PM-10 RESEARCH NEEDS

R. F. Phalen

Air Pollution Health Effects Laboratory, Department of Community and Environmental Medicine, College of Medicine, University of California, Irvine, Irvine, California, USA

R. O. McClellan

Chemical Industry Institute of Toxicology, Research Triangle Park, North Carolina, USA

Over 200 scientists participated in the 1994 Colloquium on Particulate Air Pollution and Human Mortality and Morbidity. The specialties of these participants included epidemiology, biostatistics, pulmonary medicine, occupational medicine, toxicology, physiology, cell biology, risk assessment, receptor modeling, source modeling, atmospheric chemistry, aerosol science, chemical engineering, and public health. The participants offered over 100 written suggestions for additional research related to each of the following platform sessions: epidemiological findings, epidemiologic methods, mechanisms of toxicity, and sources, levels, and characterization of PM-10. Many of the suggestions were similar enough to be combined, and all of them have been edited or paraphrased for the sake of consistency and clarity. These suggestions for research were not officially discussed at the Colloquium due to time constraints. In addition, they do not carry the imprimatur of any funding agency or regulatory agency. Rather, they are a encapsulation of the perceived needs for research as expressed by a large and diverse group of scientists who are actively involved with many aspects of the problem of understanding and dealing with the impact of particulate air pollution on the health of human populations. The suggestions are organized in this article in accordance with the Colloquium sessions. The most frequently mentioned suggestions are listed first, for emphasis.

EPIDEMIOLOGIC FINDINGS (SESSION I)

The session included presentations that both linked and failed to link human mortality and morbidity to ambient particulate air pollution. The identified research needs associated with this session were both numerous and varied.

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1. Descriptions of environmental air pollutants must be improved in the following ways: They must include more sites and be more frequent; they must include more chemical species and the levels of acidity; they must include more information on particle size distributions; they must provide information on metastable (transient) components; and they must be more long-term.
2. Human exposures must be better described for indoor environments such as nursing homes, hospitals, and other areas where the most susceptible individuals are likely to be found. These exposures need more complete specification with respect to the physical sizes and chemical makeup of air contaminants, as well as the exposure durations and ventilation rates of members of the exposed populations.
3. Exposure and dose estimates must be improved per se for studied individuals as well as for studied populations. Sophisticated inhalation dosimetry models should be incorporated into the epidemiological investigations so that the deposition efficiencies and regional depositions of various particles, gases, and vapors are included.
4. Study sites should be expanded to include cities that are diverse enough in their main air pollutants to allow scientists to clearly identify specific potentially active agents.
5. Special sensitive populations that deserve additional study emphasis include the elderly, persons with advanced chronic obstructive pulmonary disease (COPD), young children, asthmatics, users of medications that might modify responses to air pollutants, individuals with significant cardiovascular disease, and those who live near monitoring stations (where exposure is more precisely known). Those specific segments of the population actually dying from low levels of particulate air pollutants still must be identified.
6. More study is needed on the effects of weather-related variables, especially in cities or rural areas that have very low levels of anthropogenic air pollution. This could include areas that have been successful in air pollution mitigation efforts.
7. Additional longitudinal studies are needed. Especially important are those that include better exposure assessments, including personal exposures.
8. Case-control studies are needed that compare those people dying on low pollution days and on high pollution days.
9. Occupationally exposed populations, working in environments in which concentrations of specific particulate air pollutants are elevated, should be studied and analyzed for information that might help to understand environmental exposures.
10. A centralized collection of generally accepted data sets should be established, so that a methodological "shoot-out" could be performed on these data sets. There is still confusion about the facts themselves (actual air concentrations, death rates etc.).

11. A full risk assessment analysis should be performed for each identifiable major component of PM-10, and risks should be compared with those from non-PM-10 hazards.
12. Existing epidemiological studies should be reexamined and integrated in a meta-analysis that takes into account differences in methodology, as well as differences in exposure to air pollutants.
13. Studies are needed that explore possible synergy among air pollutants.
14. The temporal associations, including time lags between exposure and effects (1 day, 2 day, etc.) and short-term versus long-term effects, should be investigated more thoroughly.
15. Lung function studies should be included in epidemiological investigations in order to clearly separate effects on large airways from those on small airways.
16. The nature of dose-response relationships for mortality and morbidity should be examined more thoroughly.
17. New, affordable, continuous, direct-reading air monitors should be developed and made available for epidemiological studies.
18. Reports of increased nonlung cancer rates in women exposed to high levels of air pollutants should be followed up.

EPIDEMIOLOGIC METHODS (SESSION II)

Varied epidemiologic methods have been used by various investigators to generate their findings. Many suggestions related to the research tools were offered.

1. The exposure aspects of the exposure-response models require special attention. Improved models are needed so that personal exposures, including consideration of activity patterns and exposure locations, can be studied. Models should be refined to allow better evaluation of temporal variations in exposure, as well as variations in chemical species and physical forms of the pollutants. Just using particle mass estimates from a few scattered sampling sites is too crude for health-related studies.
2. An environmentally realistic synthetic database should be defined and used to examine the sensitivities, differences, and uncertainties inherent in the various modeling approaches.
3. A modeling "shoot-out" (as recommended in relation to Session I) is needed to better understand subtle differences in the currently used methods.
4. Uncertainty analysis methodology should undergo improvement, especially in relation to estimation of exposure.
5. Models should include methods for estimating the reductions in life expectancy due to exposure to PM-10 components, as opposed to just mortality, so that the societal costs of elevated death rates could be better estimated.

6. The available monitoring databases and methodology should be improved to include at least daily monitoring of particulate material in cities, better measures of common personal exposures, and improved characterizations of hospital-related exposures.
7. Improvements in statistical software are needed, especially regarding those packages that would help epidemiologists who are not thoroughly trained in statistical methodology.
8. The problem of autocorrelation in time-series data requires additional study.

MECHANISMS OF TOXICITY (SESSION III)

Three general types of studies—human clinical, laboratory animal, and in vitro toxicological—comprise the bulk of investigations relating to inhalation toxicology. The in vitro toxicological studies are often subdivided into categories relating to isolated organs, tissue cultures, cell cultures, and biochemical processes. Because of the unique exposure route characteristics of particle inhalation, of contaminant metabolism, and of lung diseases, most inhalation toxicology studies have been conducted with whole animals. However, research suggestions covered each of these types of studies.

1. In addition to greater use of existing animal models that are available, new animal models must be developed for the compromised human. These include models for the following: various types of active pulmonary infections; chronic asthma; COPD; emphysema; cancer (a transgenic animal model is needed); cardiovascular diseases; and fibrotic diseases.
2. Ultrafine singlet and aggregated particles, especially those smaller than 0.1 μm in diameter, must be studied with respect to their fates when inhaled, their inflammatory potentials, and their direct toxicity to various cells present in the lung. These studies should include several physical forms and chemical compositions of particles, including metal and metal-coated otherwise inert particles. (*Note*: Many investigators question the existence of a truly inert particle with respect to potential toxicity when inhaled.)
3. Toxicologic studies should be conducted to focus on some additional objectives, including identification of thresholds for effects; dose-response relationships; more realistic dust sizes (especially submicrometer in diameter); lower dust concentrations; and chronic exposures.
4. More information is needed regarding the dosimetry of inhaled particles within the respiratory tract. Studies that shed light on where individual pollutants deposit may help identify how animal species, age, and body size modulate toxicity. Comparative studies are also needed to aid in extrapolations from animals to humans. Dosimetry studies should include diseased animal models and diseased humans.

5. Greater focus is needed on the issue of biological plausibility for particles causing human deaths. Such studies should explore cardiovascular, cardiopulmonary, neurological, and immunological etiologies at the whole-animal, tissue, cellular, and biochemical levels.
6. Toxicologic studies are needed that lead to validated in vitro models for cellular injury in various lung regions; that identify cytotoxic, genotoxic, and fibrotoxic mechanisms; and that identify molecular mechanisms that could lead to acute mortality.
7. Greater focus on quantitative small airways pathology is needed, especially regarding comparative phenomena in chronically exposed humans versus commonly used animal models.
8. Studies are needed that directly compare human and laboratory animal macrophage-related phenomena; both toxicologic and mechanistic studies are required.
9. Additional biomarkers of exposures and of effects are needed so that exposure-response relationships can be improved for individual components of PM-10.
10. Additional information is needed on the dosimetry and effects of aqueous aerosol particles that carry dissolved gases and vapors into the respiratory tract.
11. Iron-coated (especially ionic Fe) particle generation systems should be developed, and should be used in inhalation studies. Similar considerations apply to fine particles of other transition metals.

SOURCES, LEVELS, AND CHARACTERIZATION OF PM-10 (SESSION IV)

As this session proceeded at the Colloquium, it became apparent that it covered a large and complex area. The suggestions for research covered diverse topics and ranged from the very basic to the highly applied.

1. Basic studies are needed on the composition of, and reactions among, metastable species in the atmosphere. Such transient species, most of which may not yet be identified, escape "filter" analyses, and may, in fact, be the culprit(s) in human mortality and morbidity. Particulate mass (as we now understand it) may be only a surrogate problem.
2. Particulate mass must be speciated both with respect to composition, and for primary particles, emission sources. Such categories might include combustion products from various fuels; silicates; carbon; pollen; molds; agricultural; industrial; free radicals; atmospheric reaction products (especially with ozone); various organic fractions; etc. Measurements that are gravimetrically based are too crude to allow for interpretation of health effects or for planning mitigation.
3. The organic fraction of PM-10 requires more study regarding its chemistry in aqueous media, exposure factors for human populations, indoor and

outdoor compositions, size characteristics, transformations on filters, and losses in sampling devices.

4. More information is needed on size distributions of the various chemical species in PM-10. This is especially true for those particles smaller than 2.5 μm in diameter, as they exist in ambient air in significant numbers.
5. Aqueous aerosol droplets require more study, especially related to their prevalence, reactions within them, and their absorption of and liberation of pollutant gases and vapors.
6. More data are needed on variations—chemical, spatial, and temporal—in outdoor and indoor aerosols. This need includes gathering more data from those cities already studied by epidemiologists.
7. Improvements are needed in several types of instruments, including those sensitive to new species of pollutants; continuous-reading instruments; those that separate particles from gases and vapors; and those that provide more and better information on size distributions.
8. The particle-size fractions and compositions in California should be better studied and better monitored so that epidemiological comparisons with eastern areas of the United States can be facilitated.
9. Episodes of air pollution should be more intensively characterized and studied at several diverse locations.
10. Methods for generating more realistic aerosols for laboratory studies are needed. This includes use of aerosol concentrators. The need applies to human exposures, laboratory animal studies, and atmospheric chemistry investigations.
11. Gas-to-particle conversions should be more thoroughly studied and modeled.
12. More thorough weather studies are needed. Better weather data will improve understanding of the effects of weather-related variables on air pollution itself, as well as understanding of the effects of weather on health.
13. Sulfate, nitrate, and acidity should be better characterized in those cities that have already been studied by epidemiologists.
14. Studies are needed to define the pollutant mixtures that will result from the widespread use of proposed "alternative" fuels.

CONCLUDING REMARKS

This exercise in soliciting suggestions for research on PM-10 from a group of actively engaged scientists is valuable to the extent that it actually improves the efficiency and payoff of future research efforts. Everyone who plans, conducts, or supports research might benefit from contemplating, weighing, and discussing these suggestions. In addition, the exercise allows us to make some immediate observations. Most striking is the realization that scientists perceived that we currently have only a meager and unsatisfactory

knowledge of the topic that stimulated the Colloquium—the relationship of particulate environmental air pollution to human mortality and morbidity. In many areas methodological limitations appear to be the major problem that blocks our progress. It is clear that a considerable amount of work still needs to be done. It is also apparent that particulate mass is perceived to be far to crude a measure for linking specific air pollutants to human health. However, one can't help but be optimistic at the clarity of the message contained in the suggestions regarding the next logical steps. Also, a remarkable similarity in research needs across specialties is seen. Perhaps in a few years, or decades, several completion checks could be entered beside items in the lists just presented. This will be the case only if the will and the means exist to mount a substantial, concerted, and sustained research effort.