nutritional specialist, custodian, and patient relatives may be in the unit for part of the day. The patient room received a human

activity score of 1. This room was unoccupied and was rarely entered except by us to change sampler filters, and by the hospital cleaning staff. The room was lightly cleaned once per week. Approximately once per month the hospital infection control staff would monitor the room to verify that the HEPA system was working properly. No detectable increase in PM_{10} levels were observed on either cleaning days or biological sampling days. Since both the nurses station and the patient room are HEPA filtered environments the difference in PM_{10} levels between the two samplers should be entirely attributable to the difference in human activity. The average PM_{10} level in the patient room was 9.7 $\mu g/m^3/24hr$. The average PM_{10} level at the nurses station was 11.4 $\mu g/m^3/24hr$. The increase in PM_{10} attributable to a moderate amount of human activity in an extremely clean occupational setting is 1.7 $\mu g/m^3/24hr$.

The increase in PM_{10} associated with changing from HEPA to bag filtration can be estimated by comparing the BMTU nurses station PM_{10} level to a bag filtration sampler site with the same human activity score, 2. At Hospital A the only sampler in a bag filtered environment with a moderate human activity score is the Nursery Room B. The average PM_{10} level for this sampler was 17.9 $\mu g/m^3/24hr$. The amount of PM_{10} leaking through the bag filtration system was 6.5 $\mu g/m^3/24hr$. A portion of this 6.5 $\mu g/m^3/24hr$, approximately 1.1 $\mu g/m^3/24hr$, may be attributable to vacuuming in the nursery. The 1.1 $\mu g/m^3/24hr$ is based on a comparison of the Nursery Room A (avg PM_{10} 17.2 $\mu g/m^3/24hr$; human activity score of 3) site which was carpeted and ICU Respiratory Therapy Island (avg PM_{10} 16.1 $\mu g/m^3/24hr$; human activity score of 3) which was not carpeted.

These differences in PM_{10} levels among the filtration systems and human activity levels may seem low. However, the inversion season over which this data was collected had abnormally low ambient PM_{10} levels. At Hospital A the average ambient PM_{10} was 18.7 $\mu g/m^3/24hr$. The 6.5 $\mu g/m^3/24hr$ increase observed when switching from HEPA to bag filtration while controlling for human activity is 34% of the ambient PM_{10}. Similarly, the increase in PM_{10} levels seen as human activity increases are also small compared to many occupational environments. However, given the compromised health status of hospital patients and the increase in latex allergies in some neonatal populations, the fact that even in a clean bag filtered air environment human activity (without smoking or cooking) can drive the PM_{10} levels above the average ambient PM_{10} level may have important health consequences.

The values found for changes in PM_{10} with different human activity patterns and ventilation systems in this study are often based on single sampler site comparisons. While the large number of days sampled at each site are reassuring, another study using more samplers and a more elaborate human activity study should be done to confirm these values before they are used to make any decisions about proper ventilation or personnel management in a hospital setting.

REFFERENCES

Anuszewski, J., T. V. Larson, J.Q. Koenig. 1992. Simaltanous indoor and outdoor particle light scattering measurments at nine homes using a portable nephelometer. Presented at: meeting of the American Association for Aerosol Research; Paper No. 3a.5.

Clayton, C. A., R. L. Perritt, R. L. Pellizzari, E. D. Thomas, K. W. Whitmore, H. Özkaynak, J. D. Spengler, L. A. Wallace. 1993. Particle total exposure assesment methodology (PTEAM) study: distributions of aerosol and elemental concentrations in personal, indoor, and outdoor air samples in a Southern California community. J. Exposure Anal. Environ. Epidemiology. 3:227-250.

Johnson, T., J. Capel, J. W. Mozier, M. McCoy. 1995. Estimation of ozone exposures experianced by outdoor children in nine urban areas using a probablistic version of NEM. Draft report prepared by International Technology Air Quality Services for U.S. Environmental Protection Agency, Office of Air Quality Planning and Standards.

Lillquist, D. R., J. S. Lee, J. R. Ramsay, K. Boucher, Z. Weiss, L. Lyon. 1996. A comparison of indoor/outdoor PM_{10} concentrations measured a three hospitals and a centrally located monitor in Utah. Applied Occupational and Environ. Hygiene. In Press

Nazaroff, W. W., L. G. Salmon, C. R. Cass. 1990. Concentrations and fate of airbourne particulates in museums. Environ. Sci. Technol. 24:66-77.

Pellizzari, E. D., K. W. Thomas, C. A. Clayton, R. W. Whitmore, R. C. Shores, H. S. Zelon, R. L. Perrit. 1993. Particle total exposure assesment methodology (PTEAM) study: Riverside, California pilot study, Volume I [Final Report]. EPA report no. EPA/600/SR-93/050.

Pellizzari, E. D., K. W. Thomas, C. A. Clayton, R. W. Whitmore, R. C. Shores, H. S. Zelon, R. L. Perrit. 1993. Particle total exposure assesment methodology (PTEAM) study: Riverside, California pilot study, Volume I [Project Summary]. EPA report no. EPA/600/SR-93/050.

Robinson J. and W. C. Nelson. 1995. National human acvtivity pattern survey data base. U.S. EPA, Research Triangle Park, NC.

Rodes, C. E., R. M. KamensR. W. Wiener. 1991. The significance and characteristics of the personal activity cloud on exposure assesment measurements for indoor contaminats. Indoors Air. 2:123-145.

Thatcher, T .L. and D. W. Layton. 1994. Deposition, resuspension, and penetration of particles within a residence. Univ. of Calif. Lawrence Livermore National Laboratory report no. UCRL-JC-116597.

Thomas, K. W., E. D. Pellizzari, C. A. Clayton, D. A. Whitaker, R. C. Shores, J. D. Spengler, H. Özkaynak, L. A. Wallace. 1993. Particle total exposure assesment methodology (PTEAM) study: method performance and data quality for personal, indoor, and outdoor aerosol monitoring at 178 homes in Southern California. J. Exposure Anal. Environ. Epidemiol. 3:203-226.

Effects of Ambient Air Total PM_{10}, Black Smoke and Resuspended PM_{10} on PEF among Asthmatic Children

Raimo O. Salonen[A], Juha Pekkanen[A], Pekka Tiittanen[A], Kirsi Timonen[A], Jari Hosiokangas[B] and Juhani Ruuskanen[B]

[A]National Public Health Institute, Division of Environmental Health, Kuopio, Finland
[B]Department of Environmental Sciences, University of Kuopio, Finland

ABSTRACT

We investigated the contribution of resuspended particles to the ambient air concentration of inhalable particulate matter (PM_{10}), and the associations between different ambient air PM exposure variables and peak expiratory flow (PEF) among 39 asthmatic school children. The study was conducted in Kuopio, a medium-sized Finnish town, during a period of 82 days in winter and spring 1994. Resuspended particles emitted from surfaces of paved roads by traffic had a large contribution to the 24-hour average PM_{10} concentration during high PM pollution episodes in spring (max. 24-hour PM_{10} 158 $\mu g/m^3$), while in winter ambient air PM_{10} originated mainly from stationary and mobile combustion processes. After a two-day lag, the 24-hour concentrations of total PM_{10} (n=78) and black smoke (n=82) tended to be associated with a decline in morning PEF of asthmatic children, whereas the 24-hour concentration of resuspended PM_{10} (n=35) tended to be associated with a more immediate decline in evening PEF. The present preliminary findings need to be tested in future epidemiological studies.

INTRODUCTION

Subarctic urban areas may have somewhat different particulate matter (PM) pollution problems from those of more temperate climates. Finland locates between latitudes 60°N and 70°N, which is about the same as Alaska in the United States, but it has a milder climate due to the influence of the Gulf stream. Still, the wintertime is relatively cold and long in Finland. Daily mean temperature stays below 0°C for about 120 days/year in the south and 190 days/year in the north.

Stack and tail pipe emissions of particulate matter (PM) are relatively low in Finland. In 1980's and early 1990's, effective desulphurization and particle removal processes have been installed to most industrial and other point sources in urban areas, which has greatly reduced the emissions of both sulfur compounds (by more

than 80 % since 1980) and particles from these sources. As electricity production and heating in urban areas is mainly from well-controlled, combined power stations, increased energy needs in winter cause only a modest rise in particle emissions. With exception of the Helsinki Metropolitan Area, the population density and traffic volumes are relatively low in Finnish urban areas, and therefore also tail pipe particle emissions are generally low. However, street sanding and use of studded tires in cars during winter cause a major problem of indirect particle emissions. In fall, when street sanding and use of studded tires begin, and especially in spring, when the snow and ice have melted and the surfaces of paved roads have dried out, there are high emissions of resuspended dust caused mainly by urban traffic flows. In spring, these emissions are highly reflected in ambient daily and monthly average concentrations of total suspended particles (TSP) and in hourly, daily and monthly concentrations of inhalable particles (PM_{10}).[1]

The aims of the present study were: 1) to characterize the contribution of resuspended particles to ambient air PM_{10} concentrations in a medium-sized Finnish town in winter and spring, 2) to examine the intercorrelations between total PM_{10}, black smoke and resuspended PM_{10} concentrations in ambient air, and 3) to investigate the associations between the different PM exposure variables, and the morning and evening values of peak expiratory flow (PEF) among asthmatic children.

SUBJECTS AND METHODS

The study was conducted in Kuopio, which is a town of 83,000 inhabitants in the eastern part of central Finland. In this town, the main sources of particulate air pollution are traffic, a peat-fired power plant (equipped with an electrostatic precipitator) connected to a municipal district heating system, and a corrugation cardboard mill. Over 80% of the buildings around the downtown area are heated by the municipal district heating system, but about 25% of the homes have also additional wood burning for heating the houses during the coldest winter period.

Study design and subjects

The present data were collected within the framework of the European multicenter study "Pollution Effects on Asthmatic Children in Europe" (PEACE) . In that study, a screening questionnaire was sent to parents of all 2,995 children, who were aged 7 to 12 years and went either to five schools in the center of Kuopio or to three schools in two suburbs of Kuopio.[2-3] A total of 2,564 (86%) questionnaires were returned, and 2,554 children were aged 7-12 years. Children with chronic respiratory symptoms, including chronic cough (only symptom in 57% of children), were asked to participate in the PEACE study, and 197 (86%; 100 in the center and

97 in the suburban area) agreed. The children were from four schools in the center and two schools in one of the two suburbs, and they were characterized with skin prick tests and spirometry.

Several previous studies have suggested that asthmatic children are more susceptible to the effects of ambient air pollution than healthy adults. Preliminary analyses of the PEACE data showed that associations between ambient air PM and PEF were restricted to children with asthmatic symptoms, i.e. the children had either doctor-diagnosed asthma or they had suffered from wheezing or shortness of breath with wheezing during the past 12 months.[4] To allow a meaningful comparison of the associations of PM exposure variables with PEF, the present analyses include only children, who reported asthmatic symptoms and lived in the center of Kuopio. From a total of 45 asthmatic children, 39 (18 girls and 21 boys) had filled in the diary on more than 60% of the possible days,[2] and only these children were included. The analyses cover the period of February 8 to April 30, 1994, with valid PEF data[4] and data on ambient PM exposure variables.

The PEACE study protocol was approved by the joint Ethical Committee of the University of Kuopio and the Kuopio University Hospital. A written consent was obtained from the parents of the children.

Air quality measurements

All air quality measurements were done at one carefully specified site in the center of Kuopio. The monitoring site was at least 50 meters from any of the surrounding streets.[2,5] Total ambient air PM_{10} was collected with a single stage Harvard impactor, and black smoke was sampled according to the OECD protocol. The elemental composition of PM_{10} filters was analyzed for every third day by using ICP-MS, and the source contributions to ambient air PM_{10} were solved with receptor modeling.[6] In this model, aluminium was a good marker for PM from resuspended dust, and therefore it was used in the estimation of the resuspended PM_{10} concentration. Gaseous pollutants were measured with continuously recording monitors: NO and NO_2 with a chemiluminescence method (Monitor Labs 8840), SO_2 with UV-fluorescence (Monitor Labs 8850), and CO with a non-dispersive infrared monitor (Thermo Environmental 48). Meteorological data (wind speed, wind direction, and temperature) were obtained mainly from a municipal weather station network, and the data on relative humidity was from a weather station at the National Public Health Institute, Kuopio. Filters for PM_{10} and black smoke measurements were always changed between 11 am and 2 pm. The 24-hour average concentrations of the other pollutants and the meteorological parameters were also calculated from noon to noon.

Lung function measurements

During the follow-up period, the children measured their PEF values every day with a mini-Wright Peak Flow Meter. The measurements were done before taking any medication, and they included three recordings both in the morning and in the evening. With the help of their parents, the children kept daily diary also on their respiratory symptoms and use of medication.[2]

Statistical methods

The daily deviations from each child's mean morning and evening PEF values (l/min) were first calculated. The deviations were then averaged to obtain the mean daily deviation (ΔPEF) separately for morning and evening PEF. Associations of ΔPEF with PM exposure variables were analyzed by using a linear multivariate first-order autoregressive model in SAS (PROC AUTOREG).[7] In these analyses, each day was weighted by the number of children reporting a PEF value on that day. Lag 0 for morning PEF was defined as the 24-hour period from yesterday noon to present day noon, and that for evening PEF from present day noon to next day noon. First, a basic model was established to adjust for the effects of autocorrelation, time trend, weekend, pollen and weather on ΔPEF. The basic model included day, day^2, day^3, dummy for weekend, pollen, minimum temperature (lag 0), relative humidity (lag 0) and first order autocorrelation. The autocorrelation was taken into account only in the analyses of ΔPEF with total PM_{10} and black smoke. After these adjustments, the residuals were found to be normally distributed and no time trends were observed. To this basic model, PM exposure variables were added one at a time. All reported coefficients are calculated for 100 µg/m^3 of each PM exposure variable.

RESULTS AND DISCUSSION

Ambient air PM pollution

In general, the variations in 24-hour average PM concentrations were relatively small during the study period (Fig. 1). However, between April 10 and 13 there was an episode of very high concentrations of total PM_{10} (max. 24-hour value 158 µg/m^3) and estimated resuspended PM_{10} (max. 24-hour value 141 µg/m^3). The PM values during this episode were much higher than those during the other episodes, and they dominated all regression analyses and made them unstable. As they also had no clear association with the PEF values of the asthmatic children, the four-day episode was excluded from further statistical analyses. After this exclusion, the median (min., max.) 24-hour average concentration of total PM_{10} (n=78) was 16.2 µg/m^3 (4.0, 61.6) and that of resuspended PM_{10} (n=35) was 4.1 µg/m^3 (0.04, 44.9).

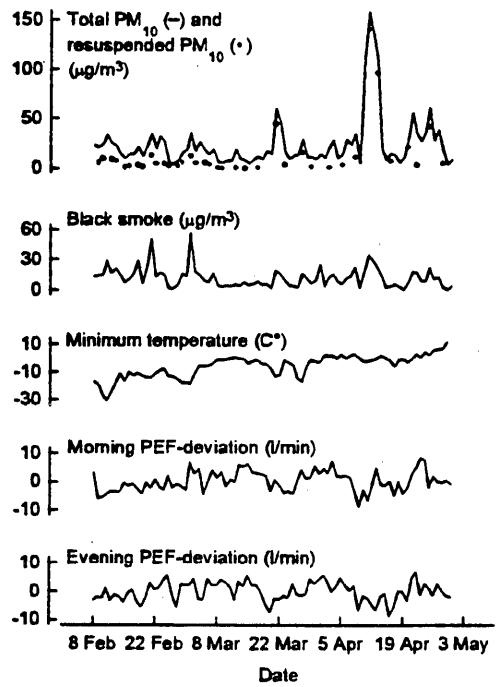


FIGURE 1. Time trends in ambient air 24-hour average concentrations of measured PM variables, minimum daily temperature and PEF-values of asthmatic school children.

The corresponding median concentration of black smoke (n=82) was 10.5 µg/m^3 (0.5, 56.9).

There were highly significant intercorrelations in ambient air 24-hour average concentrations between the measured PM variables. During the whole study period, the intercorrelations between total PM_{10} and black smoke ($r=0.78$, $p<0.0001$), and total PM_{10} and estimated resuspended PM_{10} ($r=0.80$, $p<0.0001$), were higher than the intercorrelation between black smoke and resuspended PM_{10} ($r=0.63$, $p<0.0001$). The latter intercorrelation was especially poor ($r=0.45$, $p=0.14$) after March 21, when the first PM episode with high resuspended PM_{10} occurred. These findings suggest that the estimation of resuspended PM_{10} concentration on the basis of aluminium concentration in PM_{10} mass is a useful indicator for soil and road surface material contribution to ambient air PM, whereas the contribution of stationary and mobile combustion processes is reflected clearly in black smoke concentration. The present suggestion is supported by the results of a recent principal component analysis of ambient air TSP, PM_{10} and black smoke concentrations, mean daily temperature, and wind speed from the same data.[8] In addition, a comparison of the 24-hour average black smoke concentration and the size-fractionated PM concentrations measured with an electrical aerosol spectrometer revealed that the black smoke concentration correlated best with the particle sizes 1.8-5.6 µm.[8] Thus, it seems that the estimated ambient air concentration of resuspended PM_{10} reflects largely the mass of coarse particles, although it probably includes also finer PM fractions.

Associations between PM pollution and PEF

The associations between the ambient air 24-hour average concentrations of measured PM variables and the PEF values of asthmatic school children suggested two different response patterns. After a two-day lag, the 24-hour concentrations of total PM_{10} and black smoke tended to be associated with a decline in morning PEF,

but they were not associated with any decline in evening PEF of asthmatic children (Table 1). In contrast, the 24-hour concentration of resuspended PM_{10} tended to be associated with a more immediate decline in evening PEF, but there was no similar trend in morning PEF (Table 1). The latter preliminary finding agrees with a recent study of Gordian et al.[9] in Anchorage, Alaska, where the ambient air 24-hour average PM_{10} concentration was significantly associated with the same-day and next-day outpatient visits for asthma and upper respiratory illness. In Anchorage, ambient air PM_{10} is composed mainly of earth crustal material and volcanic ash, and its mass is likely to be dominated by coarse particles. In four Finnish cities (including Kuopio), Kuusisto[10] has earlier reported a significant association between the ambient air 24-hour average TSP concentration, and the same-day respiratory symptoms, bronchodilator use and PEF values of adult asthmatic subjects.

TABLE 1. Adjusted[A] associations between ambient air 24-hour average concentrations of measured PM variables, and morning and evening PEF values of asthmatic school children (regression coefficient in l/min per 100 µg/m³).

		Morning PEF	Evening PEF
	Lag	Coeff. (p-value)	Coeff. (p-value)
Total PM_{10}	0	-0.59 (0.88)	2.66 (0.43)
	1	3.09 (0.38)	-0.07 (0.98)
	2	-6.35 (0.08)	1.58 (0.62)
	3	-4.19 (0.25)	-1.09 (0.73)
Resuspended PM_{10}	0	-3.95 (0.65)	-12.20 (0.14)
	1	-13.26 (0.12)	-11.73 (0.11)
	2	-3.22 (0.65)	-6.59 (0.14)
	3	-9.63 (0.11)	-4.70 (0.47)
Black Smoke	0	0.62 (0.88)	2.00 (0.60)
	1	5.19 (0.17)	-1.04 (0.79)
	2	-9.07 (0.02)	-4.35 (0.26)
	3	0.20 (0.96)	-4.04 (0.29)

[A] Models adjusted for autocorrelation and time trend, minimum temperature, relative humidity, weekend and pollen.

CONCLUSIONS

1. The contribution of resuspended particles to the ambient air 24-hour average PM_{10} concentration was large during high PM pollution episodes in spring. In winter, ambient air PM_{10} originated mainly from other sources such as stationary and mobile combustion processes.

2. The estimation of resuspended PM_{10} concentration on the basis of aluminium concentration in PM_{10} mass was a useful indicator for the soil and road surface material contribution to ambient air PM. The contribution of stationary and mobile combustion processes was reflected clearly in black smoke concentration.

3. The 24-hour average concentrations of PM_{10} and black smoke tended to be associated with a two-day lagged decline in morning PEF, but not with any decline

in evening PEF of asthmatic children. In contrast, the estimated 24-hour average concentration of resuspended PM_{10} tended to be associated with a more immediate decline in evening PEF.

4. In the subarctic town of Kuopio, ambient air PM_{10} seems to have a different composition in different seasons. The present preliminary findings on the respiratory health effects associated with different PM_{10} sources need to be tested in future epidemiological studies.

Acknowledgements

The data were collected within the framework of the PEACE study. The PEACE study is a study on Effects of Short-term Variations in Urban Air Pollution on the Respiratory Health of Children with Chronic Respiratory Symptoms. PEACE stands for "Pollution Effects on Asthmatic Children in Europe". The study was funded by the EU ENVIRONMENT Programme Contract EV5V-CT92-0220 (seven centres) and two additional EU PECO contracts to allow participation of five centres in Central and Eastern Europe. The Finnish, Norwegian and two Swedish centres were funded by grants from the respective Governments. The study was coordinated by the Department of Epidemiology and Public Health, University of Wageningen, P.O.Box 238, 6700 AE Wageningen, The Netherlands.

The present study was supported by The Academy of Finland, The Ministry of the Environment and The Ministry of Social Affairs and Health, Finland, and the Nordic Council of Ministers.

References

1. Hämekoski, K.J.; Salonen, R.O.: Particulate matter in northern climate of Helsinki Metropolitan Area. Proceedings of the Second Colloquium on Particulate Air Pollution and Health, Park City, Utah, 1996.
2. Effects of short-term changes in urban air pollution on the respiratory health of children with chronic respiratory symptoms. Study procedures for collaborative study funded by the Commission of the European Communities in the framework of the 'ENVIRONMENT' RDT Programme. B. Brunekreef, Ed. Wageningen Agricultural University (1993).
3. Timonen, K.L.; Pekkanen, J.; Korppi, M.; et al.: Prevalence and characteristics of children with chronic respiratory symptoms in Eastern Finland. Eur. Respir. J. 8:1155-60 (1995).
4. Timonen, K.L.; Pekkanen, J.; Salonen, R.O.; et al.: Air pollution and respiratory health of children - the PEACE panel study in Kuopio, Finland. Eur. Respir. Rev. (in press).
5. Pekkanen, J.; Timonen, K.L.; Salonen, R.O.; et al.: Urban air pollution and respiratory health among children with respiratory symptoms in Finland. In: Proceedings of 10th World Clean Air Congress, Vol. 3, pp. 613a-613d. J. Kämäri, M. Tolvanen, P. Anttila, R.O. Salonen, Eds. The Finnish Air Pollution Prevention Society. Espoo (1995).
6. Hosiokangas, J.; Kikas, Ü.; Pekkanen, J.; et al.: Identifying and quantifying air pollution sources in Kuopio by receptor modeling. J. Aerosol. Sci. 26(Suppl 1):S423-S424 (1995).
7. SAS Institute Inc.: SAS/ETS® User's Guide, Version 6, Second Edition. SAS Institute Inc. Cary, NC (1993).
8. Reponen, A.; Ruuskanen, J.; Mirme, A.; et al.: Comparison of five methods for measuring particulate matter concentrations in cold winter climate. Atm. Environ. (in press).

9. Gordian, M.E.; Özkaynak, H.; Xue, J.; et al.: Particulate air pollution and respiratory disease in Anchorage, Alaska. Environ. Health Perspect. 104(3):290-297 (1996).
10. Kuusisto, P.: Ulkoilma ja astma [Ambient air and asthma]. Ph.D. Thesis [in Finnish], University of Helsinki. Helsinki (1990).

Epidemiologic Research On Particulate Air Pollution And Mortality: Current Status And Next Steps

Jonathan M. Samet, M.D., M.S.
Scott L. Zeger, Ph.D.
Julia E. Kelsall, Ph.D.
Jing Xu, M.S., M.S.P.H.

Departments of Epidemiology and Biostatistics
School of Hygiene and Public Health
The Johns Hopkins University
615 North Wolfe Street
Baltimore, Maryland 21205

Abstract

The second colloquium on particulate air pollution marks the re-emergence of air pollution, generated by combustion sources, as a serious public health concern throughout the developed world. This paper provides a perspective on the epidemiologic evidence on particulate air pollution and health. It addresses the evolution of methods for investigating air pollution and mortality and morbidity and the interpretational framework for the findings of the studies. Our work at the Johns Hopkins University School of Hygiene and Public Health funded by the Health Effects Institute as part of its Particle Epidemiology Evaluation project provides the foundation; data are from public-use resources and are analyzed using Poisson regression. Data from previous analyses were replicated, and a detailed analysis for Philadelphia 1973-1908 was conducted to explore the sensitivity of the findings to key modeling assumptions. Our findings show that the association of TSP with mortality persisted; an effect of ozone was also noted that remained unchanged as other pollutants were considered. Varying measures of air pollution are associated with mortality in diverse communities and have been robust to choices of analytic methods. Similar analyses with single locations will contribute little to our understanding of air pollution and mortality unless there are special pollution patterns. Nonetheless, the weight of evidence from single locations indicates an adverse effect of air pollution. In deciding about the particulate matter standard, it must be remembered that we lack necessary toxicologic information. A need exists for a research program covering exposure assessment and epidemiology, and clinical and experimental toxicology; such a program could benefit the regulatory process on air pollution and health.

Key words: epidemiology, particulate air pollution, TSP. ozone, statistical modeling

Introduction

This second colloquium on particulate air pollution marks the re-emergence of air pollution, generated by combustion sources, as a serious public health concern in the United States and other countries throughout the developed world. While the well-chronicled disasters earlier in this century left no doubt about the potential for air pollution from fossil fuel combustion to cause excess morbidity and mortality, control strategies implemented from the 1950s on were generally regarded as successful in limiting effects on mortality, and air quality was widely considered to have improved, based on the monitoring systems in place. [1] Consequently, there was substantial skepticism and controversy concerning the findings of epidemiologic studies published in the early 1990s and subsequently that linked indicators of particulate air pollution to increased mortality [2-4]. In fact, one major focus of the first colloquium on particulate air pollution was on the veracity of the epidemiologic findings, which were questioned because of the novelty of the methods and the "positive findings" (proceedings volume).

Only two years later, emphasis of epidemiologic presentations at the second conference has shifted from technical concerns about the methodology and validity of the epidemiologic studies to interpretation of the mounting body of evidence on effects of air pollution on morbidity and mortality. Thus, themes running throughout the sessions of this colloquium included: 1) can statistical modeling methods separate an effect of one pollutant (e.g., particles) present in a complex mixture from the effects of other pollutants?; 2) if particles are, in fact, responsible for the observed health effects, what characteristics of the particles determine toxicity?; and 3) can the epidemiologic data be interpreted for regulatory and public health purposes, absent a full biologic understanding of mechanisms of injury? The epidemiologic studies presented at the colloquium continued to demonstrate associations between measures of air pollution and indicators of morbidity and mortality, and there was a general consensus that contemporary ambient levels of air pollution have been linked to adverse effects on public health.

Our work at the Johns Hopkins University School of Hygiene and Public Health, funded by the Health Effects Institute through its Particle Epidemiology Evaluation Project, has followed this same evolutionary sequence. In 1994, we received funding

from the Health Effects Institute to replicate previously published findings and to establish the validity of the databases and statistical methods of the studies. Findings have been reported and provided to the Environmental Protection Agency, as the Agency prepared the Criteria Document for Particulate Matter. Our first report addressed and answered concerns about obvious methodologic faults or other problems in six selected and previously reported analyses. [5] We then turned to other methodologic issues, including alternative approaches to controlling for weather, and we have also conducted an extended, multi-pollutant analysis and data from the city of Philadelphia for 1974-1988, which was presented at the second colloquium.

This paper provides a perspective on the epidemiologic evidence on particulate air pollution and health. It addresses the evolution of methods for investigating air pollution and mortality and morbidity and the interpretational framework for the findings of the studies. We draw on our work in the Particle Epidemiology Evaluation project for examples. We concluded by identifying key issues that now need to be addressed and the need for complementary epidemiologic and toxicologic research.

Considerations in Modeling the Effect of Air Pollution on Mortality

The new findings on adverse effects of particulate air pollution on health are based on time-series analyses that describe the relationship between air pollution levels and variation in health outcome measures, e.g., daily mortality counts. A statistical "model" -- a mathematical expression for the relationship between the health outcome and air pollution and other independent variables -- is used to estimate the effect of these independent variables on the outcome measure. The fitting of the model to the data is guided by a procedure that optimizes the fit.

Undoubtedly, the development of new methods for analyzing time-series data contributed to the new findings on air pollution and mortality. In particular, Poisson regression methods, appropriate for count data, became readily available through standard software packages which are used on work stations and personal computers. Additionally, new methods for fitting models to data were developed that could take into account some of the difficult issues posed by time-series data, including correlations

among outcome measures and air pollution and weather variables on a daily time frame. The most widely used method, the generalized estimating equation approach of Liang and Zeger, [6] can accommodate analyses of time series of mortality counts and air pollution data, for which mortality counts and pollution levels on consecutive days are correlated.

In modeling the relationship between mortality and air pollution, factors other than air pollution which affect mortality should be taken into account. These factors may confound the relationship between air pollution and mortality because they are both causally associated with mortality and also associated with the air pollution indexes, or they may modify the relationship between air pollution and mortality. For example, hotter temperatures could confound the relationship of air pollution with mortality, if levels of pollution tend to be higher on higher temperature days when mortality counts were increased by the direct effect of temperature. Hotter temperatures might also modify the effect of air pollution on mortality, if the effect of air pollution tended to be greater on higher temperature days. [7] Other factors to be considered are short-term effects on mortality from systematic variation by day-of-week, infectious disease epidemics, and season. Longer-term trends of disease mortality, e. g., the decline in cardiovascular mortality in the U.S. over the last 30 years, may also be relevant if there is potential for confounding with air pollution indexes which are changing on the same time frame.

The modeler faces a set of choices in approaching analysis of time series of air pollution and mortality (Table I): selecting and specifying variables to control for short-term temporal effects, for longer-term temporal effects, and for weather. The effects of these factors might plausibly vary by age, sex and race, leaving the modeler to test for variation in the effects of temporal and weather variables across strata of demographic factors. Variables for air pollution are then added to a preferred base model with variables for time factors and weather. The bases for preferring a particular model might include *a priori* knowledge, plausibility and model fit. Issues arising with regard to the air pollution variables include selection of monitors, specification of the averaging metric (e.g., average or maximum and lag structure), and pollutants for consideration. In most of the investigations, data have been used from monitors cited for regulatory

purposes and there may be a need to assess the quality of the data and the degree to which the data capture population exposure.

Finally, the specification of the health outcome needs to be addressed. Total mortality, as an outcome measure, includes both those causes of death that might be plausibly affected by air pollution and those causes for which no relationship would be anticipated, e.g., motor vehicle accidents or homicides. Stratification by cause of death may add specificity to the analyses. Thus, cardiovascular and respiratory causes are most plausibly associated with air pollution because of the susceptibility of persons with these diseases to agents that damage lung function. However, there are well-characterized limitations of the validity of death certificate certifications of cause of death, and stratification reduces power because of the smaller number of deaths within any given category compared with total mortality. Typically, the studies have reported findings for both total and cause-specific mortality.

In the analyses conducted for the Health Effects Institute, we have explored the sensitivity of findings to these analytic choices.

Particle Epidemiology Evaluation Project

Introduction

In the fall of 1994, the Health Effects Institute implemented the Particle Epidemiology Evaluation Project to address key questions regarding the epidemiologic evidence on particulate air pollution and mortality. The timing of the project and the initial set of tasks were intended to address key uncertainties in the epidemiologic evidence on those particles requiring the most immediate attention in developing the Criteria Document. Phase I of the project, now completed, was directed at key uncertainties related to interpretation of the epidemiologic information for the purpose of reviewing the Particulate Matter Standard of the Environmental Protection Agency. In Phase IA, we established the validity of a key data base, that for the city of Philadelphia, and replicated selected analyses. These findings have been fully reported. [5] In Phase IB, we assessed the analytic consequences of alternative approaches to controlling for

confounding by weather, and conducted an extended analysis for the city of Philadelphia, examining multiple pollutants in addition to TSP and SO_2, which were included in the original data set. These findings are summarized in a recent report to the Health Effects Institute. [8] Here, we provide an overview of key findings.

Methods

Databases: In Phase IA, data were analyzed from six locations (Table II). We also used data for Philadelphia, 1973-1980, provided by Schwartz and Dockery from the Harvard School of Public Health. In Phase IB, we used data for Philadelphia for 1974-1988. These data were obtained from public-use resources including tapes of the National Center for Health Statistics, the Aerometric Information and Retrieval Service (AIRS) data base of the Environmental Protection Agency, and the National Weather Center. In addition, Dr. Laurence Kalkstein of the University of Delaware provided variables for the synoptic categorization of weather patterns in Philadelphia for 1973-1980.

Analytic Methods: The data were analyzed using Poisson regression. While a variety of analytic methods were applied in Phase I and Phase IB, we used principally generalized additive models which were fit to the data with the generalized estimating equation approach. In Phase IB, we developed models for the data for Philadelphia, 1974-1988, using Akaike's Information Criterion (AIC) to guide model fit. As we considered alternative models, we selected those giving the greatest reduction in AIC. Models were fit with programs of S-Plus.

Findings -- Phase IA

As described in the report to the Health Effects Institute, previously analyzed data bases for Philadelphia assembled by Schwartz and Dockery, and by Moolgavkar and colleagues were found comparable to new files that we extracted from source data bases. We replicated analyses for six locations that had been selected for Phase IA (Table II). In more detailed analyses for Philadelphia, 1973-1980, we explored the sensitivity of the findings to key modeling assumptions. This set of analyses showed that the association of TSP with mortality was robust to model assumptions, although we did find interdependence of the effects of TSP and SO_2 and modification of the effect

of TSP by season. With regard to weather specifically, the association of TSP with mortality was comparable when comparing the empirically derived set of weather variables used by Schwartz and Dockery and our approach, based on LOESS smoothing.

Findings -- Phase IB

In interpreting the epidemiologic studies on air pollution and mortality, there had been persistent concern about the possibility of uncontrolled confounding by weather because both colder and hotter temperatures affect mortality and levels of air pollution are also affected by meteorological factors. In reported analyses, diverse empiric approaches had been followed to control for weather. For example, Schwartz and Dockery, in analyzing the data for Philadelphia, had used both continuous variables for temperature and a discrete variable for hotter temperatures while we had used a smoothing approach for temperature and humidity. Kalkstein had proposed that use of synoptic categories which describe weather patterns from a meteorologic perspective might provide tighter control of confounding.

Consequently, working with Dr. Kalkstein, we compared use of synoptic categories with alternatives that had been previously used. For this analysis, we used data for the city of Philadelphia, 1973-1980. Kalkstein provided two sets of synoptic categories for these years: the Total Synoptic Index (TSI) and the Spatial Synoptic Categorization (SSC), two distinct types of categorization of weather patterns. The latter variables were available only for the summer and winter months. In general, we found that the associations of the air pollution indexes, TSP and SO_2, did not vary markedly with the specific weather variables included in the model. Models using the empiric methods, based on data fitting, were not surprisingly found to better fit to the data than models using the externally derived synoptic categories, which are intended to classify weather patterns. We concluded that residual confounding by weather variables does not explain the association of TSP with mortality.

We also conducted a *de novo* analysis of data for the City of Philadelphia 1974-1988, which used the major criteria pollutants of concern: TSP, SO_2, CO, NO_2, and ozone. Levels of these pollutants were found to be correlated (Table III). The

concentrations of the primary combustion-related pollutants (TSP, SO_2, CO, and NO_2) tended to be moderately correlated, while correlations of the secondary pollutant, ozone, with levels of these pollutants were lower. We systematically built a model for the effect of air pollution on mortality, using the AIC and *a priori* considerations as the bases for model specification and selection. We sequentially built models which progressively added terms for long-term and short-term time trends and for weather. We found that the data were fit better by a model that attained the effect of weather to vary by age.

Our published report provides a full description of the models and the findings. The association of TSP with mortality persisted as the effects of other pollutants were considered (Table IV). An effect of ozone on mortality was also noted that remained unchanged as other pollutants were considered. All pollutants were included in one model, although model coefficients need cautious interpretation because of the correlations among the pollutants. Nonetheless, in this model, effects of TSP and ozone were confirmed.

Synthesis

In the last five years, there has been a remarkable growth in the evidence on the public health impact of outdoor air pollution. With many countries having made improvements in outdoor air quality across previous decades, there was a general, albeit unformalized, consensus that levels of outdoor air pollution had been reached in developed countries that were not likely to affect mortality. Emphasis of epidemiologic researchers had shifted to studies of morbidity and to sensitive populations; this shift was mirrored in experimental and clinical toxicologic investigations of air pollution which tended to focus on biomarkers of response at ambient levels of pollution and on the sensitivity of susceptible populations. The now emerging findings on air pollution and mortality were unexpected and inconsistent with widely held views on air pollution and mortality.

Consequently, the findings of the epidemiologic studies on air pollution and mortality were controversial and received extensive review and criticism. Areas of

concern included the statistical methods for analysis of time-series data, which were novel at the time; the possibility of incorrect application of analytic methods or other problems in the development of the data bases and conduct and interpretation of the analyses; and the lack of biologic and clinical plausibility for the findings. Concerns about analytic errors have been set aside as the findings have been replicated by multiple investigators, including our work in Phase IA of the Particle Epidemiology Evaluation Project. However, uncertainties about underlying biologic mechanisms persist, as we have yet to develop and use appropriate toxicologic models. Mechanisms have been postulated that could underlie the association of particles with mortality, but only preliminary data have become available from toxicologic models.

Even lacking this toxicologic framework, the weight of the evidence shows that measures of air pollution are associated with mortality in diverse communities. These associations have been found with varying measures of air pollution, although emphasis has been placed on measures of particulate air pollution; the associations have been robust to choices of analytic methods. Our analyses of Philadelphia data and other sensitivity analyses show a substantial robustness of the association of air pollution measures with mortality. While analyses of data from single cities may be needed for purposes related to advancing local public health, further analyses comparable to those already reported will contribute little to our understanding of air pollution and mortality. As shown by the discussions at this meeting, we continue to wrestle with the difficult task of interpreting the available epidemiologic information. Some have interpreted the epidemiologic information as indicative of a causal association of particles, most likely fine particles, with mortality. This interpretation is based on the consistent finding of an association of measures of particulate air pollution with mortality across a range of locations where other pollutants are present to a variable extent. Studies of morbidity are also considered to be consistent with this interpretation. Others, in interpreting the same evidence, have emphasized the ambiguity of the observational data and the difficulty of assigning a causal role to a single mixture component, e. g., particles, in a complex pollution mixture. We have concluded that analyses within location need cautious interpretation in the presence of multiple pollutants with correlated concentrations.

Arguments for either pole on this interpretational axis are weakened by the lack of toxicologic information. Promising animal models have been developed but only preliminary findings are available. We know little about the responses of persons with advanced heart and lung diseases to inhalation of particles and other pollutants. We do not anticipate substantial advances in the toxicologic evidence for the short term. Nonetheless, the regulatory schedule has required a review of the evidence on particulate air pollution and mortality for the purpose of considering revision of the Particulate Matter Standard for the United States. The review was scheduled at a time when the epidemiologic evidence provided warning of possible public health impact of particulate air pollution. However, the evidence is incomplete in many respects and any specific decision by the Environmental Protection Agency on the control of particles will be made in the face of substantial uncertainty. We cannot be certain that the risks attributed to particles by the regression models are predictive of benefits to be gained by reducing particle levels. These risks are likely to reflect the effects of pollutant mixtures in urban air and not of single components. If the risks do reflect injury by particles alone, we still lack information on the determinants of toxicity, e.g., particle acidity or elemental composition.

While the regulatory process of the Environmental Protection Agency mandates a decision, there is a need for a coherent research program that covers the broad spectrum of exposure assessment and epidemiology and of clinical and experimental toxicology. This program should target key uncertainties and have a timeline that could bring results in synchrony with needs of the regulatory process.. The current discussions about particles and mortality offer another lesson on the need for an appropriately targeted and sustained research agenda on air pollution and health.

References

1. Holland WW, Bennett AE, Cameron IR, et al. Health effects of particulate pollution: Reappraising the evidence. Am J Epidemiol 1979; 110:533-659.

2. Utell MJ, Samet JM. Particulate air pollution and health. New evidence on an old problem. Am Rev Respir Dis 1993; 147:1334-5.

3. Lipfert FW. Air Pollution and Community Health: A Critical Review and Data Sourcebook. New York, New York, Van Nostrand Reinhold; 1994.

4. Waller RE, Swan AV. Invited Commentary: Particulate air pollution and daily mortality. Am J Epidemiol 1992; 135:20-2.

5. Samet JM, Zeger SL, Berhane K. The Association of Mortality and Particulate Air Pollution. Cambridge, Massachusetts, Health Effects Institute; 1995.

6. Liang KY, Zeger SL. Longitudinal data analysis using generalized linear models. Biometrika 1986; 73:13-22.

7. Katsouyanni K, Pantazopoulou A, Touloumi G, et al. Evidence for interaction between air pollution and high temperature in the causation of excess mortality. Arch Environ Health 1993; 48:235-42.

8. Samet JM, Zeger SL, Kelsall JE, et al. Weather, Air Pollution and Mortality in Philadelphia, 1973-1980. Interim Report to the Health Effects Institute on Phase IB of the Particle Epidemiology Evaluation Project. Cambridge, Massachusetts, Health Effects Institute; 1996.

Table I

Specifying Models For Air Pollution And Mortality

- Selection of statistical method, e.g., Poisson regression.
- Selection of method for fitting the model to the data.
- Specification of variables to adjust for temporal trends, long-term and short-term.
- Specification of variables to adjust for weather.
- Selection of pollutants and monitors.
- Specification of lag structure.
- Stratification by age, sex, race.
- Stratification by cause of death.

Table II

Summary Of Regression Model Results For Particulate Matter Indexes In Phase IA

Location	Particulate Matter Index	Particulate Matter Exposure Metric	Other Pollutants	$\hat{\beta}$ (x 1000)[A]	SE ($\hat{\beta}$ x 1000)[A]	Corrected *t* Value[B]
Philadelphia	TSP ($\mu g/m^3$)	Mean of concurrent and one prior day	SO_2 ppb	0.50	0.16	2.8
St. Louis	PM_{10} ($\mu g/m^3$)	Prior day		1.5	0.71	2.1
Eastern Tennessee	PM_{10} ($\mu g/m^3$)	Prior day		1.6	1.4	1.0
Utah Valley	PM_{10} ($\mu g/m^3$)	Five-day-lagged average		1.6	–	2.8
Birmingham	PM_{10} ($\mu g/m^3$)	Mean of PM_{10} on the 3 prior days		1.0	0.4	2.5
Santa Clara[C]	Coefficient Of Haze	Concurrent day		6.7	3.0	–

[A] Coefficients are from the IWFLS log-linear model, except those for Santa Clara.

[B] Corrected for over-dispersion.

[C] Coefficient is from linear regression.

Table III

Pearson Correlations (x100) Between Pairs Of Pollutants By Season And For The Full Year, Philadelphia, 1974-1988

Pollutants[A]	Winter	Spring	Summer	Fall	All Year
TSP & O_3	-36.7	19.8	36.8	13.4	11.6
SO_2 & O_3	-47.0	3.1	29.3	3.5	-2.0
NO_2 & O_3	-51.6	-6.5	27.9	4.1	0.1
CO & O_3	-46.2	-29.4	2.6	-24.1	-19.8
TSP & CO	57.4	38.8	30.8	56.4	48.0
SO_2 & CO	53.5	34.4	21.4	44.2	41.7
NO_2 & CO	72.7	66.4	48.2	65.7	63.0
TSP & NO_2	70.0	62.4	57.2	75.7	66.6
SO_2 & NO_2	68.3	57.8	55.1	66.0	60.9
TSP & SO_2	71.6	58.4	55.2	69.7	64.8

[A] Residuals after regressing each of the pollutants on time and weather variables

Table IV

Pollutant Coefficients[A] For Models[B] With Different Combinations Of Other Pollutants, Philadelphia, 1974-1988

Other Pollutants	TSP	SO_2	NO_2	CO	LCO[‡]	O_3
Alone	1.15(3)	1.08(3)	0.20	0.06	1.13(4)	2.28(3)
TSP	—	0.30(1)	-0.93(2)	-0.54(1)	1.17(4)	2.04(2)
SO_2	0.74(1)	—	-0.63(1)	-0.38(1)	1.16(4)	2.25(3)
NO_2	1.79(4)	1.45(3)	—	-0.05	1.14(4)	2.27(3)
CO	1.43(3)	1.23(3)	0.21	—	1.14(3)	2.37(3)
LCO[C]	1.21(3)	1.12(3)	0.23	0.12	—	2.11(3)
O_3	0.96(2)	1.05(2)	0.14	0.27	1.04(3)	—
All others	1.04(1)	1.08(2)	-1.14(2)	0.08	1.07(3)	1.95(3)
All except CO	1.06(2)	1.08(2)	-1.10(2)	—	1.10(3)	1.91(3)

[A] Coefficients are expressed as approximately the percent change in mean mortality for an increase of one interquartile range of the corresponding pollutant. The numbers in parentheses are rounded down absolute *t*-values. A value of 2 or greater is usually taken to indicate significance.

[B] Including long-term time trends, seasonal and weather effects in the model.

[C] Mean of CO values for the third and fourth prior days

The 1994 ICRP66 Human Respiratory Tract Dosimetry Model as a Tool for Predicting Lung Burdens from Exposures to Environmental Aerosols

M.B. Snipes[A], A.C. James[B], and A.M. Jarabek[C]

[A]Inhalation Toxicology Research Institute, Albuquerque, NM; [B]ACJ and Associates, Richland, WA; [C]U.S. Environmental Protection Agency, Research Triangle Park, NC

ABSTRACT

The International Commission on Radiological Protection Human Respiratory Tract Dosimetry Model was used to predict average particle deposition and retention patterns for two example trimodal (fine, intermodal, and coarse modes) environmental aerosols (Phoenix, AZ and Philadelphia, PA). Deposited dose metrics are presented as mass (and number) of particles normalized to either respiratory tract region surface area (cm^2) or to mass (g) of epithelium. Deposition metrics ranged over several orders of magnitude, with extrathoracic > tracheobronchial > alveolar-interstitial. Dissolution-absorption half-times for fine, intermodal, and coarse particles were defined as 10, 100, and 1000 days, respectively, to allow modeling chronic exposures. Default values for particle physical clearance parameters were used. Retained dose for the alveolar-interstitial region is presented as the steady-state mass of particles (μg)/g epithelium. Modeling results indicated similar retention patterns for the fine particles, but substantially different patterns for the intermodal and coarse particles. Intermodal and coarse particles dominated the Phoenix aerosol, resulting in predictions that long-term retained lung burdens would be about 4 times higher in individuals chronically exposed in Phoenix versus Philadelphia. This modeling approach improves the understanding of relationships between exposures to environmental aerosols and deposition/retention patterns in the human respiratory tract. Modeling demonstrated that significant thoracic deposition of environmental aerosol particles larger than the cut-point of a $PM_{2.5}$ sampler occurs, supporting the conclusion that using the PM_{10} fraction as an exposure index should be

a good indicator of potential health effects. Therefore, aerosol sampling should retain PM_{10} sampling in order to include the entire respirable size range and to provide adequate information for predicting deposition and retained dose metrics for environmental aerosols. Ventilatory activity patterns are also necessary to characterize total personal exposure, and the dissolution-absorption of environmental aerosol particles must be determined to allow accurate modeling of their long-term retention in the lung.

Key Words: Environmental aerosols, humans, inhalation, ICRP66 Model, dosimetry.

INTRODUCTION

Humans are exposed to environmental aerosols that have a broad range of physical, chemical, morphological, and thermodynamic attributes. These aerosols contain a wide range of particle sizes and have naturally occurring constituents, as well as those produced by human technologies. Particle size is an important characteristic of aerosols because aerodynamic or thermodynamic size markedly influences deposition patterns for inhaled particles. Particle composition is also important because many constituents of environmental aerosols exhibit toxicity to cells and tissues that could affect clearance mechanisms, thereby altering the residence time of retained particles, or influence other response mechanisms such as phagocytosis by alveolar macrophages. Composition also affects dissolution/absorptive rates, which influence the residence time and the response to particles retained in respiratory tract tissue as well as remote tissues that are targets for absorbed constituents.

A growing epidemiological data base indicates that exposures to environmental aerosols produce adverse biological responses. Unfortunately, relationships among environmental aerosol concentrations, deposited doses of inhaled particles, and retention of inhaled environmental aerosol constituents are poorly understood. Characterizing the respiratory tract deposition and retention patterns in individuals exposed to environmental aerosols should improve the interpretation of exposure-dose-response relationships that are needed for assessments of epidemiological data to determine human health risks.

Selection of dose metrics for deposition and retention of particles for dose-

response assessment should be based on insight about mechanisms of action for observed responses to deposited or retained particles. However, mechanistic insights on the health effects observed in the epidemiologic studies are only beginning to be elucidated for particulate matter (PM).[1] At present, when considering epidemiologic data, effects can be categorized as acute and chronic. It is not known whether mass, surface area, or particle number is most appropriate for assessing potential toxicity. Further, questions remain about how the dose should be normalized (e.g., per ventilatory unit or critical cell type). Acute effects of PM are probably best related to deposited particle burdens of short duration, whereas a steady-state retained burden may be most appropriate to characterize chronic responses.

Models are useful for predicting deposition and accumulation patterns of inhaled materials. To date, however, no model specific for predicting these patterns in the human respiratory tract has been developed for repeated inhalation of environmental aerosols. The revised ICRP Human Respiratory Tract Dosimetry Model for Radiological Protection[2] was developed to predict radiation dose rates and cumulative radiation doses from acute or chronic inhalation exposures of humans to radioactive aerosols. Figure 1 is a schematic representation of the ICRP66 Model. Compartments of the model with clearance pathways are shown; details of the model structure and rates associated with the pathways are discussed elsewhere.[2] The ICRP66 Model was used in this paper to demonstrate respiratory tract deposition and accumulation patterns for selected environmental aerosols. Model limitations and needs relevant to understanding

relationships between inhalation exposures to environmental aerosols and the consequent deposition and accumulation patterns of constituents of environmental aerosols are discussed.

METHODS

The ICRP66 Model was developed for use in radiological protection and is structured to predict absorbed radiation doses resulting from inhalation of radioactive aerosols. However, because radiation dose rate is mathematically analogous to mass of particles per unit (mass, volume, or surface area) of tissue, the ICRP66 Model can be used to simulate deposition patterns and resulting tissue burdens for human inhalation exposures to nonradioactive particles, including environmental aerosols. The deposition data used to develop the model were from human radioactive tracer studies in which accurate measurements were obtained using very low particulate mass burdens. The small respiratory tract burdens precluded the possibility of experimental artifact due to lung overload phenomena. Assuming that exposures to environmental aerosols do not cause altered rates of lung clearance, the model can be used to simulate accumulation and retention patterns of particles in the alveolar-interstitial (AI) region for chronic inhalation exposures to environmental aerosols. Software developed for use with the ICRP66 Model (LUDEP®, version 1.1; National Radiological Protection Board, 1994), was used to perform the simulations described in this paper.

For this application, the ICRP66 Model was simplified for ease of presentation

and to provide a level of detail approximately commensurate with the observed effects reported in epidemiological studies. The two extrathoracic compartments (ET_1 and ET_2) were combined and defined as the extrathoracic (ET) region; the two tracheobronchial compartments (BB and bb) were combined and defined as the tracheobronchial (TB) region. The AI region defined in the ICRP66 Model was not changed.

Deposition for the ET, TB and AI regions and retention patterns for the AI region were modeled for environmental aerosols (Figure 2) that were characterized for Philadelphia, PA, and Phoenix, AZ.[3] These environmental aerosols were chosen to represent a comparison between an eastern and western U.S. city. The size distributions of the aerosols from both cities were described as trimodal (fine, intermodal, and coarse modes). It is not known at this time whether the intermodal mode is real or an artifact of sampling procedures.[1] The distribution of mass, particle numbers, and particle surface area for the Philadelphia and Phoenix aerosols are indicated in Table 1.

Air concentrations for both environmental aerosols were assumed to be 50 $\mu g/m^3$, and inhalation of the aerosols was considered continuous for 24 hours/day, 7 days/week. Deposition rates (μg/day) were modeled for normal augmenters and adult male mouth breathers. Normal augmenters are individuals who normally breath through their noses, but who involuntarily switch to a combination of nose and mouth breathing as the ventilation rate increases (Figure 3). This change in breathing pattern occurs at a ventilation rate of about 2.1 m^3/hour, at which time about 60 percent of the minute ventilation is through the nose and about 40 percent is through the mouth. At a

ventilation rate of 5 m^3/hour, about 60 percent of the air is inhaled and exhaled through the mouth and 40 percent through the nose. Note that mouth breathers inhale and exhale about 70 percent through the nose at rest and about 30 percent through the nose at a breathing rate of about 5 m^3/hour. There is always a flow of at least 30 to 40 percent of inspired and expired air through the nose, with heavy exercise dictating that 60 to 70 percent of this inspired and expired air will flow through the mouth.

Three different ventilation activity patterns were used for modeling deposition, corresponding to the general population, light workers, and heavy workers. The patterns represent different amounts of time spent per day at different levels of exertion and therefore, ventilation (Table 2). Whereas particle size and distribution are key input parameters governing deposition of inhaled particles and represent key attributes of the ambient aerosols, ventilatory activity pattern is the major physiologic parameter.

For this modeling effort, daily average deposited particle mass and number burdens were normalized to either regional respiratory tract surface area (cm^2) or mass (g) of epithelium in each region were chosen as dose metrics to characterize acute exposures. Because chronic effects of particles are likely best attributed to particle burdens or damage over many years, steady-state average particle retention was modeled only in the AI region where clearance processes occur over weeks to years. Particle burdens in the AI region resulting from chronic exposures to the two example environmental aerosols were modeled for the normal augmenter from the general population. Model results for average retained particle burdens in the AI region were

normalized to the mass of AI epithelium and presented as specific lung burden (μg particles/g AI epithelium) as a function of time.

A very important input parameter to model chronic inhalation exposures was the dissolution-absorption half-time of the deposited particles. The ICRP66 Model accounts for clearance from the respiratory tract as a result of dissolution of particles or elution of their constituents, followed by absorption of the dissolved constituents into cells proximate to the particles, or into the circulatory system for redistribution or excretion. Information about the dissolution-absorption rates for particles in these environmental aerosols is not available. Rates for dissolution-absorption were assumed on the basis of particle size and probable chemical attributes of the three aerosol modes. The dissolution-absorption half-times for the fine, intermodal, and coarse aerosol modes were assumed to be 10, 100, and 1000 days, respectively, for both example aerosols. Another important variable for modeling chronic inhalation exposures to the AI region of the respiratory tract is the physical clearance rate for deposited particles. Default values recommended in the ICRP66 Model were used as physical clearance rates of these aerosol particles. Table 3 summarizes the assumptions used to model chronic exposures of adult male normal augmenters to these two trimodal environmental aerosols.

RESULTS

Predicted daily average mass deposition (μg/day) in the TB and AI regions as a function of particle size for an exposure concentration of 50 $\mu g/m^3$ is presented in Figure

4 for the Philadelphia environmental aerosol, and in Figure 5 for the Phoenix aerosol. Predictions are given for adult male normal augmenters versus mouth breathers and activity patterns for the general population, light workers, and heavy workers. When compared to normal augmentation, larger amounts of particles can penetrate to the TB or AI regions with mouth breathing because of the lower filtration efficiency of the mouth. Penetration to the lower respiratory tract is especially enhanced for the larger particles ($\geq$ 2 μm MMAD), which normally deposit preferentially in the ET region as a result of impaction. For heavy workers, in which about 70 percent of the ventilation is through the mouth (Figure 3), deposition of particles less than 2 μm diameter is almost independent of mode of breathing because the small particles deposit by sedimentation and diffusion, and only a very small portion of the fine aerosol fraction usually is deposited in the ET region. The differences between the regional deposition patterns for the Philadelphia and Phoenix aerosols are due to the fact that the mass of particles was about equally split between the fine and coarse modes of the Philadelphia aerosol, whereas 3/4 of the mass of the Phoenix aerosol was particles larger than 1 μm and 1/4 less than 1 μm.

Table 4 presents the predicted average daily mass deposition fraction of the example environmental aerosols as ng particles/cm^2/day for the ET, TB, and AI regions of a normal augmenter from the general population. The relative masses of particles per cm^2 reflect the large differences in surface area (see footnote to Table 4) for the three regions. Substantially more mass is deposited per cm^2 of the ET region than in the TB

or AI regions. However, particles that are deposited in the ET region clear rapidly via the mucociliary pathway. Likewise, whereas substantially more mass deposits per cm^2 on the surface of the TB region than the AI region, most of the particles that are deposited in the TB region are also believed to be cleared quickly. Table 5 presents the predicted daily deposition per gram of target tissue (ng particles/gram/day) for the ET epithelium, the TB epithelium, and the AI tissue.[1] Data in Tables 4 and 5 demonstrate that there are large differences in initial deposition metrics for the ET, TB, and AI regions when deposition is expressed as mass of particles either per surface area or per mass of epithelial tissue. It is noteworthy that a substantial mass of particles from the coarse aerosol modes is deposited on the TB epithelium, and this deposition should not be ignored, especially if a portion of the deposited particle burden is cleared slowly.[5]

Figure 6 shows predicted daily average particle number deposition normalized to respiratory tract surface area as a function of particle size. When average deposition is expressed as numbers of particles/cm^2/day, regional concentrations of deposited particles are different by 1 to 4 orders of magnitude, with ET > TB > AI. Particle numbers in these two environmental aerosols are dominated by the fine aerosol modes, so numbers of particles deposited/cm^2 in the ET, TB, and AI regions were predicted to be higher for particles less than 1 μm. However, about equal numbers of particles/cm^2 are predicted to deposit in each respective region of the respiratory tract for the very small particles and particles about 1 to 5 μm.

The modeling results for predicted average AI time-dependent burdens of particles

resulting from chronic exposures to the two environmental aerosols at a concentration of 50 $\mu g/m^3$ are presented in Figure 7. Equilibrium between deposition and clearance was predicted to occur after about 70, 700, and 7000 days, respectively, for the fine, intermodal, and coarse aerosol modes. The same total mass of aerosol particles was predicted to deposit per day in the AI region for both aerosols (Table 3). However, 1.5 times as much intermodal and 10 times as much coarse-mode Phoenix aerosol were deposited per day as compared with the Philadelphia aerosol. More particle mass occurred in the coarse mode for the Phoenix aerosol and a dissolution-absorption half-time of 1000 days was assumed in modeling the clearance of the coarse mode particles. Therefore, a higher equilibrium lung burden was predicted for the Phoenix aerosol than for the Philadelphia aerosol. Overall, individuals exposed for long periods to the Phoenix aerosol are predicted to have almost 4 times as much total dust in their lungs as individuals exposed to the Philadelphia aerosol, primarily because of the difference in the amount of coarse aerosol mode for these two environmental aerosols.

For chronic inhalation exposures to the Phoenix or Philadelphia environmental aerosols, assuming relatively constant physical and chemical attributes over time, equilibrium amounts of dust are predicted to be achieved after about 18 years. The steady-state retained burdens of particles would be comprised mainly of particles from the coarse aerosol mode, and the specific lung burden would remain constant as long as exposure conditions remained relatively constant.

DISCUSSION

The revised ICRP human respiratory tract dosimetry model was used to evaluate average daily deposition patterns in the ET, TB, and AI regions of the respiratory tract for example environmental aerosols characterized for Philadelphia, PA, and Phoenix, AZ. Model results indicate substantial differences between these environmental aerosols in deposition and retention metrics for the coarse mode particles. Such differences in deposition suggests that differences should be noted in biological responses to these aerosols if the coarse mode particles cause the responses.

The fine particle modes of these environmental aerosols contain more than 99 percent of the number distribution of particles. Because fine aerosol particles are deposited primarily by sedimentation and diffusion, they can penetrate deeply into the respiratory tract. Therefore, fine particles contribute a large fraction of the average thoracic deposition. The deposition metrics were similar for the fine modes of the two aerosols, which suggests that any differences in biological responses should be associated with differences in chemical constituents and/or surface area of the fine mode particles if they are responsible for biological responses.

Examination of alternative deposition metrics yields interesting information about deposition versus particle size in the TB and AI regions. For example, large numbers of all particle sizes are deposited per cm^2 (or per gram) of epithelium in the TB region. These deposition metrics for the TB region are two orders of magnitude larger than the same metrics for the AI region. Model results for either numbers of particles deposited

per cm^2 or per gram of TB epithelium suggest that all particle sizes in these environmental aerosols should be evaluated in terms of their potential importance to biological responses to inhaled environmental aerosols.

Particles from the coarse mode of environmental aerosols dominate long-term retention and cannot be excluded from evaluations of biological effects of environmental aerosols. This is an important consideration when directed toward regulating ambient aerosols with samples of size cut-points other than PM_{10} (for example $PM_{2.5}$). The PM_{10} samplers collect a range of particle sizes that approximates particles that are deposited in the human thorax (i.e., TB and AI regions) during inhalation exposures, even if breathing is via the mouth (Figure 8). A $PM_{2.5}$ sampler adequately collects ultrafine and fine particles of the environmental aerosol, but excludes a portion of the coarse aerosol mode particles that potentially could deposit in the respiratory tract. This modeling effort indicates that significant deposition of particles larger than the cut-point of a $PM_{2.5}$ sampler occurs and supports the use of the PM_{10} fraction as an exposure index of particles with the potential for thoracic deposition and retention. There is no clear dosimetric motivation for the use of a $PM_{2.5}$ fraction in relation to deposited or retained particle mass. However, a rationale for a fine particle standard could be based on consideration of differences in composition and potential toxicity of the fine versus coarse modes.[1]

Adequate information on key input parameters is an important factor in using the ICRP66 human respiratory tract dosimetry model, or any other model, to predict the

consequences of exposures to environmental aerosols. Breathing mode (normal augmentation versus mouth breathing) and ventilatory activity pattern were shown to be key determinants of initial deposition. Also, the predicted deposition and retention patterns represent averages. Local doses can be influenced by local ventilatory patterns in the thorax, but adequate information is not available to assess the degree of noniformity of particle deposition and retention resulting from differences in local ventilation patterns. Average dose predictions probably underestimate actual doses to specific local areas in the respiratory tract where deposition is enhanced by air flow patterns or by non-uniform clearance. Anatomical data are needed to support models that can be used to compute local versus average doses, especially across gender, age, and disease states (e.g., chronic obstructive pulmonary disease). Additionally, aerosol flow patterns during inspiration and expiration can influence particle deposition patterns. Air sampling strategies should collect data on microenvironment exposures so that dose construction efforts can take advantage of dosimetry models that account for inhalation dynamics by using ventilatory patterns as input and which thereby more accurately characterize total personal human inhaled dose.

Physical attributes (i.e., particle size and distribution) and other physicochemical factors (e.g., composition and hygroscopicity) are also important. These factors are relatively easy to quantify, and their routine reporting would aid dosimetry modeling efforts. With respect to constructing accurate retained dose metrics for particles in the respiratory tract, *in vivo* dissolution-absorption rate characteristics are key determinants

of particle clearance. These characteristics are more difficult to determine and were not done for the different modes of the Philadelphia and Phoenix aerosols. The approximations for dissolution-absorption rates used in this paper could therefore yield only illustrative modeling results that would be improved with accurate values for these parameters.

CONCLUSIONS

The ICRP human respiratory tract model can be used to help evaluate deposition of environmental aerosol particles in all regions of the respiratory tract. Various deposition metrics can be selected, including average mass or number of particles per unit of area or mass of the target tissues. The model can also be used to simulate chronic inhalation exposures that result in long-term, retained constituents of environmental aerosols.

Substantial amounts of environmental aerosols are deposited in the TB region. While clearance is rapid for most of the deposited particles, some fraction of the deposited particles remains associated with the TB epithelium for a significant amount of time after deposition and might be important to consider in evaluating immediate and long-term biological responses to environmental aerosols. Because a $PM_{2.5}$ sampler does not account for all particles with the potential for deposition in the thoracic region, especially for mouth breathers, these model results suggest that ambient air quality regulations should retain a PM_{10} standard.

Breathing mode and ventilatory activity pattern are key parameters that determine initial deposition. Data on differences in ventilatory activity pattern due to age, gender, and disease status would likely provide critical information on variability in susceptibility of the population due to the influence of these factors on dosimetry. Further, in order to construct total personal exposures, ventilatory activity patterns corresponding to the microenvironments (e.g., activities outdoors versus indoors) for which particles are sampled would be ideal data to facilitate the use of dosimetry models. The dissolution-absorption characteristics of an environmental aerosol are important parameters necessary for improved estimates of cumulative lung burdens of retained particles resulting from chronic inhalation exposures. This information is currently unavailable and is a requirement for making accurate long-term model projections.

DISCLAIMER

The views in this paper are those of the authors and do not necessarily reflect the views or policies of the U.S. Environmental Protection Agency. The U.S. government has the right to retain a nonexclusive royalty-free license in and to any copyright covering this article.

REFERENCES

1. U.S. Environmental Protection Agency: Air Quality Criteria for Particulate Matter. Research Triangle Park, NC: National Center for Environmental Assessment - RTP Office; EPA Report No. EPA/600/P-95/001aF-cF. 3V. Available from: NTIS, Springfield, VA; PB96-168224. 1996.

2. International Commission on Radiological Protection: ICRP Publication 66, Human Respiratory Tract Model for Radiological Protection. Elsevier Science Inc., Tarrytown, NY (1994).

3. Lundgren, D.A.; Hausknecht, B.J.: Ambient Aerosol Mass Distribution of 1 to 100 μm Particles in Five Cities. Presented at 75th Annual Meeting, Air Pollution Control Association, New Orleans, LA, paper no. 82-45.4, June, 1982. Air Pollution Control Association, Pittsburgh, PA (1982).

4. Miller, F.J.; Martonen, T.B.; Ménache, M.G.; *et al.*: Influence of Breathing Mode and Activity Level on the Regional Deposition of Inhaled Particles and Implications for Regulatory Standards. In: Inhaled Particles IV: Proceedings of an International Symposium and Workshop on Lung Dosimetry, Cambridge, 1985. Ann. Occup. Hyg. 32(suppl. 1):3-10. J. Dodgson, R. I. McCallum, M. R. Bailey, D. R. Fisher, eds. (1988)

5. Scheuch, G.: Size Dependent Particle Clearance and Retention in the Human Tracheobronchial Region. Appl. Occup. Environ. Hyg. (in press).

Table 1. Percent of the total mass, particle number, or surface area of each of the three modes for Philadelphia and Phoenix aerosols.

Aerosol	Philadelphia			Phoenix		
Mode	Mass	Number	Surface	Mass	Number	Surface
Fine	48.2	99.946	95.4	22.4	99.6	85.5
Intermodal	7.4	0.050	2.5	13.8	0.3	7.4
Coarse	44.3	0.004	2.1	63.9	0.1	7.1

Table 2. Human activity patterns and associated respiratory minute ventilation[a]

Activity Pattern	Sleeping (0.45 m^3/h)		Sitting (0.54 m^3/h)		Light Activity (1.5 m^3/h)		Heavy Activity (3.0 m^3/h)		Total/Day	
	Hours	Total m^3	Hours	Total m^3	Hours	Total m^3	Hours	Total m^3	Hours	Total m^3
Adult male, general population	8	3.6	8	4.32	8	12	0	0	24	19.9
Adult male, light work	8	3.6	6.5	3.5	8.5	12.75	1	3	24	22.85
Adult male, heavy work	8	3.6	4	2.16	10	15	2	6	24	26.76

[a] International Commission on Radiological Protection (Ref. 2).

Table 3. Model assumptions used to predict average particle mass retention in the AI region of the respiratory tract of an adult male normal augmenter with a general population activity pattern for chronic exposures (24 hours/day, 7 days/week) to environmental aerosols containing 50 μg particles/m^3.

- Average daily deposition (μg) in the AI region:

	Fine	Intermodal	Coarse	Total
Philadelphia	37.1	11.3	1.2	49.6
Phoenix	26.5	17.2	11.9	55.6

- Dissolution-absorption half-times for aerosol modes:
  - fine = 10 days;
  - intermodal = 100 days; and
  - coarse = 1000 days.

- Default ICRP66 values for particle physical clearance parameters (see Figure 1).

Table 4. Predicted daily mass of particles deposited per unit of tissue surface area (ng particles/cm^2/day) in a normal augmenter for example environmental aerosols inhaled for 24 hours/day, 7 days/week at a concentration of 50 $\mu g/m^3$.

	Philadelphia			Phoenix		
Region[a]	Fine	Intermodal	Coarse	Fine	Intermodal	Coarse
Extrathoracic (ET)	81	96	560	16	140	890
Tracheobronchial (TB)	3.2	1.3	0.9	3.0	1.8	3.5
Alveolar-Interstitial (AI)	0.025	0.0077	0.00078	0.018	0.012	0.0081

[a] Surface area of ET epithelium = 470 cm^2; TB epithelium = 2690 cm^2; AI epithelium = 1.475×10^6 cm^2 (from Ref. 2, Table 1).

Table 5. Predicted daily mass of particles deposited per unit of tissue mass (ng particles/gram tissue/day) in a normal augmenter for example environmental aerosols inhaled for 24 hours/day, 7 days/week at a concentration of 50 $\mu g/m^3$.

	Philadelphia			Phoenix		
Region[a]	Fine	Intermodal	Coarse	Fine	Intermodal	Coarse
Extrathoracic (ET)	16,000	19,000	110,000	3,200	28,000	180,000
Tracheobronchial (TB)	1,700	670	470	1,500	920	1,800
Alveolar-Interstitial (AI)	34	10	1	24	16	11

[a] Mass of ET epithelium = 2.4 g, calculated from surface area of 470 cm^2 x average thickness of 50 μm; TB epithelium = 5.2 g, calculated from surface area of 290 cm^2 for the BB epithelium x average thickness of 15 μm, plus surface area of 2400 cm^2 x average thickness of 15 μm; AI epithelium = 1100 g (Ref. 2, Figures 5 and 6; Table 1).

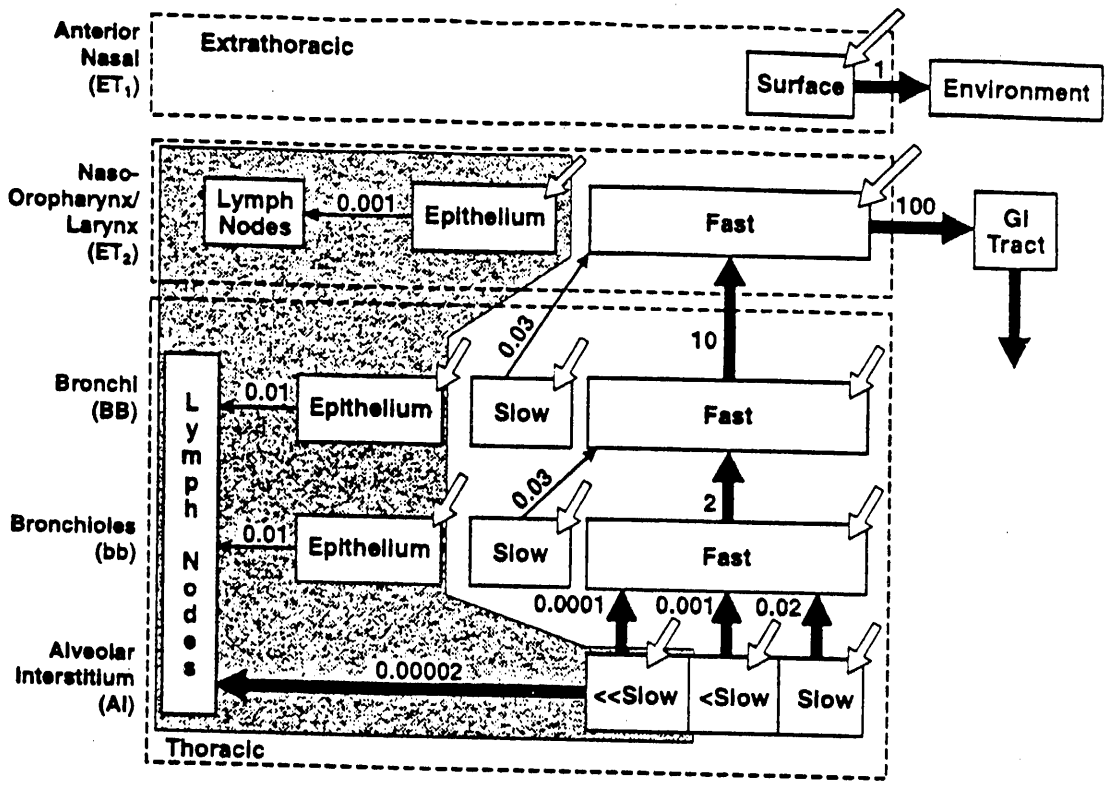


Figure 1. Schematic representation of the ICRP66 Human Respiratory Tract Dosimetry Model (Ref. 1). Open arrows show regions into which inhaled particles can deposit. Solid arrows represent time-dependent particle transport pathways from each region. Particle transport rate constants shown beside each solid arrow are default values in units of d^{-1}. Stippling indicates the compartments with clearance pathways sequestered in tissue rather than associated by surface transport. ET_1 = anterior nose; ET_2 = posterior nasal passages, larynx, pharynx, and mouth; BB = bronchial region; bb = bronchiolar region (bronchioles and terminal bronchioles); AI = alveolar interstitial region (respiratory bronchioles, alveolar ducts and sacs with their alveoli, and interstitial connective tissue).

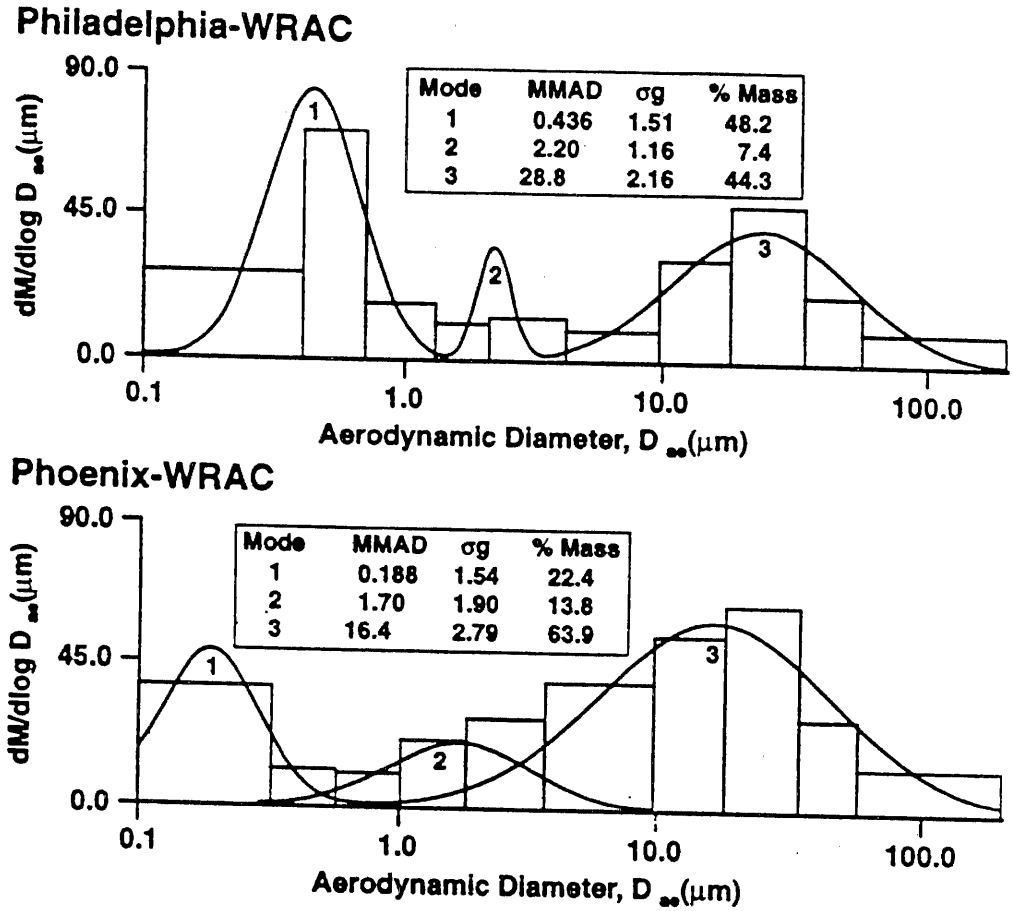


Figure 2. Example environmental aerosols for two U.S. cities. The aerosols were collected using a Wide Range Aerosol Classifier (WRAC)(modified from Ref. 3).

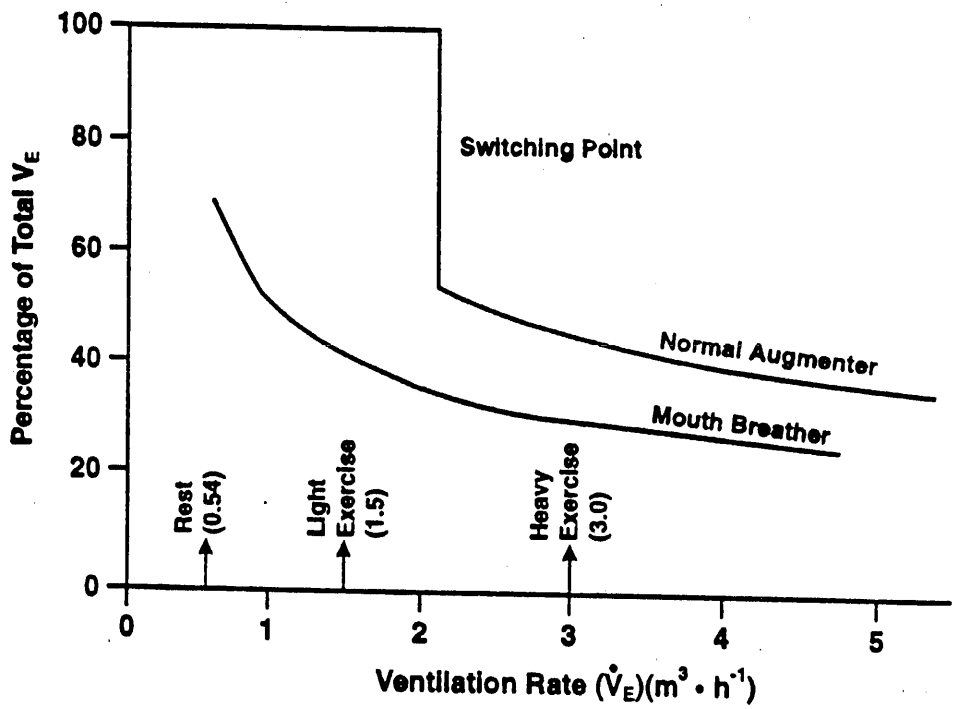


Figure 3. Percentage of total ventilation ($\dot{V}_E$) passing through the nasal route of human normal augmenters (solid curve) and habitual mouth breathers (broken curve). Source: Ref. 1, as derived from Ref. 4).

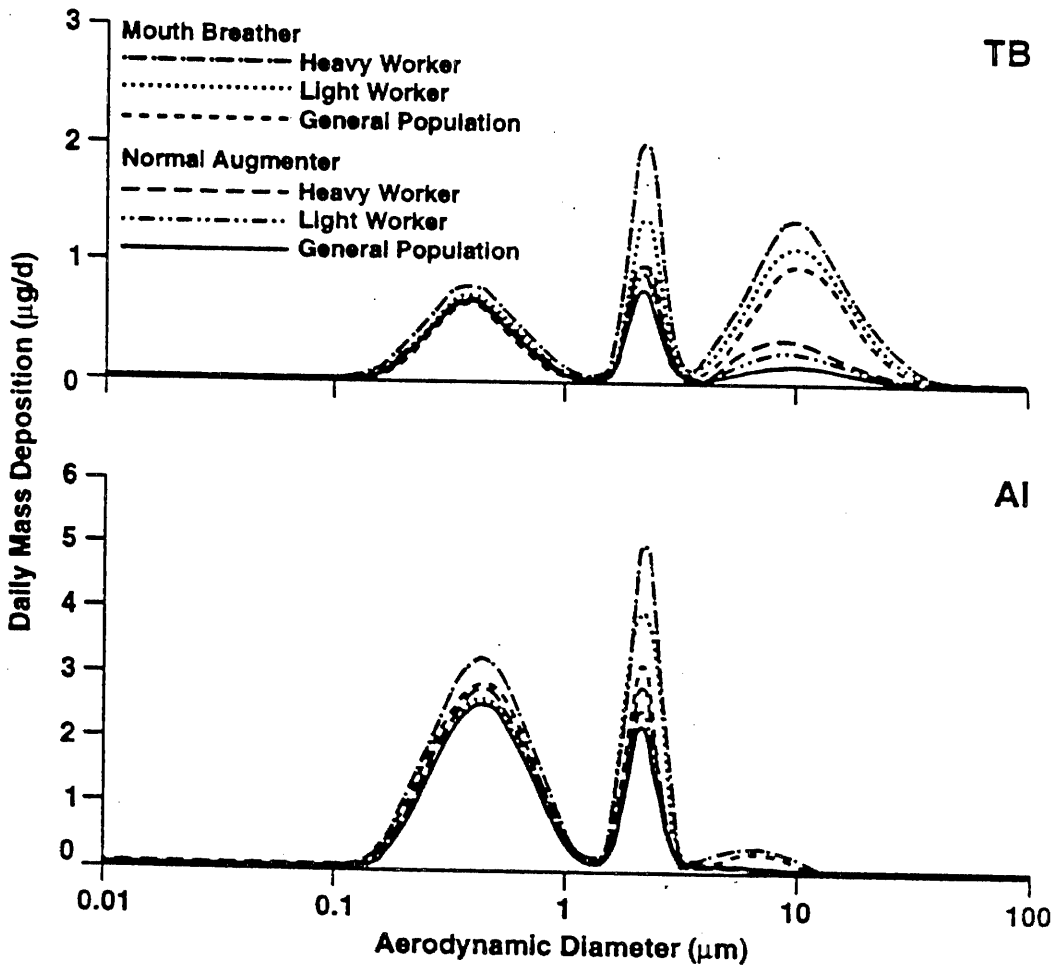


Figure 4. Predicted average daily mass deposition (μg/day) as a function of aerodynamic particle size (MMAD) for the Philadelphia environmental aerosol inhaled at a concentration of 50 $\mu g/m^3$.

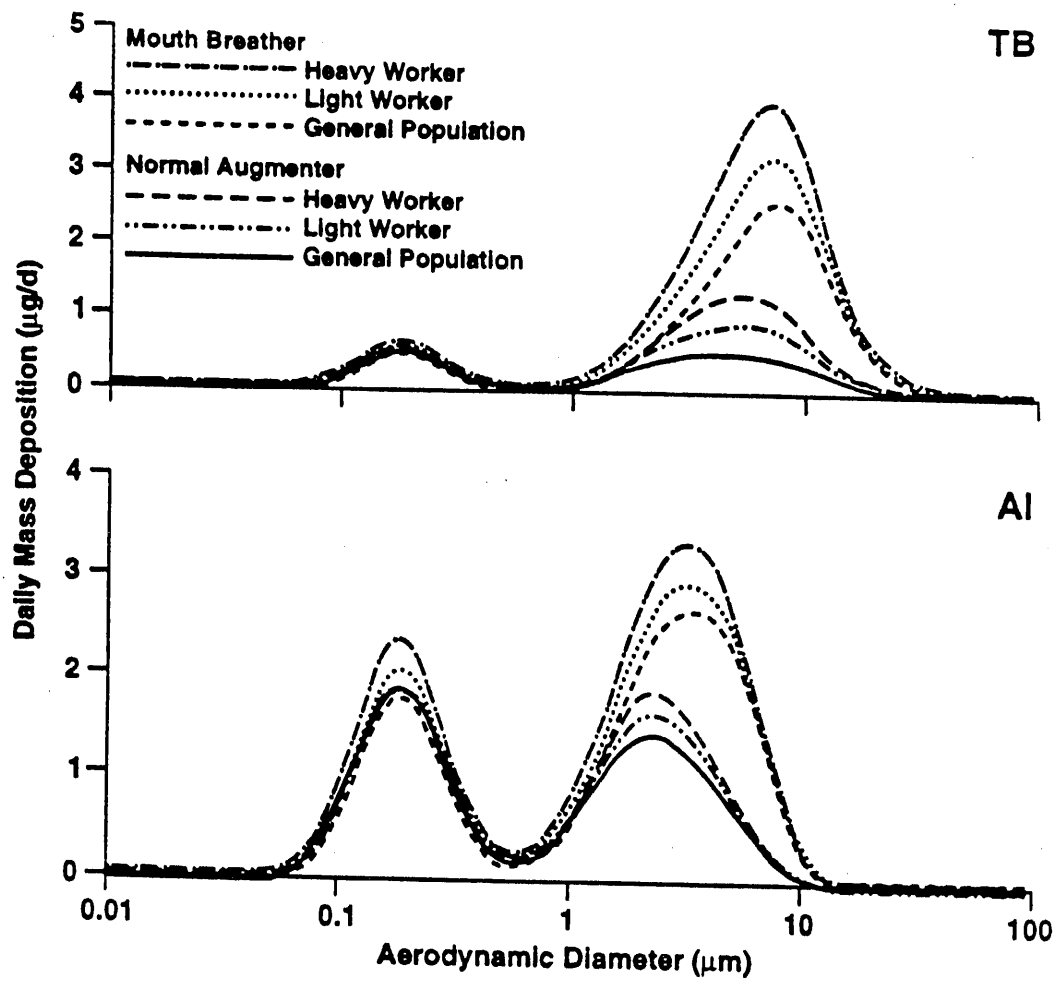


Figure 5. Predicted average daily mass deposition (μg/day) as a function of aerodynamic particle size (MMAD) for the Phoenix environmental aerosol inhaled at a concentration of 50 $\mu g/m^3$.

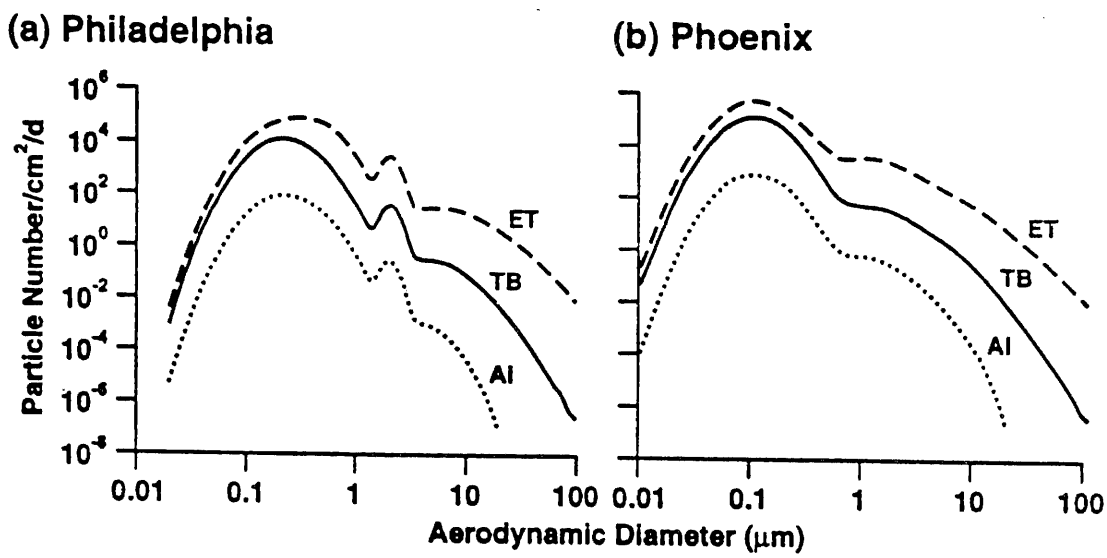


Figure 6. Predicted average daily mass particle deposition per unit of surface area (particles/cm^2/day) in a normal augmenter from the general population as a function of aerodynamic particle size (MMAD) for the Philadelphia and Phoenix environmental aerosols inhaled at a concentration of 50 μg/m^3.

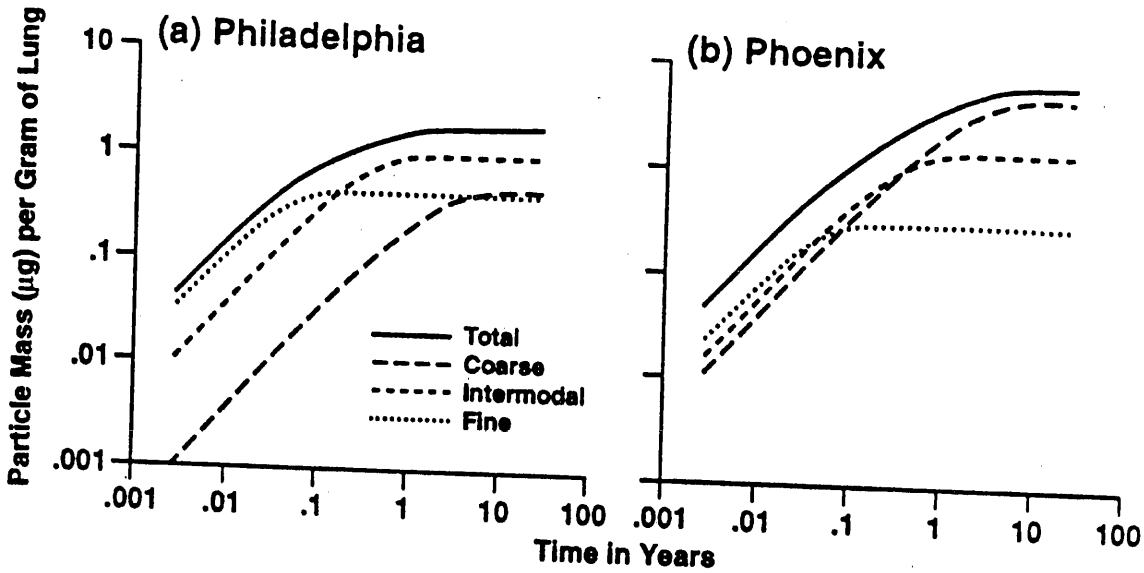


Figure 7. Specific average lung burdens of particles (μg particles/g lung) predicted for a normal augmenter from the general population exposed 24 hours/day, 7 days/week to Philadelphia or Phoenix environmental aerosols containing 50 μg particles/m^3.

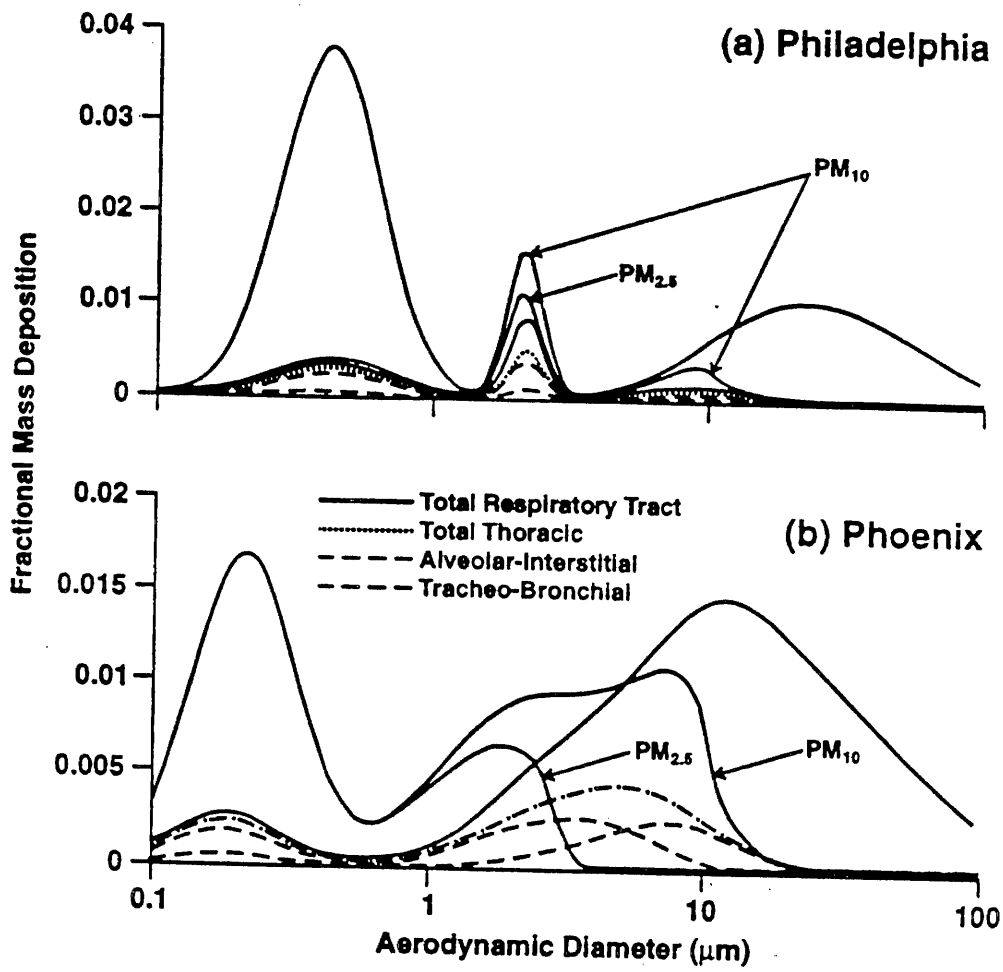


Figure 8. Fractional mass deposition in PM_{10} and $PM_{2.5}$ aerosol samplers compared with predicted deposition in adult male mouth breathers.

PERSONAL EXPOSURE OF ADULTS WITH CARDIORESPIRATORY DISEASE TO PARTICULATE ACID AND SULFATE IN SAINT JOHN, NEW BRUNSWICK, CANADA

David M. Stieb[A], Jeffrey R. Brook[B], Irvin Broder[C], Stan Judek[A], and Richard T. Burnett[D]

[A]Air Quality Health Effects Research Section,
Health Canada;
[B]Atmospheric Environment Service,
Environment Canada;
[C]Gage Research Institute,
University of Toronto;
[D]Biostatistics Division,
Environmental Health Directorate,
Health Canada

Correspondence and reprint requests should be addressed to David M. Stieb, Air Quality Health Effects Research Section, 0803C Tunney's Pasture, Ottawa, ON, Canada, K1S 0P9
(613) 957-3132 (phone), (613) 941-4546 (fax), dave_stieb@isdtcp3.hwc.ca (e-mail)

Paper presented at the 2nd Colloquium on Particulate Air Pollution and Human Health
Park City, Utah, May 2, 1996

ABSTRACT

Saint John is the site of an ongoing study of the relationship between cardiorespiratory emergency department visits and airborne particles, including particulate acid and sulfate. The purpose of the present study was to assess the extent to which fixed site monitors reflect average personal exposure to fine particle sulfate and acidity among adults visiting the emergency department with cardiorespiratory disease. Study participants had made an emergency department visit for cardiorespiratory disease in the previous 12 months and resided within approximately 5 km of the fixed site monitor which records the highest sulfate and acid concentrations in Saint John. Twenty-one volunteers wore personal annular denuders, during the period 7:00 a.m. to 6 p.m. (mean duration 7.6 hours) for up to 4 separate days between July 6 and August 11, 1995, and completed a time-activity diary for each sampling period. Subjects ranging from 49 to 85 years of age completed a total of 62 sampling periods. The mean proportion of time spent indoors, outdoors and in vehicles was respectively 81.8, 7.6 and 10.5 percent. Mean personal sulfate (29.8 $nmol/m^3$) and acid concentrations (17.1 $nmol/m^3$) were lower than measurements at fixed site monitors (mean sulfate 49.1 $nmol/m^3$; mean acid 37.6 $nmol/m^3$). The correlation (R^2) between mean personal and fixed site sulfate was 0.90 ($p<0.0001$), and high daily concentrations measured at the fixed site were reflected in high mean personal concentrations. There was little correlation between mean personal and fixed site acid measurements ($R^2=0.06$; $p=0.29$), although some high personal measurements corresponded to high fixed site concentrations. In this population of adults visiting an emergency department with cardiorespiratory disease, fixed site sulfate monitors appear to accurately reflect daily variability in average personal exposures to particulate sulfate. Personal exposure to particulate acid does not appear to be well-represented by fixed site monitors.

KEY WORDS: Air pollution, particulates, aerosols, sulfate, acid, personal monitoring, exposure assessment

PERSONAL EXPOSURE OF ADULTS WITH CARDIORESPIRATORY DISEASE TO PARTICULATE ACID AND SULFATE IN SAINT JOHN, NEW BRUNSWICK, CANADA

Introduction

There is a growing body of literature linking air pollution with adverse health effects on the basis of the association between data from fixed site air pollution monitors, and "administrative" data on such outcomes as deaths (1), hospital admissions (2), emergency department visits (3), physician billings (4), and school attendance (5). The essential characteristic of these data is that they were originally collected for a purpose other than examining the relationship between air pollution and health, and the lack of data on individual exposure may result in exposure misclassification (6). A number of recent studies suggest that for some pollutants, personal exposure is not necessarily well represented by measurements made at fixed site monitors (7-9).

In this study, we examine the relationship between personal measurements of sulfates (SO_4^{2-}) and particle strong acidity (H^+), and measurements made at fixed site monitors, among adults with cardiorespiratory disease, who had recently made a visit to the emergency department. The primary objective was to determine whether average personal exposure in this population is accurately reflected by fixed site monitors. This study was conducted in the context of an epidemiologic study being carried out in Saint John, New Brunswick, Canada. This daily time series study is intended to determine: the relationship between air pollution and the frequency of cardiorespiratory ED visits; the role of air pollution relative to other triggers; and the broad health, quality of life and economic burden of air pollution-attributable cardiorespiratory disease episodes (10).

Methods

Study participants were recruited from a database on cardiorespiratory emergency department visits to Saint John Regional Hospital. To be included in the study, participants had to have made an ED visit for cardiorespiratory disease in the previous 12 months, and to have resided within approximately 5 km of the central site monitor which records the highest H^+ and SO_4^{2-} concentrations in Saint John (11). We originally intended to restrict participation to individuals 60 years of age or older, who were thought to be at greater risk of adverse health effects of air pollution. However we were unable to recruit a sufficient number of subjects using this criterion and therefore included some subjects under 60 years of age.

Subjects wore personal annular denuders (PADs) for a continuous period of approximately 8 hours, generally during the period from 7:00 a.m. to 6 p.m. for up to 4 days between July 6 and August 11, 1995. These samplers, which have been described in detail elsewhere (7,9), weigh approximately 5 pounds, including pump and batteries, and were worn in a knapsack or shoulder bag carried by the subject. The PADs were loaded with single Teflon filters (Gelman Sciences 37 mm Teflon), and the upstream denuders

were coated with citric acid to remove ammonia from the air stream. Study technicians visited subjects on the morning sampling was to start, and instructed them on use of the sampler. Pump flow was set at 4 L/min and flow was measured at the beginning and end of the sampling period. For each day that personal samples were collected, a sampler was also operated at the fixed site for the same duration as the personal samples. This was done because the existing fixed site sampler operated on a 24 hour schedule. Duplicate fixed site measurements were made on one third of these days. For all personal samples, subjects completed a time-activity diary which documented the duration of the sampling period by location (eg. home, office, car, store), geographic zone (based on the first 3 digits of the postal code), whether outdoors or indoors with windows open or closed, whether they were in the presence of tobacco smoke, and their breathing level (normal or fast).

Teflon filters from the PADs were extracted in a perchloric acid solution (pH=4). The extracts were analyzed for acidity using pH measurement, and for sulfate, nitrate, and ammonium using ion chromatography. The denuder extracts were not quantified (i.e. the denuder was simply used as an ammonia scrubber). The detection limit for acidity, which was based on the standard deviation of the acidity measurements from the blank filters (n=5), was 21 nmol/m^3. The detection limits for sulfate, nitrate and ammonium, which were also determined from the field blanks, were less than 1 nmol/m^3, but at these low concentrations measurement precision was poor. However, for sulfate concentrations above 20 nmol/m^3, precision in chemical analysis was better than 10%.

Statistical analysis was carried out on a personal computer using PC-SAS for Windows (release 6.10). Negative H^+ concentrations were set to zero for statistical analysis. The relationship between personal and fixed site measures was examined using the REG and GLM procedures in SAS (12). Regressions based on daily means of a number of personal samples were weighted by the number of samples per day. Regressions based on individual personal samples assumed that multiple measurements on the same individual were independent. Model goodness of fit was assessed using the R-square and model p-value.

Results

Characteristics of the study subjects are summarized in table I. Twenty one subjects completed a total of sixty-two sampling periods, according to the schedule shown in figure 1. The average duration of personal sampling was 7.6 hours, with a range of 4.3-9.8 hours, and the average duration recorded in activity diaries was 7.5 hours, with a range of 3.9-9.8 hours, indicating that a small proportion of personal sampling time was not captured in activity diaries. Sampling time for fixed site monitors averaged 7.7 hours, with a range of 3.7-8.8 hours.

The total duration of each activity diary was used as a weight in calculating average activity patterns. These data revealed that on average, the majority of sampling time was spent in the house, and other indoor locations, followed by in cars or other

vehicles, while a small proportion of time was spent outdoors (see table II). Compared to a general population sample of various age groups in Saint John (table II), study subjects spent more time indoors and at home, and less time outdoors (Personal communication, Dr. J. Leech, Health Canada, 1996). Windows were reported as open 51.9 % of the time spent indoors and 41.7 % of the time spent in a car. Although none of the subjects were current smokers, 11.9 % of sampling time was reported to be in the presence of tobacco smoke. Faster than normal breathing was reported during 7.6% of sampling time. All subjects lived within zone J outlined in figure 2, where they spent the majority of sampling time. The proportion of sampling time spent in other selected geographic zones around Saint John is also shown in this figure.

Summary data from personal and fixed monitors, which are shown in table III, indicate that both personal SO_4^{2-} and H^+ were lower than fixed site concentrations, although the ratio between personal and fixed site concentrations tended to be lower for H^+ than SO_4^{2-}. Duplicate fixed site measurements are shown in table IV, and reveal that SO_4^{2-} measurements were more precise than H^+ measurements, as reflected by both the mean absolute and relative difference between duplicates.

Figures 3A and 3B plot personal and fixed site SO_4^{2-} and H^+ concentrations by date. These plots reveal that temporal variability in personal SO_4^{2-} exposure was mirrored closely by fixed site concentrations, although there were a small number of outliers, where personal concentrations exceeded fixed site concentrations by a wide margin (July 18 and 31, and August 4). For personal H^+ exposure, although some peak personal and fixed site concentrations occurred together, they generally appeared poorly correlated. Linear regressions between mean personal and fixed site measurements are shown in figures 4A and 4B, and again reveal a much stronger relationship between personal and fixed site SO_4^{2-} than between personal and fixed site H^+. Although we were primarily interested in the relationship between average personal exposure in this population and fixed site concentrations, we also examined the relationship between individual personal measurements and fixed site concentrations. As seen in figures 5A and 5B, personal and fixed site SO_4^{2-} remained much more strongly associated than was the case for H^+. The relationship between both mean daily personal and individual personal SO_4^{2-} and fixed site concentrations were strengthened slightly by exclusion of the outliers noted earlier.

The influence of potential mediators of personal exposure on the relationship between personal and fixed site measurements was assessed by introducing interaction terms into regressions of personal versus fixed site measurements. Factors assessed included percent of time outdoors ("$percent_{out}$"), percent of time outdoors or indoors (including in vehicle) with windows open ("$percent_{out/wopen}$"), percent of time in zone "j" ("$percent_{zonej}$"), and distance of the subject's residence from the fixed site monitor ("distance"). Selected models which include these interaction terms are summarized in table V. (While interaction effects for both $percent_{out}$ and $percent_{out/wopen}$ were considered for both SO_4^{2-} and H^+, only the strongest of the two effects is presented in table V.) Only percent of time outdoors (SO_4^{2-}) and percent of time outdoors or indoors with windows

open (H^+), were associated with statistically significant interaction terms.

The effects of these interactions on the relationship between personal and fixed site concentrations are shown in figures 6A and 6B. In these figures, the regression line relating personal and fixed site concentrations is plotted for 4 discrete values of $percent_{out}$ (for SO_4^{2-}), and $percent_{out/wopen}$ (for H^+), representing selected percentiles in the distribution of these variables. The individual personal measurements are also displayed, "÷" symbols representing samples during which $percent_{out}/percent_{out/wopen}$ was greater than a given cutpoint, and "." symbols representing all other samples. For both SO_4^{2-} and H^+, the slope relating personal and fixed site concentrations increases as percent of time outdoors/ and/or indoors with windows open increases. Although these interaction terms were statistically significant, they generally did not significantly improve the fit of the models as compared with models without interaction terms, as judged by the model p-value and R-square. The only exception to this was the H^+ model which included an interaction term for $percent_{out/wopen}$. Even this model, however, explained less than 10 per cent of the variability in personal acid measurements. A variety of alternative specifications of the interaction terms was also assessed (i.e. quadratic, linear quadratic, and log), again with negligible improvement in fit versus models without interaction terms.

Discussion

To our knowledge, there are no other published studies of personal exposure to SO_4^{2-} and H^+ in a population of older adults with cardiorespiratory conditions. Although, *a priori*, one might expect this population to be less highly exposed to outdoor air pollution because of limited vigorous outdoor physical activity compared to the general population, the slope and R^2 we report here relating individual personal SO_4^{2-} measurements to fixed site monitors, are very similar to those reported by Suh et al. in their study of 24 children in Uniontown, Pennsylvania (7), as well as by Brauer et al. in their study of adult volunteers in Boston (9). Thus we reproduced these results quite closely despite the fact that our study subjects probably spent considerably less time outdoors, that our sampling times were shorter (8 hours versus 12 and 24 hours in the Suh and Brauer studies respectively), and that ambient SO_4^{2-}concentrations were much lower in Saint John. This suggests that SO_4^{2-} penetrates effectively indoors, and that variability in measurements of SO_4^{2-} concentrations made at fixed site monitors accurately reflect variability in average personal exposure to SO_4^{2-}, even in populations which spend a small proportion of their time outdoors, and in regions with low to moderate ambient sulfate concentrations.

As in Suh's study (7), we found that measurements of H^+ made at fixed site monitors did not accurately reflect personal exposures, although the correlation between fixed site and personal measurements was lower in our study. The smaller proportion of time spent outdoors by our subjects, a shorter sampling period, and lower ambient acid concentrations in Saint John, may account for the weaker correlation observed in our study. In contrast, in Brauer's study (9), the correlation between personal and fixed site

H^+ concentrations was higher than that for sulfates, despite the fact that mean fixed site concentrations were actually lower than in our study. The much closer correlation in Brauer's study may relate to their sampling strategy, in which subjects increased the amount of time they spent outdoors when high concentrations of H^+ were anticipated.

Although the effects of certain potential mediators of the relationship between personal and fixed site measurements (eg. activity patterns) were statistically significant when included in models as interaction terms, none significantly improved our ability to explain variability in personal measurements.

In the context of the daily time series analysis being carried out in Saint John, it appears that temporal variability in fixed site SO_4^{2-} concentrations may be used as an accurate measure of variability in average personal exposure, even for individuals who spend less time outdoors than the general population. H^+ measurements made at fixed sites, on the other hand, do not appear to accurately represent personal exposure. Interestingly, some studies have nonetheless found significant associations between H^+ measured at fixed site monitors and adverse health effects (13,14), and in general, it has been suggested that H^+ may be a potent constituent of particulates in terms of contributing to adverse health effects. The poor correlation between personal H^+ exposure and fixed site concentrations suggests that if H^+ is in fact an important constituent of particulates, it may not contribute to health effects directly, but may potentiate the effects of other constituents of particles.

Conclusions

In this population of adults visiting an ED with cardiorespiratory disease, fixed site SO_4^{2-} monitors appear to accurately reflect daily variability in average personal SO_4^{2-} exposures. Personal exposure to H^+ does not appear to be well-represented by fixed site monitors.

Recommendations

Our results support the use of fixed site monitors to represent average personal exposure to SO_4^{2-} in daily time series studies, even in populations who spend less time outdoors than the general population, and in regions where SO_4^{2-} concentrations are low to moderate. Our results also suggest that weighting fixed site concentrations of SO_4^{2-} using activity patterns or other variables may not significantly improve exposure classification in these studies. Given the poor correlation between personal exposure and fixed site measurements of H^+ at low ambient H^+ levels, further investigation is required to understand the direct and/ or indirect mechanisms through which H^+ may exert effects on health, to identify other specific hazardous constituents of particles, and to validate their associations with adverse health effects.

References

1. Pope, C.A.; Schwartz, J.; Ransom, M.R.: Daily mortality and PM_{10} pollution in Utah Valley. Arch. Environ. Health 47:211-217 (1992).
2. Burnett, R.T.; Dales, R.; Krewski, D.; Vincent, R.; et al.: Associations between Ambient Particulate Sulfate and Admissions to Ontario Hospitals for Cardiac and Respiratory Diseases. Am. J. Epidemiol. 142(1):15-22 (1995).
3. Schwartz, J.; Slater, D.; Larson, T.V.; Pierson, W.E.; et al.: Particulate Air Pollution and Hospital Emergency Room Visits for Asthma in Seattle. Am. Rev. Respir. Dis. 147:826-831 (1993).
4. Gordian, M.E.; Morris, S.; Özkaynak, H.; Xue, J.; et al.: Particulate Air Pollution and Respiratory Disease in Anchorage, Alaska. In Particulate Matter: Health and Regulatory Issues-- Proceedings of an International Specialty Conference, Pittsburgh, Pennsylvania, 1995, pp. 143-166. Air and Waste Management Association, Pittsburgh (1995).
5. Ransom, M.R.; Pope, C.A.: Elementary school absences and PM_{10} pollution in Utah Valley. Environ. Res. 58:204-219 (1992).
6. Özkaynak, H.; Ryan, P.B.; Spengler, J.D.; Laird, N.M.: Bias due to misclassification of personal exposures in epidemiologic studies of indoor and outdoor air pollution. Environ. Int. 12:389-393 (1986).
7. Suh, H.H.; Spengler, J.D.; Koutrakis, P.: Personal Exposures to Acid Aerosols and Ammonia. Environ. Sci. Technol. 26(12):2507-2516 (1992).
8. Liu, L.-J.S.; Koutrakis, P.; Leech, J.; Broder, I.: Assessment of Ozone Exposures in the Greater Metropolitan Toronto Area. J. Air Waste Manage. Assoc. 45:223-234 (1995).
9. Brauer, M.; Koutrakis, P.; Spengler, J.D.: Personal Exposures to Acidic Aerosols and Gases. Environ. Sci. Technol. 23:1408-1412 (1989).
10. Stieb, D.M.; Beveridge, R.C.; Brook, J.R.; Burnett, R.T.; et al.: The Saint John Particle Health Effects Study - Measuring Health Effects, Health Costs and Quality of Life Impacts using Enhanced Administrative Data: Design and Preliminary Results. In Particulate Matter: Health and Regulatory Issues-- Proceedings of an International Specialty Conference, Pittsburgh, Pennsylvania, 1995, pp. 131-142. Air and Waste Management Association, Pittsburgh (1995).
11. Brook, J.R.; Wiebe, H.A.; Stieb, D.M.; Burnett, R.T.: Saint John, NB, Particle Health Effects Study: Determination of Ambient Exposures to Respirable Particles. In Particulate Matter: Health and Regulatory Issues-- Proceedings of an International Specialty Conference, Pittsburgh, Pennsylvania, 1995, pp. 347-357. Air and Waste Management Association, Pittsburgh (1995).
12. SAS Institute Inc.: SAS/STAT® User's Guide, Version 6, Fourth Edition, Volume 2, SAS Institute Inc., Cary, NC (1989).
13. Thurston, G.D.; Ito, K.; Hayes, C.G.; Bates, D.V.; et al.: Respiratory Hospital Admissions and Summertime Haze Air Pollution in Toronto, Ontario: Consideration of the Role of Acid Aerosols. Environ. Res. 65:271-290 (1994).
14. Neas, L.M.; Dockery, D.W.; Koutrakis, P.; Tollerud, D.J.; et al.: The Association of Ambient Air Pollution with Twice Daily Peak Expiratory Flow Rate Measurements in Children. Am. J. Epidemiol. 141(2):111-122 (1995).

Table I.-- Characteristics of study subjects

Variable	Mean (range) / Percent
Age (years)	66 (49-85)
% female	71.4
Smoking:	
% former smokers	52.4
% never smokers	47.6
Primary diagnosis (% of sample)	
Asthma	14.3
Chronic Obstructive Pulmonary Disease	9.5
Other Respiratory (Pneumonia/ Bronchitis)	28.6
Heart Disease	47.6
Distance of residence from fixed site monitor (km)	2.2 (0.6-3.9)

Table II.-- Percent of sampling time spent in various locations

Location	Percent of sampling time			
	Personal Monitoring Study	Canadian Human Activity Patterns Survey Saint John sample, summer 1995 (7 a.m. - 7 p.m.)		
	(n=21)	Adults (≥ 18) (n=189)	Youth (12-17) (n=32)	Children (≤11) (n=57)
House	64.0	39.8	50.0	48.3
Office	7.3			
Store	4.8			
Other	5.7			
INDOORS (total)	81.8	71.0	66.0	61.3
Street	2.0			
Lawn/ outside house	3.6			
Other	2.0			
OUTDOORS (total)	7.6	15.5	26.2	31.3
CAR/ VEHICLE	10.5	13.5	7.7	7.4

Table III.-- Summary of personal and fixed site sampling data

Variable	n	Mean (SD)	Range
Personal SO_4^{2-} (nmol/m^3)	62	29.8 (34.3)	0.5-171.1
Fixed site SO_4^{2-} (nmol/m$^{3)}$	28	49.1 (53.1)	1.4-214.3
Personal H^- (nmol/m^3)	62	17.1 (15.7)	0-83.1
Fixed site H^+ (nmol/m^3)	28	37.6 (37.2)	0-121.8

Table IV. -- Precision of duplicate fixed site measurements of SO_4^{2-} and H^+

Date	SO_4^{2-}				H^+			
	Maximum (nmol/m^3)	Minimum (nmol/m^3)	Max - Min (nmol/m^3)	(Max - Min)/ Max (%)	Maximum (nmol/m^3)	Minimum (nmol/m^3)	Max-Min (nmol/m^3)	(Max - Min)/ Max (%)
July 6	12.9	11.4	1.5	11.6	32.9	30.5	2.4	7.3
July 13	63.3	58.0	5.3	8.4	102.3	65.3	37.0	36.2
July 20	31.6	26.4	5.2	16.5	51.6	46.8	4.8	9.3
July 21	155.3	154.0	1.3	0.8	121.8	96.9	24.9	20.4
July 27	97.8	92.6	5.2	5.3	59.6	57.9	1.7	2.9
July 31	4.4	3.9	0.5	11.4	2.3	1.3	1.0	43.5
Aug. 8	25.4	22.4	3.0	11.8	16.5	0.0	16.5	100.0
MEAN	55.8	52.7	3.1	9.4	55.3	42.7	12.6	31.4

Table V.-- Influence of selected factors on the relationship between personal and fixed SO_4^{2-} and H^+

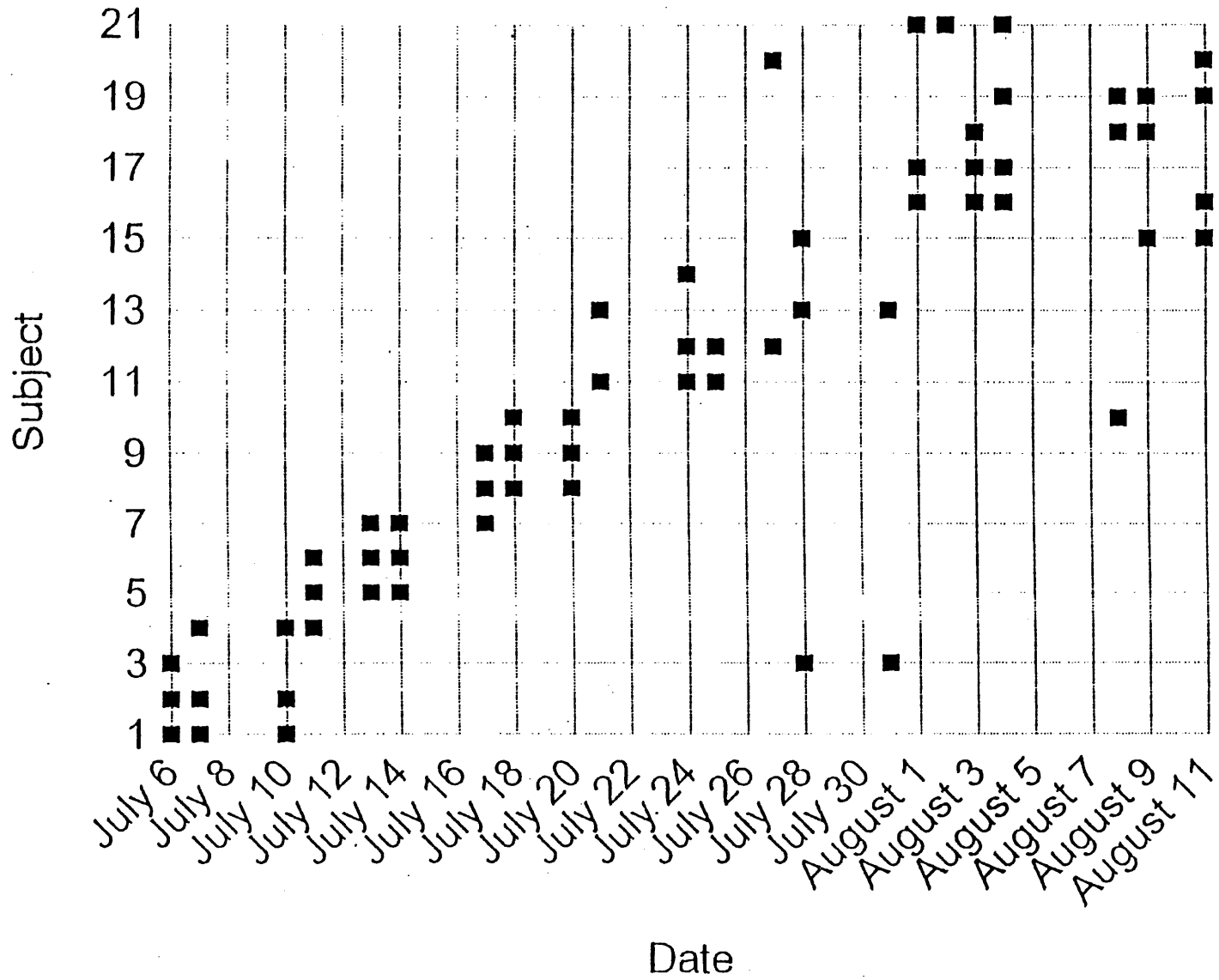
Dependent Variable	Explanatory Variable[a]	β(S.E.)	Parameter p-value	Model p-value	Model R-square
personal SO_4^{2-} (nmol/m^3)	$(SO_4^{2-})_f$	0.53 (0.05)	<0.0001	<0.0001	0.74
	$(SO_4^{2-})_f$ * $percent_{out}$	0.91 (0.35)	0.01		
	$(SO_4^{2-})_f$	0.39 (0.15)	0.01	<0.0001	0.72
	$(SO_4^{2-})_f$ * $percent_{zonej}$	0.18 (0.15)	0.23		
	$(SO_4^{2-})_f$	0.38 (0.12)	0.003	<0.0001	0.72
	$(SO_4^{2-})_f$ * distance	0.07 (0.04)	0.12		
personal H^+ (nmol/m^3)	$(H^+)_f$	-0.06 (0.08)	0.47	0.04	0.10
	$(H^+)_f$ * $percent_{out/wopen}$	0.23 (0.10)	0.03		
	$(H^+)_f$	-0.15 (0.21)	0.47	0.24	0.05
	$(H^+)_f$ * $percent_{zonej}$	0.24 (0.21)	0.26		
	$(H^+)_f$	0.08 (0.16)	0.62	0.46	0.03
	$(H^+)_f$ * distance	-0.001 (0.06)	0.98		

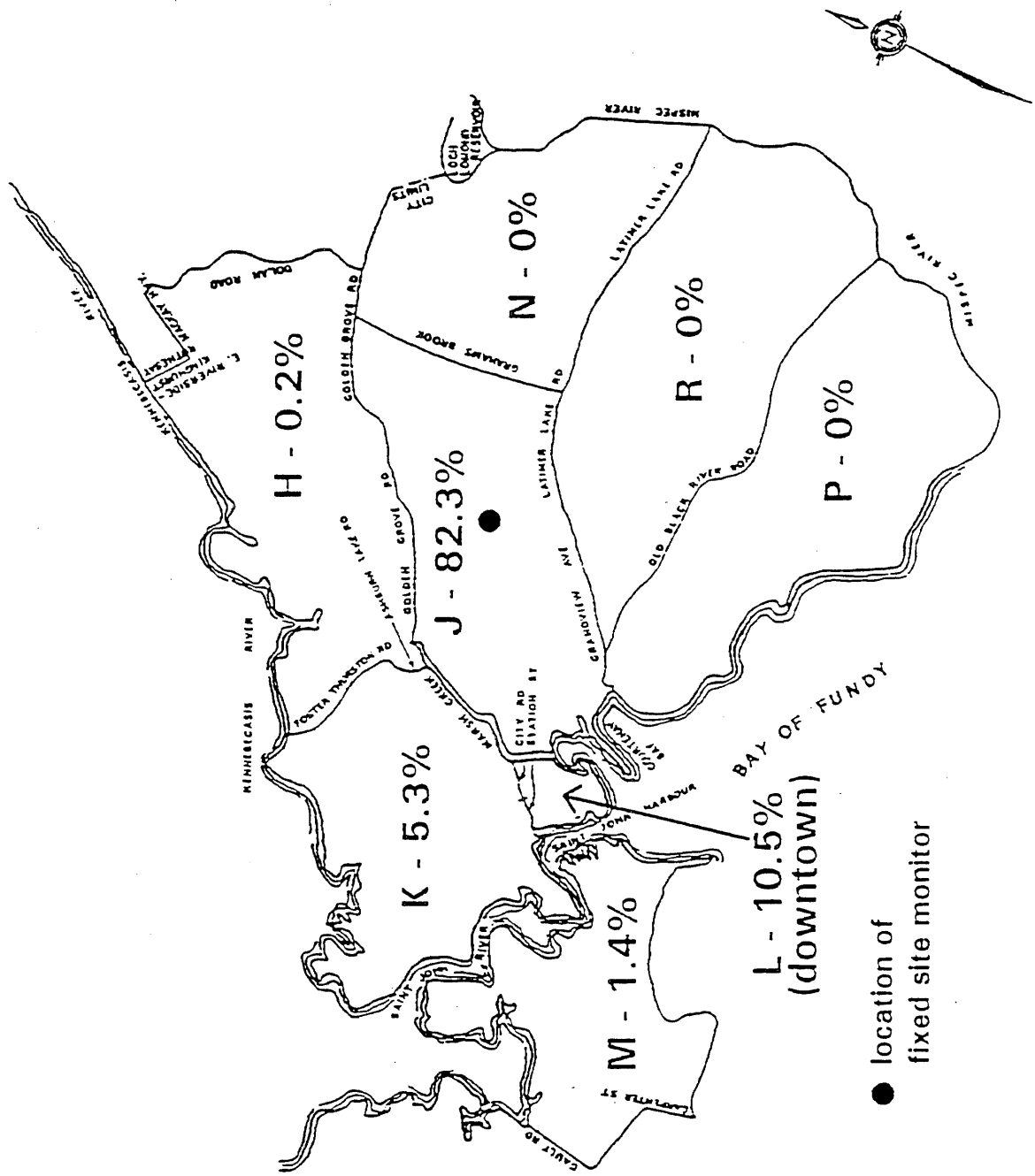
[a]subscript "f" denotes fixed site concentration (nmol/m^3); $percent_{out}$ denotes percent of sampling time outdoors; $percent_{zonej}$ denotes percent of sampling time in zone j; $percent_{out/wopen}$ denotes percent of sampling time outdoors or indoors with windows open; and distance denotes distance between subject's home and fixed site monitor in kilometres.

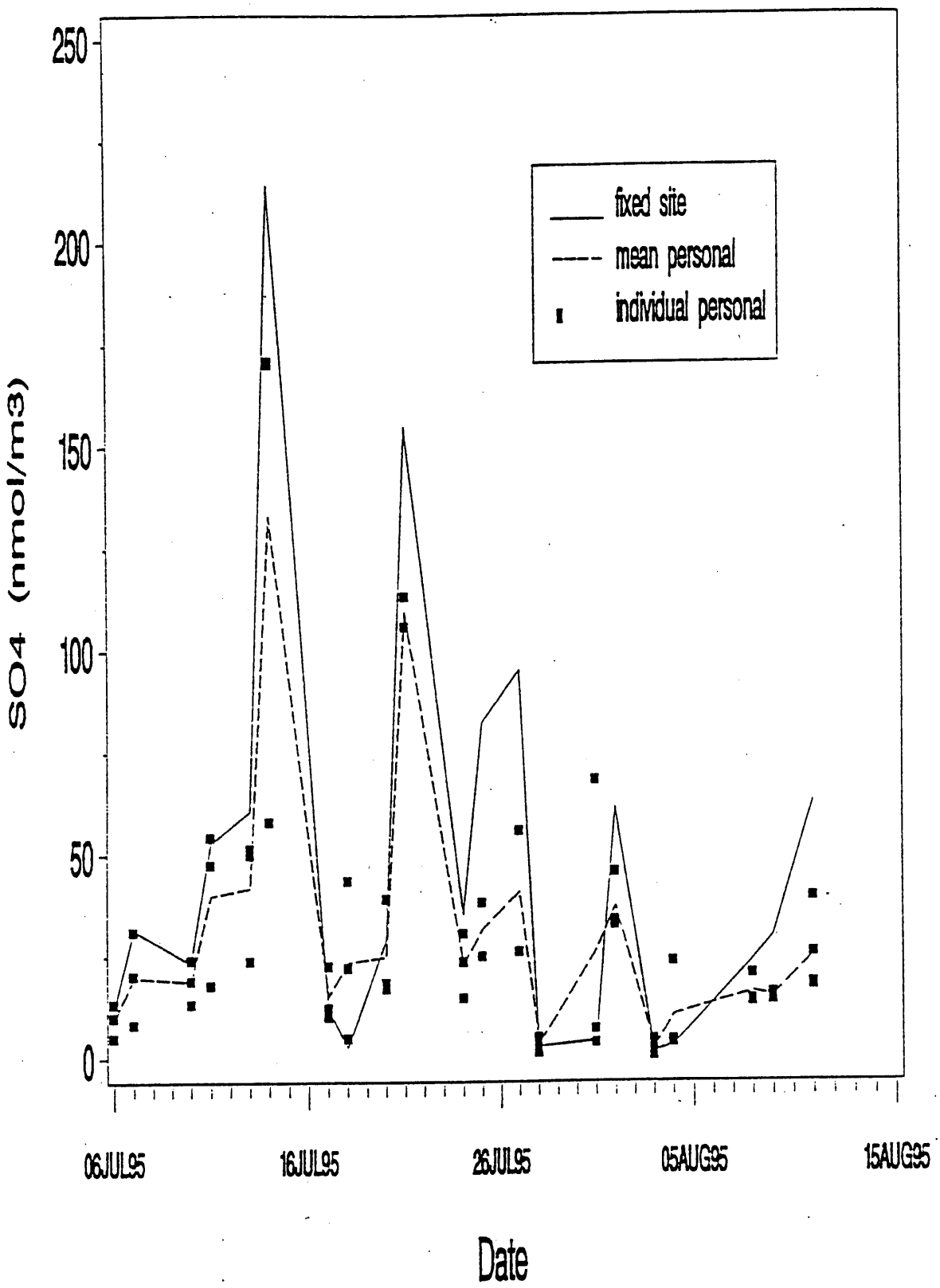
Acknowledgements
The authors would like to thank Helen Suh and Mike Wolfsson for advice regarding study design issues and the use of personal annular denuders, the California Air Resources Board, for lending personal pumps for use in our study, Sandy Woodhouse for conducting chemical analysis of samples, and Dr. Robert Beveridge, for facilitating subject selection. This study was funded by Health Canada and Environment Canada.

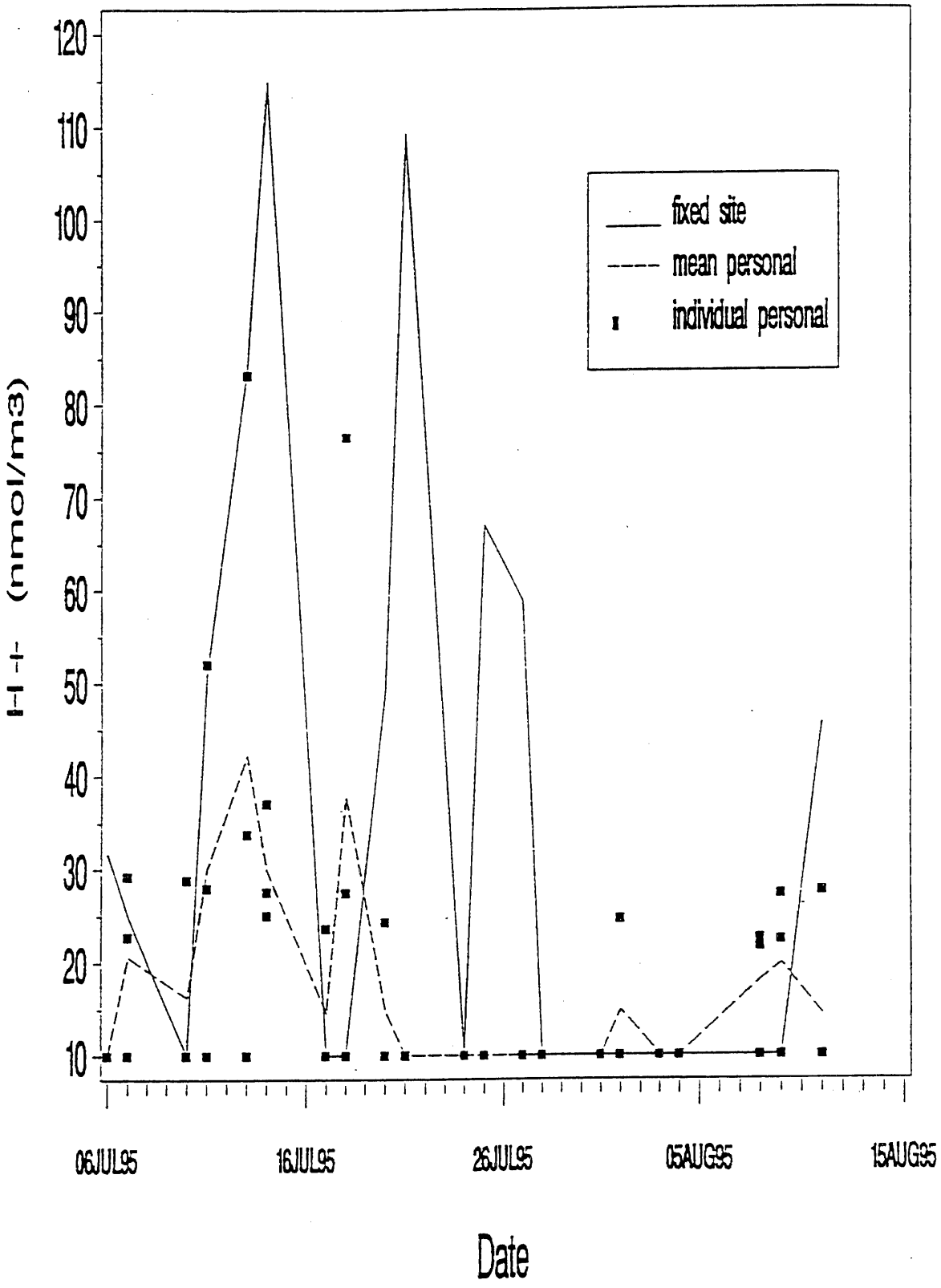
Figure Captions

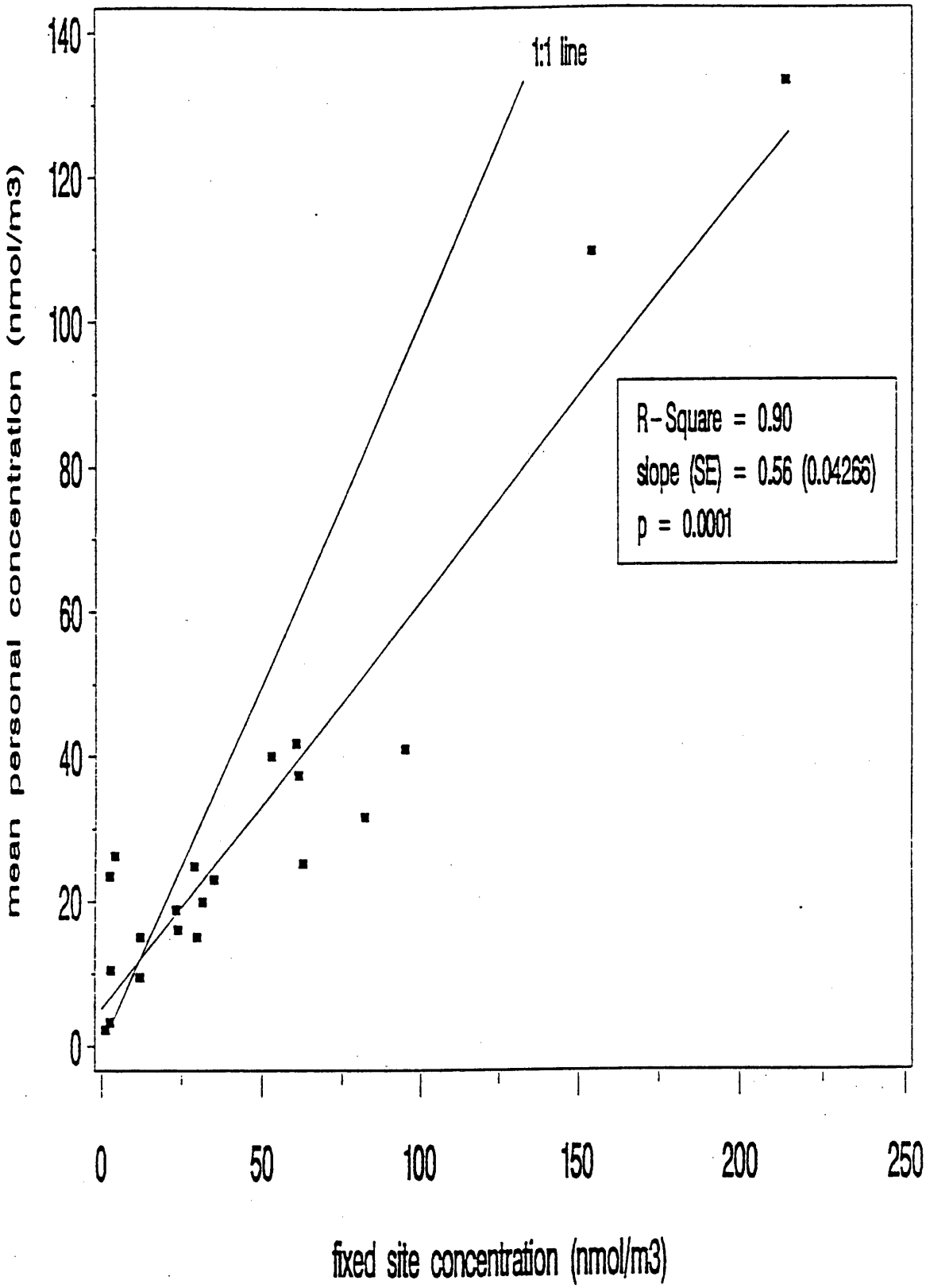
Figure 1.-- Personal samples by subject and date
Figure 2.-- Proportion of sampling time spent in selected geographic zones (note: area shown is approximately 21 km x 24.5 km)
Figure 3A.-- Personal and fixed site sulfate concentrations by date
Figure 3B.--Personal and fixed site acid concentrations by date
Figure 4A.-- Mean personal versus fixed site sulfate concentrations
Figure 4B.-- Mean personal versus fixed site acid concentrations
Figure 5A.-- Individual personal versus fixed site sulfate concentrations
Figure 5B.-- Individual personal versus fixed site acid concentrations
Figure 6A.-- Personal versus fixed site sulfate concentrations by percent of time spent outdoors
Figure 6B.-- Personal versus fixed site acid concentrations by percent of time spent outdoors or indoors with windows open

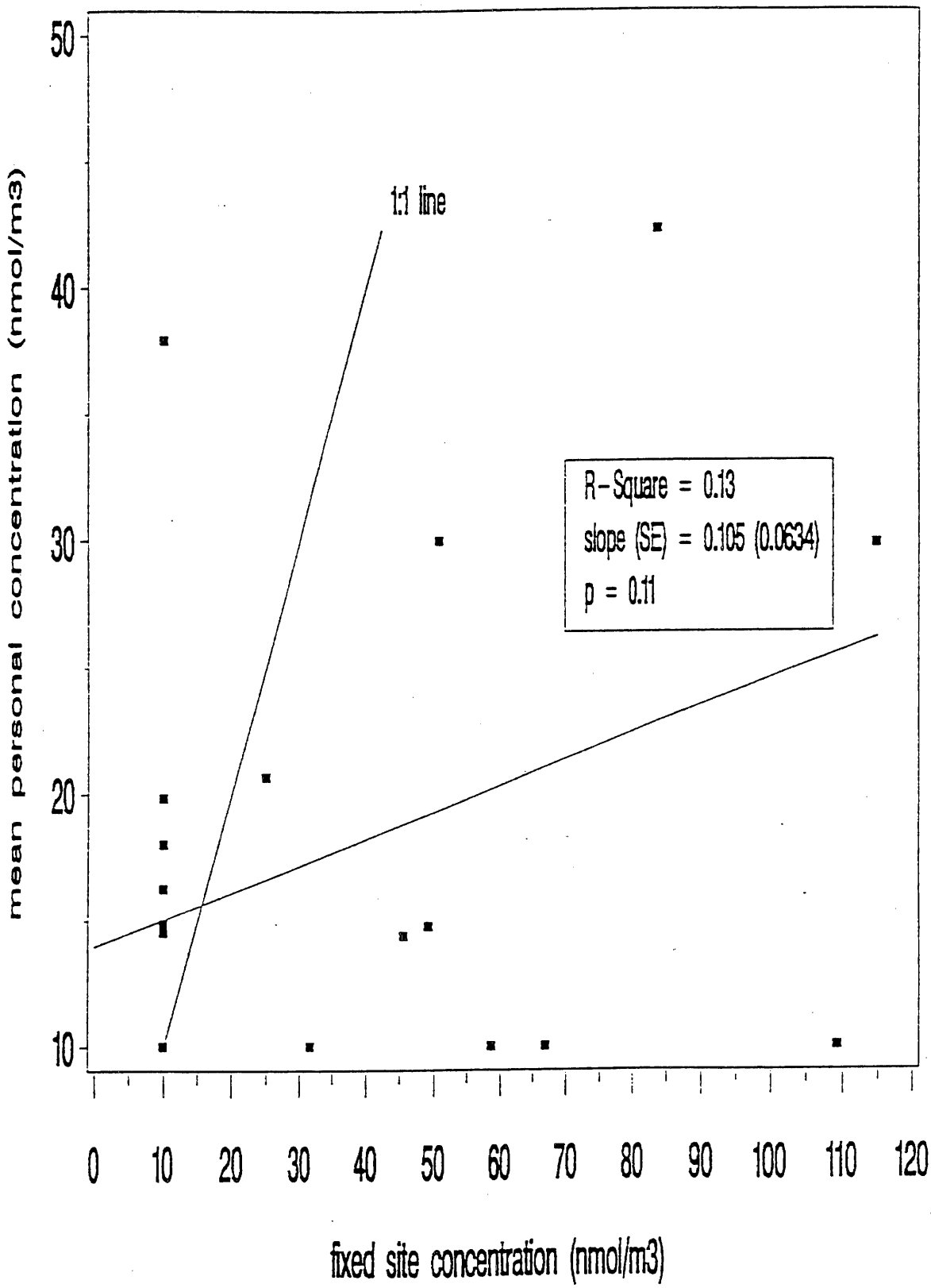

Subject
21
19
17
15
13
11
9
7
5
3
1
July 6
July 8
July 10
July 12
July 14
July 16
July 18
July 20
July 22
July 24
July 26
July 28
July 30
August 1
August 3
August 5
August 7
August 9
August 11
Date

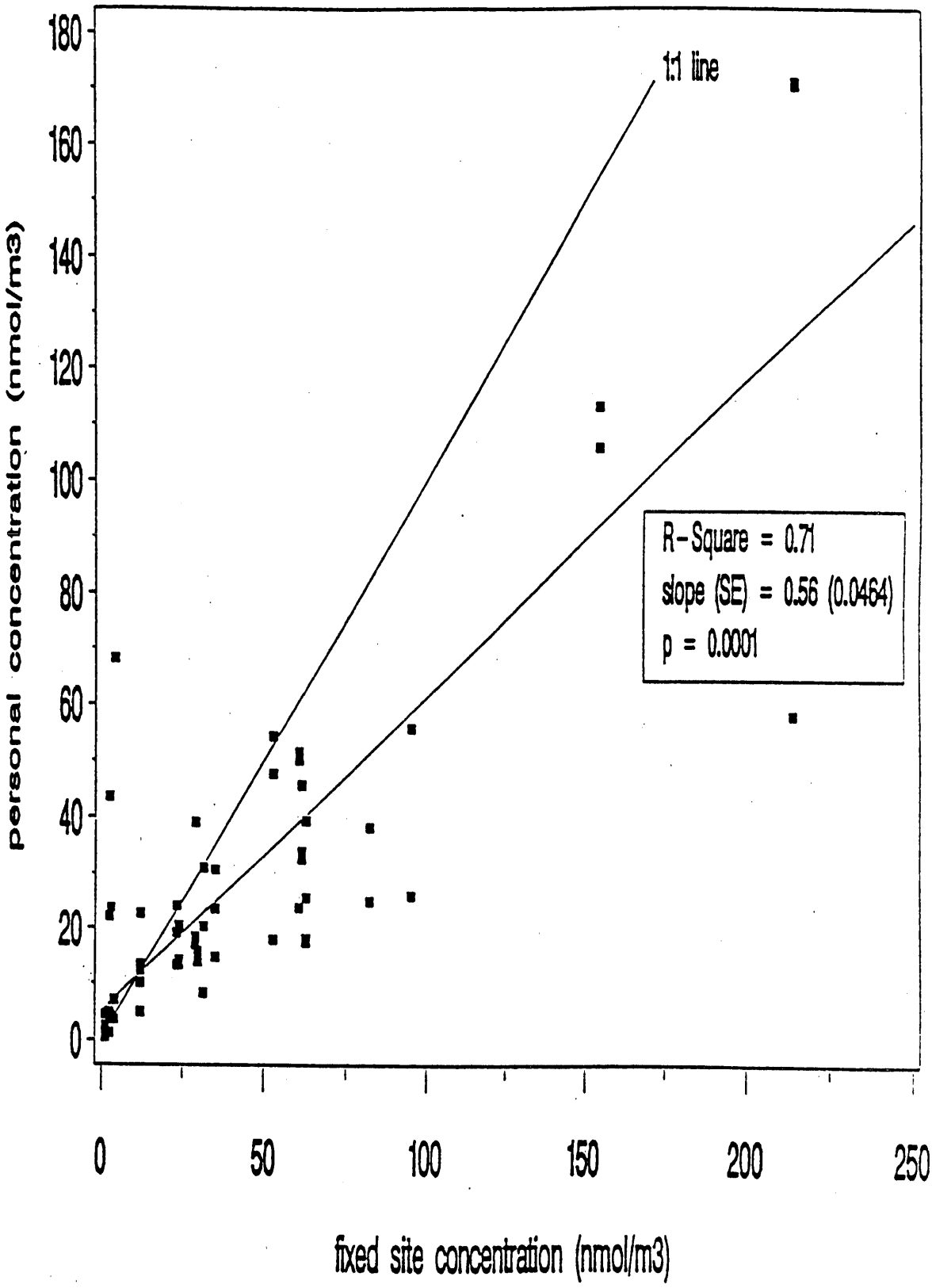

H - 0.2%
J - 82.3%
K - 5.3%
L - 10.5%
(downtown)
M - 1.4%
N - 0%
R - 0%
P - 0%
BAY OF FUNDY
location of
fixed site monitor

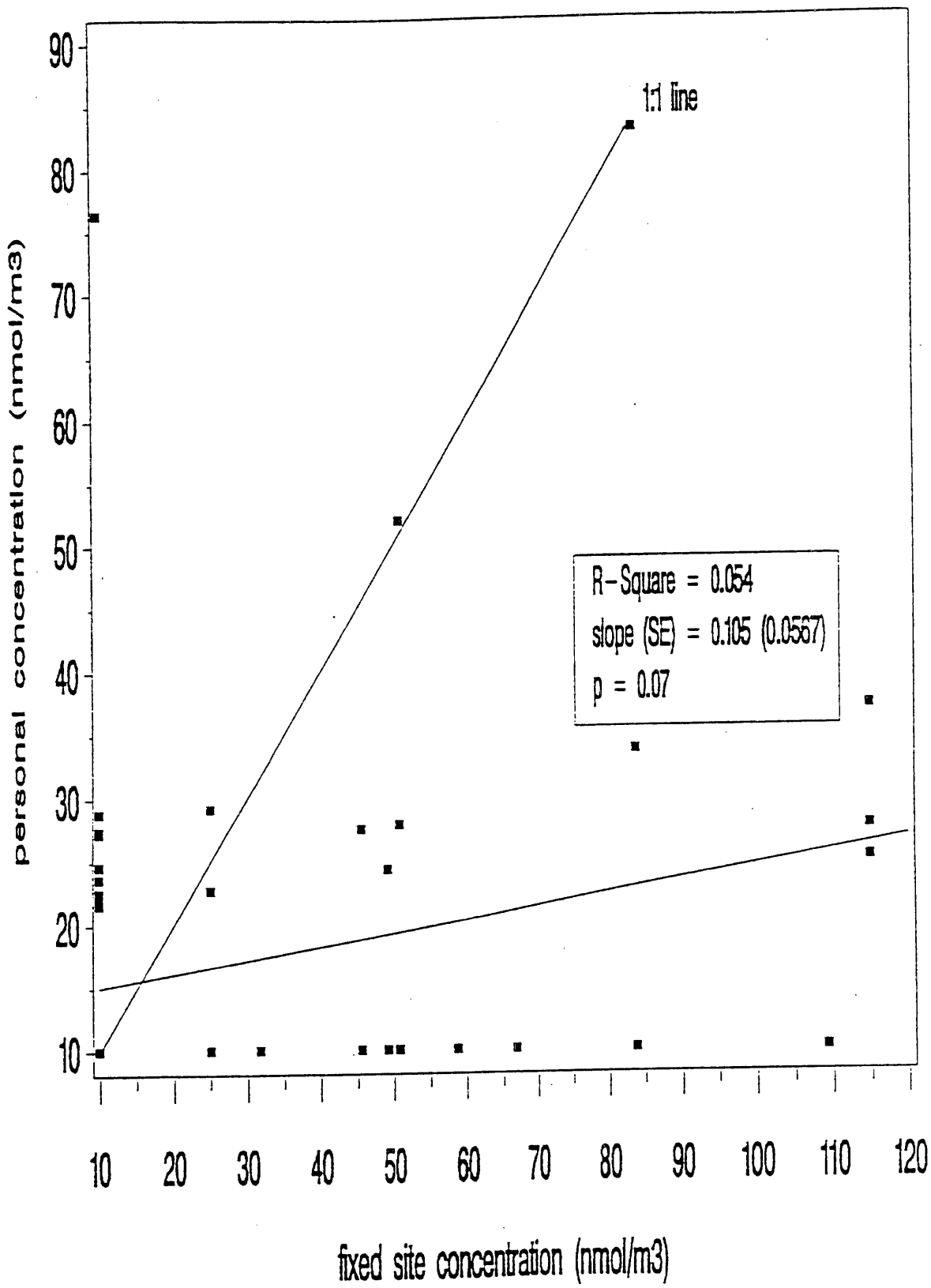

250
200
150
100
50
0
SO4 (nmol/m3)
fixed site
mean personal
individual personal
06JUL95
16JUL95
26JUL95
05AUG95
15AUG95
Date

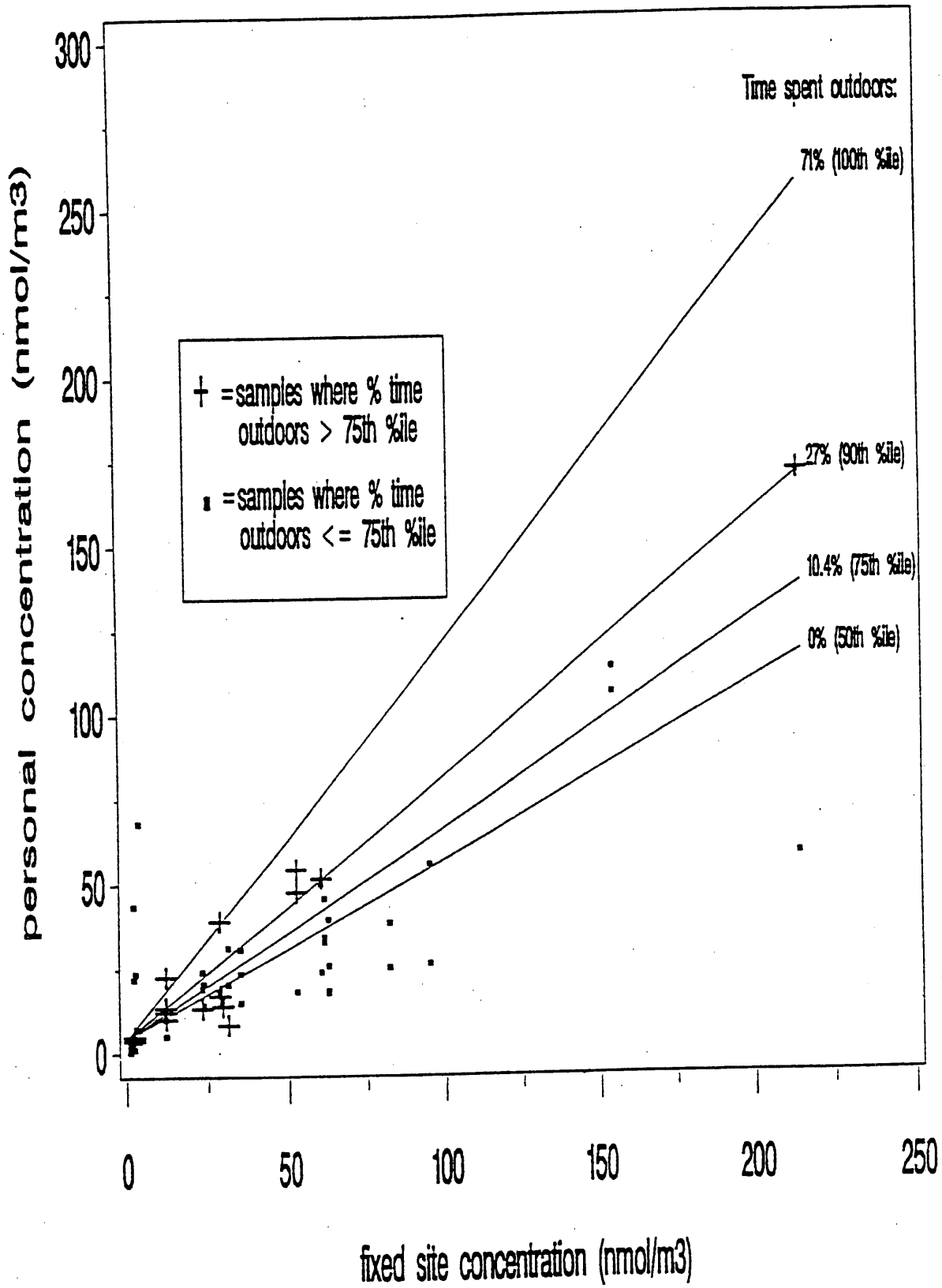

120
110
100
90
80
70
60
50
40
30
20
10
H+ (nmol/m3)
fixed site
mean personal
individual personal
06JUL95
16JUL95
26JUL95
05AUG95
15AUG95
Date


1:1 line
R-Square = 0.90
slope (SE) = 0.56 (0.04266)
p = 0.0001
mean personal concentration (nmol/m3)
fixed site concentration (nmol/m3)
0
20
40
60
80
100
120
140
0
50
100
150
200
250


mean personal concentration (nmol/m3)
50
40
30
20
10
1:1 line
R-Square = 0.13
slope (SE) = 0.105 (0.0634)
p = 0.11
0
10
20
30
40
50
60
70
80
90
100
110
120
fixed site concentration (nmol/m3)


1:1 line
R-Square = 0.71
slope (SE) = 0.56 (0.0464)
p = 0.0001
personal concentration (nmol/m3)
fixed site concentration (nmol/m3)
0
20
40
60
80
100
120
140
160
180
0
50
100
150
200
250


1:1 line
R-Square = 0.054
slope (SE) = 0.105 (0.0567)
p = 0.07
personal concentration (nmol/m3)
fixed site concentration (nmol/m3)
10
20
30
40
50
60
70
80
90
100
110
120


Time spent outdoors:
71% (100th %ile)
27% (90th %ile)
10.4% (75th %ile)
0% (50th %ile)
+ =samples where % time outdoors > 75th %ile
▪ =samples where % time outdoors <= 75th %ile
personal concentration (nmol/m3)
fixed site concentration (nmol/m3)
0
50
100
150
200
250
300

IV-54B

REQUIREMENTS FOR A CREDIBLE EXTRAPOLATION MODEL DERIVED FROM HEALTH EFFECTS IN RATS EXPOSED TO PARTICULATE AIR POLLUTION

– A Way to Minimize the Risks of Human Risk Assessment ? –

Werner Stöber, Fred J. Miller, Roger O. McClellan
Chemical Industry Institute of Toxicology
Research Triangle Park, NC 27709

ABSTRACT

For some years, several regulatory agencies have attempted to develop rather simple mathematical and biostatistical models to yield quantitative assessments of human risk derived from data of experimental rat exposures to typical particulate air pollutants. In our view, these models have failed to adequately consider some important biological aspects. The assessments would have to bridge the gap between the low levels of human exposures and the intentionally high levels used in rat exposure studies which is even controversial without the interspecies problem. Four crucial questions may be raised that have not been addressed in past efforts:

a) What constitutes the effective dose of particulate matter of long biopersistence in the lung ?

b) Is the effective dose mechanistically the same in humans and rats ?

c) Are the dose-response curves linear, and if not, are the nonlinearities the same for humans and rats ?

d) Are the models suitable for extrapolating from high to low exposures and from rat to humans ?

As the mechanistic similarity will remain an open question for some time, so will the lack of suitable data for human retention continue to impede accurate rat-to-man extrapolations. For the other problems, however, improvements are possible and necessary. Invariably, published procedures treat particles as chemically active agents whether they are soluble or not. Furthermore, much emphasis is placed on the phenomenon of lung overload. However, the evaluation of diesel exhaust exposure studies shows, that the retention of particles in the environmental range of ambient exposure concentrations up to 150 $\mu g/m^3$ is not influenced by impairment of alveolar macrophages. Focusing on insoluble particles, this paper shows that particle mass accumulated in the lung can not *per se* be the relevant effective dose. Such a dose must be related to a target tissue or cell population and is represented by an integral of the total particulate surface and its residence time in the target area. Based on this effective relative dose, it can be shown by using data of lifetime exposures of rats that even crude dose-response relationships for lung tumor incidences show a strong nonlinearity. No-threshold probit analyses of rat data indicate that ubiquitous exposure concentrations for rats at diesel soot levels between 40 and 85 $\mu g/m^3$ are "virtually safe" from lung cancer incidences. This must be a very conservative assessment, because in reality, this suspicious, nonchemical, nongenotoxic, rat-specific carcinogenicity can be seen only under heavy lung overload and involves most likely a no-effect threshold. Another major drawback of published risk assessment procedures is the exclusive use of inappropriate lung retention models. Most frequently,

postexposure models have been applied to chronic exposures. Almost all models are "models of data" that, according to a definition by DiStefano and Landaw, are only acceptable for interpolations (*e.g.*, the radiological applications of the ICRP model). However, physiologically based "models of systems" discriminating between various compartments in the pulmonary region give plausible disposition patterns of the retained particles and thus more credible extrapolations.