The Annapolis Center
For Science-Based Public Policy

PARTICULATE MATTER HEALTH EFFECTS

Preface

The Annapolis Center seeks to improve the public debate about the potential risk associated with environmental, health, and safety factors. On January 16-17, 1997, The Annapolis Center convened a workshop at which recognized experts summarized the scientific information related to the consequences of the public's exposure to particulate matter (PM) in the air. The U.S. Environmental Protection Agency (EPA) has proposed revisions to the air standards for this pollutant, and there has been confusion as to the scientific basis for the revisions. A facilitated discussion of the quantity, scope, and importance of the available information on PM was held by diverse experts who attended the workshop and they subsequently suggested how additional research and discussion might be beneficial.

The discussion proved to be lively and respectful of the diversity of interpretations of the evidence. At the conclusion of the 2-day discussion, it was clear that a complete and certain picture of the science related to PM could not be drawn. Some epidemiologic studies link current levels of ambient air pollution to statistical increases in the number of deaths per day. An association between particulate air pollution and mortality is also suggested by the pattern of findings in these studies as the results are examined in total. Other studies also suggest that measures of illness or morbidity, such as the numbers of hospitalizations among the elderly, are affected by PM. Scientists usually seek to confirm such observational evidence by performing toxicologic studies to gain an understanding of the mechanisms of injury. However, past studies focused on concentrations and particle sizes that are not directly relevant to today's lower levels of exposure and did not elucidate what it is about PM that might be contributing to observed health effects even at the higher concentrations used in the experiments. That gap in our knowledge constitutes a key uncertainty in interpreting the observational data. It is the iterpretaion of the epidemiologic studies that has been at the center of the current debate. The debate continues because a full toxicologic and mechanistic understanding of PM is absent. It would be more productive to focus debate on the identity of the agents responsible for the observed health effects and whether the proposed regulatory actions are appropriate for mitigating these agents. These data, as became clear during the workshop , do not exist.

EPA is in the regrettable position of having to meet a court-imposed deadline regarding the pollutant standards. The Administrator is required by law to set a standard that protects public health against adverse effects with "an adequate margin of safety." That legal construct implies that there is some level of exposure below which there are no biological effects and that there is even a margin of safety to be found below that level. Nature might not always cooperate with such simplistic legal constructs.

The Administrator is required to act on the basis of a review of all available scientific evidence. But the EPA and the Congress have, over the years, provided scant resources for a regulatory matter that might cost the American public billions of dollars.

Last year, the expenditure for research related to PM was only $18 million, compared to a total budget for EPA of about $7 billion.

You are invited to consider this summary of the workshop as a tool to assist you in your thinking about modifying the PM standards and evaluating additional research. Please share this document--written in laymen's terms--with others who might be interested in the scientific basis for the PM standards.

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SUMMARY OF WORKSHOP
ON PARTICULATE MATTER HEALTH EFFECTS

Seeking to inform the debate concerning the potential health benefits of revising the particulate matter standard (hereafter referred to as PM), The Annapolis Center held a workshop in Annapolis, Maryland on January 16-17, 1997. An array of recognized experts engaged in a facilitated discussion on the quality of the evidence on PM health effects and related matters, and on disagreements and uncertainties that require additional study. The following summarizes the major subjects addressed during the workshop and highlights the key points made in the discussion.

Why is there a concern about PM?

In the past, the ill effects on health caused by extremely high concentrations of particulate matter in the atmosphere resulting from human activities were obvious. In the 1940s and 1950s, when episodic high concentrations of PM and other pollutants in London were associated with illness and death, it seemed to many that air pollution was the cause. Today in the United States, improvements in air quality (including PM) make the identification of health effects from the relatively low exposures to PM more difficult for scientists. But the issue is still important because in large populations even small effects could have sizable public-health consequences either directly or by making people with existing diseases more ill. Epidemiology—the study of patterns of disease in populations—investigates associations between people experiencing adverse health effects and exposure to external or endogenous agents. With generally lower levels of air pollution, epidemiological studies must be designed and performed carefully if they are to identify potentially harmful agents for further investigation. Ideally, epidemiological studies of present lower levels of air pollution would include large numbers of people, and results would be analyzed with sophisticated statistical tools.

A body of evidence from epidemiological studies comparing mortality in a given city at times of higher and lower monitored levels of PM concentrations indicates a positive association between mortality in a city and PM. In many cases the higher levels are below the current Environmental Protection Agency (EPA) regulatory standard which limits particles having aerodynamic diameters less than 10μm (PM_{10}) to an annual mean concentration below 50 micrograms per cubic meter of air (μg/m3). The 24-hour standard is attained when the expected number of days per calendar year above 150 μg/m3 is no more than one. The indicated increase in total mortality is about 3-4% per 100μg/m3 of PM as measured for PM in the size range of 10μm and below.

Results of studies comparing lung function in children who have lived in communities with different concentrations of PM and other pollutants suggest decreases in lung function (in children an average 3% lower volume of air that can be expired in a second) in communities with higher concentrations compared to communities with lower concentrations. There are only a few studies which assess the relationship between lung function and PM in children, however. Often, a decrease in life span (on the order of several years) is also reported in communities with higher concentrations of pollutants

including PM. Again, there are not many of these studies. Confounding factors such as potential differences in lifestyle and other factors (including socioeconomic factors, other pollutants, ethnicity, season, and climate) across these communities and/or over time complicate these results and epidemiologists endeavor to adjust their analyses for them.

Epidemiological studies have also been used to estimate the magnitude of the effect by defining a relationship between various exposures and health responses (a "dose" response relationship). Care must be taken in relating ambient measures of pollutants to the actual level of exposure that an individual experiences as these may differ depending on the day-to-day practices of an individual. When feasible, laboratory animals are exposed to candidate agents, and scientists look for health responses similar to those identified in epidemiological studies. In clinical studies, individuals are observed before and after carefully controlled exposure to environmental agents. Sometimes individuals with characteristics similar to those identified in epidemiological studies are selected for clinical studies. Often these studies are conducted using concentrations of the environmental agent that are higher than those found in ambient air so that rare health responses are more likely to be seen during the clinical test.

The Annapolis Center workshop on particulate matter examined available information in the following way: first, the epidemiological studies on PM were discussed and the adequacy of various studies was reviewed. Next, the findings of animal tests and clinical trials were discussed. Finally, because it is not known how PM specifically affects the human body, the plausibility of different hypothetical mechanisms for PM causing health responses was discussed.

What is particulate matter?

Particulate matter is the phrase used for all the solid and liquid particles found in ambient or indoor air. PM ranges in size from particles visible to the eye to particles that are microscopic. PM is created by natural processes (such as soil dust) and by human activities (such as the products of combustion in automobiles, electric power plants, and household activities). For the current discussion of PM smaller than the regulated size of PM_{10}, PM can be categorized according to particle size. The "coarse" fraction (mean diameter, 2.5-10μm[1]) can arise from erosion of soil and other mechanical processes. The "fine" fraction (mean diameter 0.1 to 2.5 μm) is largely associated with human activities but also includes bacteria. These particles generally remain suspended in the atmosphere for longer periods of time than the coarse fraction. Particles less than 0.1 μm in diameter are referred to as "ultrafine."

The importance of particle size is that it largely defines the potential for particles to be inhaled and reach different regions of the lung: the smaller the particle, the larger the chance that it will travel more deeply into the lung (except for the ultrafine particles which may behave essentially as gases and not deposit in the lung). Particles larger than 10 μm in diameter are almost always deposited in the nasal passages unless breathing is done through the mouth. About 80% of the particles between 5 and 10 μm are captured

[1] μm (or micron) is a unit of length equal to one millionth of a meter

in the larger passages leading to the lung, and those smaller than 2.5 μm have a greater chance of being deposited in the lung. The smaller the particle the farther it is likely to travel toward the smallest of the air passages in the deep lung. The relationship of size to likelihood of deposition in the deeper lung regions is the principal reason to assume that fine particles are the most likely contributors to some health outcomes in the lung, but there is no current accepted biological explanation for how the PM deposited in the deep lung is involved in the variety of adverse health responses that have been observed. And in fact, for some diseases such as asthma the relevant receptors are in the upper regions of the lung. For other diseases, such as chronic obstructive pulmonary disease, relatively few particles deposit in the deepest recesses of the lung.

PM is also characterized according to chemical composition. Particle size dictates what portion will be deposited and the likely region of deposition in the lung, but some scientists believe that chemical composition determines whether particles will cause a health response after deposition. The chemical composition of a particle is related to its origin; for example, particles that result from combustion include sulfate, nitrate, metals, and carbon-based materials. The chemical composition of particles can be modified as they combine in the atmosphere with other particles and gases. The specific characteristics of PM that cause a biological reaction leading to the observed health outcomes are not known. More will be said on this in the section on biological mechanisms.

What is the regulatory background?

The Clean Air Act of 1970 recognized the public-health concern with PM and directed the Environmental Protection Agency (EPA) to set a regulatory standard "requisite to protect the public health" and in so doing provide "an adequate margin of safety...." The Act also directs EPA not to consider its economic consequences in setting the standard. The original EPA standard required that the average concentration of all PM, that can be captured by high volume samplers, that is particles less than 40μm diameter, (referred to as "total suspended particulates," or TSP) measured at central monitoring stations over the course of a year be limited to 75μg per cubic meter. As with many situations where a potential environmental hazard is under regulation, few PM measurements other than TSP were made after the standard was set because measurements are taken as part of monitoring for compliance with the standard. Thus, when the time came for regulators to consider whether the TSP standard provided an "adequate margin of safety," few measurements of specific size (such as 10 μm or 2.5 μm) of PM had been made.

In the 1980s, the standard was revisited as required by the Clean Air Act. Health outcomes associated with PM were still being observed in some studies. The TSP standard had substantially reduced the mass of PM in the air; however, there was still concern that adverse health outcomes might be related to exposure to PM at lower concentrations. Some scientists considered it most likely that particles of less than about 15 μm were responsible for the health outcomes attributed to PM. There was considerable discussion about what the indicator for a new standard should be; focusing primarily on the size of the particles that can be inhaled. However, there was limited definitive scientific information on the effects of particles of different size, inasmuch as

measurements other than TSP were rare. The standard limiting the concentrations of particles equal to or smaller than 10 μm (PM10) was in 1987.

Epidemiological studies

Many studies in the United States and abroad since the 1970s have tested the hypothesis that observed health outcomes were associated with ambient PM and other air pollutants. Studies have been done of both immediate and longer-term health effects. The first deals with acute outcomes, immediate responses to periods of increased air pollution (including PM) in the ambient air. The second deals with the chronic or longer-term responses to repeated exposure to increased air pollution in the ambient air in a geographic area.

Results from studies of acute responses indicate an association between daily increases in PM (as measured in various size ranges including the 2.5μm and 10μm size ranges) and daily deaths after up to 5 days in time. The increase in mortality appears to be largely related to cardiorespiratory causes. But the specific causes of death have been examined in only a few studies. The exact causes of death have not been clearly established; information in these studies is drawn from death certificates, which can be imprecise as to cause of death. The rapid response of mortality should not be confused with a large increase in the number of deaths. The proportional increase in mortality is relatively modest and can be readily measured only by studies that consider fairly large populations exposed to PM over several years. It is assumed by most scientists that the mortality observed is accounted for by people whose pre-existing respiratory or cardiac conditions are exacerbated to the point where death occurs- -slightly prematurely. Most epidemiologists would say that this "harvesting" effect should result in a decrease in mortality in the weeks after the period of increased PM. Some would argue that this effect could be observed in the earlier studies of major pollution episodes in London. This effect has not been investigated thoroughly and has been suggested in only a few of the recent studies.

The longer-term studies compared people in different communities having different levels of ambient air pollution. It is important to recognize that variable levels of PM are present in all communities. Critical factors that affect health—such as whether people smoke, where they work, how old they are, and their socioeconomic standing and lifestyle—must be taken into account in longer-term studies; we know that these variables do significantly affect life span; air pollution might also affect it. Many earlier studies did not properly account for those factors, so the contribution of, say; differences in the amount of smoking to differences in health outcomes among cities could not be determined. Some long-term mortality studies looking at whole populations rather than individuals, have suggested that mortality associated with air pollution decreases as additional confounding factors are considered. More recently, 3 studies have been carried out in a manner that accounts for several of these potentially confounding factors where the research addressed specific individuals, not populations. When comparing specific individuals the investigator can account for differences in life habits to the extent they have been recorded or are remembered by the individuals. Two of these, the Harvard 6-city study (air quality measurements made from 1978-1988) and the American

Cancer Society 151-city study (air quality measurements made from 1979-1981) included data on particles the size of EPA's current proposed standard—namely, 2.5 μm (the third study, examining a population of Seventh-Day Adventists in California found no association between increased mortality and PM where PM was measured as TSP and no measurements of PM_{10} or $PM_{2.5}$ were made). The two studies found statistically significant effects in mortality (increase). The Harvard 6-city study found effects in cardiopulmonary mortality (increase) in communities with higher concentrations of air pollution and PM. Subsequent studies have found small, but not statistically significant, changes in lung function. Other studies have found statistically significant decreases in lung function (2-3%). These observations of a decrease in the volume of air that can be forced out of the lungs during exhalation, may be important and some susceptible persons may be affected more significantly. Progressive decreases in lung function can indicate more serious disease.

Participants in the workshop discussed whether the American Cancer Society 151-city study and the Harvard 6-city study had in fact sufficiently adjusted for the possible confounding factors. There were varied opinions on whether PM studies have made adequate adjustments for confounders, which could form an explanation for those outcomes. The participants noted the importance of clearly delineating and adjusting study methodologies to reduce the likelihood of independent risk factors modifying the association of PM and mortality. The numerous confounding factors discussed by the participants included: other pollutants, day of the week, season, temperature, humidity, barometric pressure, smoking, exercise, diet, socioeconomic status, migration, ethnicity.

The participants in the Annapolis workshop on PM also discussed a recent re-analysis of past studies commissioned by the Health Effects Institute (which receives about half its funding from EPA and half from companies in the automotive industry) because of the debate about the findings of the various studies done to date. The study was carried out by Jonathan Samet and his colleagues at the Johns Hopkins School of Public Health. It reexamined data on mortality and air pollution from Philadelphia; some earlier investigators had claimed that the data demonstrated a health effect of PM, and others had claimed that they did not. The Health Effects Institute study systematically reviewed the effects of using different assumptions and statistical treatments. The reanalysis confirmed the earlier finding that "daily mortality from all causes combined, and from cardiovascular and respiratory causes in particular, increased as levels of particulate air pollution indexes increased." The second phase of their study examined the inter-relationships among the pollutant measurements and for total suspended particulate matter and sulfur dioxide concluded that "it is not possible, based solely on these Philadelphia data, to identify one or the other pollutant as the principal cause of increased mortality." This latter finding illustrates the fact that PM is rarely found in the absence of other air pollutants. Therefore isolating its effects is difficult. This work illustrates an important point—that the debate about recent PM epidemiological studies is not whether errors have been made but rather whether there is more than one "correct" answer to the question being addressed.

Workshop participants identified 2 important shortcomings in current epidemiological studies that should be taken into consideration in viewing the overall scientific picture of the health effects of PM. They are:

- The fine particles (2.5μm) that are the subject of the PM debate have been measured in only 3 of the many studies that have been performed. Earlier studies measured the occurrence of particles 10-μm and smaller, and even earlier ones the more-general TSP, which is even less indicative of the occurrence of fine particles. That was done because EPA regulated PM first as TSP, then as the concentration of particles of 10 μm, and has only recently been considering lowering to 2.5μm the size of particles to be regulated. As a result, monitoring stations that provide data for regulatory compliance and only incidentally for the conduct of epidemiological studies have measured sizes required by regulations of the day, not all of the sizes that scientists might have wished. Thus, for the current discussions regarding regulatory changes, most of the epidemiolocal evidence relates to particles larger than 2.5μm.

- The accuracy of extrapolation from concentrations of PM measured at central monitoring stations to people's actual exposures in their daily lives is not well understood and thought by many to be very imprecise. People spend more than 90% of their time indoors, most of that in their homes (this is even greater for health-compromised individuals). How well do central monitoring-station data relate to exposures in the home? Not well, as studies show. The relationship is confused by the fact that people are exposed to high concentrations of particles generated in their homes during normal activities, such as movement, cooking, vacuum cleaning, and cigarette smoking and particles of all sizes that infiltrate from outside.

Having discussed the methodological flaws in some of the epidemiological studies, particularly the difficulty in doing valid studies of long-term or chronic health effects where the effects are small, workshop participants considered the full range of epidemiological findings to date. They concluded that **there is a statistical association between increased mortality from respiratory and cardiovascular disease and increased ambient concentrations of PM (as measured in all size ranges) even when those concentrations are below current National Ambient Air Quality Standards. They also concluded that current studies do not identify whether the short-term association represents an advancement of the time of death of highly susceptible persons by a few days.**

However, they did not believe that current epidemiological studies clearly identified the causal agent in air pollution (for example, PM) or, more specifically, the PM fraction that is responsible for the health outcomes and our current understanding of plausible biological mechanisms cannot explain the effect at observed outdoor PM levels.

The participants turned to an examination of laboratory studies on humans and studies on animals to see whether they provide further evidence for specific agents or biological changes due to an agent that would account for the observed health outcomes that follow an increase in ambient PM.

Identifying the causal agent

Because the weight of evidence from epidemiological studies does not give a clear picture of the agent(s) responsible for observed health outcomes; we should look to an analysis of toxicological studies of the effects of hypothesized agents on animals and humans.

Using animal studies to investigate the effects of PM

Animal studies suffer from the obvious disadvantage that animals are not human beings and that reactions to a given agent may be different in animals and humans. But animal studies do have some advantages. Experiments with fairly rigorous controls can be run. The length of time that animals are exposed and the concentrations of a test agent can be precisely set. Relationships can be examined between different concentrations and exposures to the agent, which can be crucial for setting regulatory standards that, are appropriately protective. And animals can be killed to make it possible to examine tissues closely.

Animal studies on the health effects of other EPA "criteria air pollutants" have helped to elucidate some of the mechanisms of their biologic action on the human body and to determine dose-response relationships. For example, animal studies have shown that exposure to NO_2 at about 10 times the normal ambient concentration decreases the ability of particular lung cells to combat some bacteria and viruses and that exposure to O_3 damages lung cells.

Animal studies have also been used to examine the health effects of PM. They are complicated by the fact that recreating a mixture of particles in the laboratory that is similar in size distribution and composition to the mixture experienced outside the laboratory is very difficult. Ideally, these studies would use animals that have diseases similar to those of humans who are believed to be the most sensitive to PM such as people with asthma and chronic obstructive lung diseases. But such animals are not readily available. Recent findings using animals with experimentally compromised cardiac and respiratory systems and particles gathered from real air have given indications that health effects (for example, cardiac arrythmias) may be seen in animals at concentrations of PM that are comparable to those in ambient air in heavily polluted communities (or about six times the concentration of the new standard for PM in the 2.5μm size range being proposed by the EPA).

Studies in which healthy laboratory animals were exposed to substantial concentrations of fine PM (0.25μm mass median diameter) PM (at least twice and as much as 45 times the allowed daily concentration) over long periods (years) have shown no difference in animal mortality attributable to PM exposure. Participants in the workshop concluded that **animal studies have yet to identify the agent, whether chemical or mechanical, in PM that could account for the association between PM and acute or chronic health outcomes demonstrated in epidemiological studies.**

Using human studies to identify the causal agents

Clinical studies, although they have the obvious advantage that there is no need to extrapolate animal results to humans, also have limitations. As in animal experiments, creating a realistic mixture of PM that mimics both the size distribution and the chemical composition of that in ambient air is difficult. And people in groups suspected to be at greatest risk for a health effect are not appropriate to use if there is a chance of harming them. Finding subjects who will participate in long-term exposure studies of more than a few days is difficult.

Many of the recent clinical studies on PM have focused on acidic particles. That is because biologists have hypothesized that acidic particles would logically be likely to cause harm to lung tissues. Two sensitive populations have been studied: asthmatics and people with chronic obstructive lung disease. In general, among adults there is not a notable response in asthmatics, although asthmatic children do appear to have a slight constriction of the larger airways, but at levels higher than measured in current ambient environments. No reaction to acid in particles has been seen in people with chronic obstructive lung disease. Furthermore, no clinical studies have seen evidence of the rapid biological response to PM suggested by the rapid (on the order of several hours to several days) response in mortality associated with increased levels of PM demonstrated in the epidemiological studies. The workshop participants concluded that **studies in which people in sensitive populations were exposed to acidic particles have not demonstrated effects that can be readily interpreted as related to the observed association between PM** (as measured in both the 2.5μm and 10μm size ranges) **and acute health outcomes demonstrated by epidemiological studies.**

Biological mechanisms of health outcomes associated with PM

The failure of animal and clinical studies to identify the exact agents responsible for the association between increased PM and increased mortality is reason to revisit possible biological mechanisms that might be responsible for the associations observed in epidemiological studies. This approach—first hypothesizing a mechanism and then trying to identify the agent responsible for it—left workshop participants with several avenues for further research.

The immediate appearance of an increase in mortality that is associated with increased levels of PM and other air pollutants suggests that the mechanism should be quite distinct. Isolating the causes of death of people who died during the period of increased PM is not an easy task, and it has not been done. Observations dating back to the early London fog incident have convinced most scientists that the people most likely to be affected by whatever agent is in or associated with PM are older people with pre-existing coronary or respiratory disease. Thus, the mechanism leading to mortality is thought to be something that takes place rapidly and exacerbates a pre-existing disease.

The long-term, or chronic, outcomes associated with PM include a small decrease in the function of the lungs in children and a decrease in longevity in communities with higher air pollution and PM concentrations. It is thought by some that the same mechanism associated with the short-term increase in mortality might also cause the longer-term health outcomes among people who are not as susceptible to the short-term effects.

Therefore, we must look for a biological reaction that is so rapid and severe that it can cause death in the sensitive populations and yet has an action that is not so striking that doctors can easily identify deaths as being associated with ambient PM. But the mechanism working in less-susceptible populations leads to both a reduction in the lung function (that might not be noticeable except when specifically investigated) and a reduction in longevity that is also somewhat subtle.

It is important to note that the same mechanism might not be responsible for the 2 patterns of health outcomes that are seen in the short and longer term. To confuse the picture further, different agents with different mechanisms of toxicity could be involved in the acute and chronic outcomes.

Respiratory tract inflammation

A number of agents lead to respiratory inflammation that might, in the case of such sensitive populations as asthmatics, lead to a life-threatening situation. Among the agents that might cause this inflammatory response are acidic particles; particles of biological origins that induce allergic reactions, such as pollen; transition metals; and ultrafine particles; or possibly agents such as peroxides.

Acidic particles. Many particles created via the process of combustion contain compounds that make them acidic. Some researchers have believed that this acidity might be the cause of inflammation in the respiratory tract that leads to observed health outcomes, but this hypothesis is not supported by current epidemiological evidence. Asthmatics do not appear to respond markedly to acidic particles. And acidic particles appear to be substantially neutralized in the respiratory tract by the ammonia that occurs naturally there. The lack of adverse health effects with acidic particles is primarily drawn from work on "droplets" such as sulfuric acid and ammonium bisulfate aerosols. The significance of acid coated insoluble particles (for example, carbon particles) is unclear. There are some animal studies that suggest acid coated particles may be considerably more toxic than acid droplets alone.

Biological particles. After exposure to a specific allergen to which a person has previously been exposed and sensitized, a severe respiratory inflammation can occasionally occur. Allergic reactions like this are seen in up to 20% of the general population and perhaps 50% of asthmatics are allergic as defined by skin tests and/or blood tests. The rapid response of the body to allergens resembles the rapid increase in death associated with increased levels of PM. It is likely that allergens—such as pollen, molds, and fungi—can be found with and in many airborne particles. The question arises whether allergens occur at the same times as increased PM. To date, the day-to-day variations in these substances do not correlate well with PM concentrations or the associated changes in mortality. Allergic reactions, alone or in combination with PM, could contribute to hospitalization for asthma and the associated increased morbidity

Transition metals. While having transition metals—such as iron, copper and manganese—in low doses in our diet is important to maintain good health, when inhaled as constituents of PM, they can catalyze reactions in our lungs that create superoxides. Superoxides produced in this manner, although not able to produce as rapid a response as allergens, do produce a greater inflammatory effect than say, peroxides. Like peroxides,

superoxides through a chemical process called oxidation cause a breakdown in vital parts of the cell. The cell is constantly repairing this damage, which takes place throughout its life. The importance of transition metals in health outcomes rests on whether they increase the oxidation in the cell beyond what is normally dealt with by the cell's natural defense mechanisms. The capacities of these natural repair mechanisms are not well understood.

Ultrafine particles (less than 0.1μm). The role of ultrafine particles is not well understood. Some scientists have suggested that these particles, usually surrounded by water and a largely uncharacterized variety of dissolved chemical, may be the agent in question. This may be related to physical abrasion of lung cells or the chemical constituents of the watery shell of these particles affecting the lung. The lifetime of ultrafine PM in the ambient environment is thought to be short as they coagulate easily and form larger particles.

Peroxides. Recently, it has been hypothesized that ambient peroxides could be particles of concern. This class of compounds is closely associated with sulfates in the air, which are closely associated with PM and are produced as part of the photochemical smog process. Submicrometer aerosols contain a great deal of water: when the relative humidity is 70%, submicrometer particles contain 50% water and when the humidity is 46% the submicrometer particles contain 15% water. Concentrations of peroxides in PM have not been measured, but their concentrations in air can be used to estimate the amount of dissolved peroxide in fine PM. Because peroxides have their origin in the photochemical reactions of ozone, ozone control would be a means of reducing peroxides if they were shown to be an agent of concern. Nevertheless, there is very limited information about peroxides in the environment and an inadequate understanding of potential airway response to these agents.

Workshop participants believe that a number of the mechanisms and agents discussed might contribute to the observed changes in human health associated with PM. All need further investigation to determine whether they are operative.

Research needs

PM is the only regulated pollutant that is not chemically specific. Fine particles, especially those less than 1 μm, are subject to chemical reactions in the air and to the uptake of water. Their chemical composition is complex and not well understood. A research program aimed at characterizing the chemical composition of PM is an obvious step. A more-complex research initiative would involve a concerted effort to investigate particular agents and their effects on the heart and lung, and on morbidity and mortality.

It became obvious to workshop participants that an insufficient prospective, long-term well-designed epidemiological study is one cause of the controversy over interpretation of the data on PM and other air pollutants. Without the appropriate sample size, and consideration of confounding factors, future studies will not alleviate this situation. Our current understanding of how measurements at central monitoring stations relate to an individual's exposure to PM indoors is weak and further work is essential for properly understanding the contribution of PM to

observed health effects. Identification of plausible causal agents and their mechanisms would also improve the ability of these studies to inform the discussion on the potential health effects of PM. Laboratory studies of the toxicological effects of PM and specific PM constituents might identify biological mechanisms by which PM affects humans. Such studies are necessary to properly interpret the findings of past epidemiological studies and to design appropriate monitoring programs for candidate causal agents in future epidemiological studies.

Biographies of Particulate Matter Workshop Participants

Experts

Peyton Eggleston, MD is a Professor of Pediatrics at the Johns Hopkins University School of Medicine. Dr. Eggleston's areas of expertise are pediatric allergy, asthma, and aerosol immunology. Relevant to the area of particulate matter, Dr. Eggleston has studied cat and rat induced asthma, asthma morbidity relations to indoor allergens, and allergens immunotherapy.

Sheldon Friedlander, PhD, is Parsons Professor of Chemical Engineering and Director of the Aerosol Technology Laboratory at the University of California, Los Angeles. Dr. Friedlander's area of expertise is aerosol science and technology. Relevant to the area of particulate matter, Dr. Friedlander has been involved with U.S. Environmental Protection Agency (EPA) workshops on the health effects of particulate matter and has Chaired the Clean Air Scientific Advisory Committee (CASAC); he has studied measurements of aerosol morphology; he is the inventor of receptor modeling for source resolution of atmospheric aerosols using chemical signatures, and the author of the widely used textbook entitled "Smoke, Dust, and Haze."

Fred Lipfert, PhD, is a staff scientist at Brookhaven National Laboratory and an independent consultant whose area of expertise lies in air quality and epidemiology. Dr. Lipfert has conducted research on particulate matter issues for over 20 years and has published many papers on the subject. Most notably, Dr. Lipfert authored a book on the subject entitled "Air Pollution and Community Health a Critical Review and Data Source Book."

Roger O. McClellan, DVM is the President of the Chemical Industry Institute of Toxicology. Dr. McClellan's area of expertise lies in toxicology and risk assessment. Dr. McClellan has had a long-standing interest in the health risks of air pollutants with special interest in integrating the results of epidemiological investigations, controlled human exposure studies and in vivo laboratory animal studies. Previously, Dr. McClellan served as Chair of the EPA Clean Air Scientific Advisory Committee (CASAC) and served on numerous advisory panels including service on the most recent CASAC Review Panel for ozone and particulate matter.

Lucas M. Neas, MD is an Assistant Professor of Environmental Health and Epidemiology in the Faculty of Public Health at the Harvard School of Public Health. Dr. Neas is an expert in the area of epidemiology especially pulmonary function in children. Relevant to the particulate matter issue, Dr. Neas has studied the relationship between indoor particulate matter and expiratory flow rate, conducted longitudinal studies of peak expiratory flow, studied the health effects of particle strong acidity, and studied the health effects of bioaerosols.

Jonathan M. Samet, MD, MS is Professor and Chairman of the Department of Epidemiology and the School of Hygiene and Public Health at the John Hopkins University. Dr. Samet also serves on the Science Advisory Board and the Clean Air Scientific Advisory Council (CASAC) for the U. S. Environmental Protection Agency and he is presently Chairman of the Biological Effects of Ionizing Radiation Committee VI of the National Research Council. He has written widely on the health effects of active and passive smoking and has edited monographs on the epidemiology of lung cancer and on indoor air pollution.

Mark J. Utell, MD is a Professor of Medicine and Environmental Medicine and the Director, Pulmonary/Critical Care and Occupational Medicine Divisions at the University of Rochester Medical Center. Dr. Utell is an expert in pulmonary medicine, occupational and environmental medicine, and inhalation toxicology. He is also a member of the U.S. EPA's Clean Air Scientific Advisory Committee on particulate matter and ozone and has conducted research on controlled human exposures with particles. In addition, Dr. Utell has authored several papers and made several presentations on the health effects of particles.

Ron Wyzga, PhD is a Senior Program Manager with the Electric Power Research Institute (EPRI). Dr. Wyzga's areas of expertise are public health, environmental risk assessment, biostatistics, epidemiology, and air quality issues. He has undertaken several analyses of mortality and air pollution data and has written several papers on that topic. In addition, Dr. Wyzga oversees the EPRI research program regarding all aspects of research on the particulate issue.

Annapolis Center Board Members

Paul Gilman, PhD is Executive Director of the Commission on Life Sciences of the National Research Council at the National Academy of Sciences. Dr. Gilman is also Vice-Chairman of the Annapolis Center. As Executive Director, Dr. Gilman is responsible for the management of all scientific, financial and administrative operations of the Commission. Prior to joining the Academy in 1993, Dr. Gilman served as executive assistant and technical advisor to Secretary of Energy James D. Watkins and in the Executive Office of the President as Associate Director of the Office of Management and Budget for Natural Resources, Energy, and Science.

Lois Swirsky Gold, PhD is Director of the Carcinogenic Potency Project at the University of California, Berkeley, and a senior scientist at the Lawrence Berkeley National Laboratory. Dr. Gold is a member of the Board of Directors of The Annapolis Center. For the past 18 years, Dr. Gold has been developing the widely used Carcinogenicity

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