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Sulfur Oxides

Committee on Sulfur Oxides
Board on Toxicology and Environmental Health Hazards
Assembly of Life Sciences
National Research Council

NATIONAL ACADEMY OF SCIENCES
Washington, D.C. 1978

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This report has been reviewed by a group other than the authors according to procedures approved by a Report Review Committee consisting of members of the National Academy of Sciences, the National Academy of Engineering, and the Institute of Medicine.

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Chapters 1, 2, and 3 (the introduction, the summary and conclusions, and a statement of policy issues) represent the combined output of the full Committee.

Chapter 4, on sulfur oxides in the atmosphere, was prepared by Mr. Elmer Robinson and Drs. Rudolf B. Husar and James N. Galloway.

The preparation of Chapter 5, on the effects of sulfur oxides on aquatic ecosystems, was the responsibility of Dr. James N. Galloway, who received invaluable assistance from Drs. George R. Hendrey and Carl L. Schofield.

Chapter 6, which discusses the effects of sulfur oxides on vegetation, is the result of a joint effort of Drs. Delbert C. McCune and T. Craig Weidensaul.

Dr. Robert Frank prepared Chapter 7, on clinical and toxicologic evaluations.

The coverage of epidemiologic studies in Chapter 8 was the joint responsibility of Drs. Frank E. Speizer and Benjamin G. Ferris, Jr.

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The Assembly staff officer for the Committee was Mr. John Redmond, Jr. The editor was Mr. Norman Grossblatt.

Ms. Ute S. Hayman prepared and, with the assistance of Mrs. Edna W. Paulson, verified the references. Mrs. Eileen G. Brown typed the report.

1 INTRODUCTION

In preparing this document for the Environmental Protection Agency (EPA), the Committee on Sulfur Oxides has attempted to update the current evaluation of the air-pollution aspects of the sulfur oxides--their emission, their transformation and transport, their effects on aquatic ecosystems and vegetation, and toxicologic, clinical, and epidemiologic studies of their effects on humans. The report is intended to serve as a source document in the EPA's upcoming revision of the air-quality criteria document on sulfur oxides. The Committee has not recommended concentration limits to be set by regulations, but rather has evaluated the enlarged data base on which the Administrator of the EPA can make his judgments. In general, the subjects covered are those normally covered in air-quality criteria documents, except that effects on materials are not included. The Committee was not asked to discuss control technology, which could itself be the subject of a complete document.

Since the publication of air-quality criteria for the sulfur oxides in 1969, there have been numerous studies of emission, transformation, transport, animal and clinical toxicology, and epidemiology of the sulfur oxides. During the same period, there have been a number of reviews, particularly of the health effects of sulfur oxides. This Committee has elected not to review historical data, but rather to build on the 1969 criteria document and later significant reviews. As in any critical review, it has attempted to point out the strengths and weaknesses in studies that have been done and to judge where the truth probably lies, on the basis of available data.

The need to use more coal to reduce the nation's reliance on imported oil and the tremendous cost of air-pollution control equipment for energy-producing plants make it important that decisions be based on the best current knowledge. The Committee has endeavored to evaluate the scientific questions, and a

summary and conclusions are presented as Chapter 2. There are still many subjects on which decisions must be made on social or political grounds. Chapter 3 lists some of the Committee's thoughts regarding these subjects, without any suggestion as to what decisions should be made.

Throughout this report, the reader will find concentrations of, for example, sulfur dioxide expressed in parts per million (abbreviated "ppm"), micrograms per cubic meter ("$\mu g/m^3$"), or both. Most of the research summarized or cited here was conducted by people other than the authors of this report. Hence, it was often difficult to determine precisely the conditions under which the concentrations had been measured--in particular, the air temperature and the atmospheric pressure. Because those conditions influence the factor used to convert between parts per million and micrograms per cubic meter and because it was desirable to avoid misinterpretation of reported findings, the Committee decided not to convert statements of concentration from one unit to another, but rather to present them as they appeared originally in the published literature. Full references are given in each case, however, so the reader can consult the original reports for further details.

2 SUMMARY AND CONCLUSIONS

The following material is arranged in the order of its presentation in the text.

SULFUR OXIDES IN THE ATMOSPHERE

Emission

Emission of anthropogenic sulfur pollutants to the atmosphere of the United States in 1974 exceeded 31 × 10^6 metric tons (tonnes). This was almost all in the form of gaseous sulfur dioxide. Its main source was fuel combustion, which accounted for 78%; coal was the chief fuel involved (53%). Some 75% of the sulfur dioxide was emitted east of the Mississippi River.

Naturally emitted sulfur compounds probably include compounds other than sulfur dioxide, with hydrogen sulfide and a variety of organic sulfur compounds assumed to make up the natural or background atmospheric sulfur burden. In the eastern United States the natural emission is about 10% of the anthropogenic.

Although oxidized sulfur compounds, other than sulfur dioxide, are not commonly emitted, sulfates and sulfuric acid are formed in the atmosphere, and they are widely believed to constitute an important part of the atmospheric sulfur pollutant burden. The atmospheric processes by which sulfur dioxide is transformed into these other compounds cannot yet be described quantitatively.

In recent years (1970-1974), there has been a small--about 2%/yr--downward trend in national sulfur dioxide emission. This has accompanied a longer-term trend toward fewer but larger sulfur dioxide sources involving higher stack emission points and a trend in emission locations away from urban areas and toward rural locations. This has caused the emitted sulfur to be distributed over a wider area. There has also been a trend away

from peak emission during winter and toward a more uniform time distribution, or even a summer peak.

Concentrations

Generally, the data on sulfur dioxide concentrations are satisfactory only in urbanized areas, and even here the data tend to emphasize the areas of probably high concentrations--i.e., the "hot spots"--rather than some type of area average value. In general, the urban areas of the nation are in compliance with the National Air-Quality Standard (NAQS) for sulfur dioxide, in that, in 1974, the annual mean NAQS of 80 $\mu g/m^3$ was exceeded at only 31 of 1,030 reporting stations, and the 24-h standard of 365 $\mu g/m^3$ was exceeded at 99 of 2,241 stations. These results are an improvement over those of 1970, when the annual standard was exceeded at 16% of the stations and the 24-h standard at 11% of the stations.

The data base for sulfate concentrations is weak, both because of station coverage and because of sampling and analytic problems. On a national basis, the highest sulfate concentrations occur east of the Mississippi River. In rural areas of the eastern United States, there appears to be an upward trend in sulfate concentration.

There are essentially no data for particulate sulfate compounds other than as "total sulfate ions," except for a few research studies. Thus, evaluations of exposures to specific sulfur compounds, such as ammonium sulfate or sulfuric acid, cannot be established quantitatively, on the basis of monitoring results.

Concentration data tend to emphasize long-term average values, e.g., the annual mean of sulfur dioxide. However, it is reasonable to assume, on the basis of toxicologic evidence, that hazards from sulfur dioxide and the other sulfur compounds would more likely depend on the magnitude and frequency of high concentrations. Thus, some more advanced statistical variables, which are sensitive to peak concentrations, may be important as a concentration measure in addition to the long-term average.

There are no data that can adequately describe actual human exposures, in view of the large differences between the indoor and the outdoor atmosphere.

Sulfates constitute about 30-40% of the atmospheric fine-particle mass concentration, and their mean size range coincides with the range of most efficient light-scattering per unit mass. Furthermore, atmospheric sulfates are hygroscopic or deliquescent; this increases their role in light-scattering and visibility reduction. The coincidence of visibility degradation and

the presence of sulfates has been documented through correlations at fixed locations and through comparisons of visibility reduction and sulfate concentrations in various geographic regions. However, the relative contribution of sulfates to total visibility degradation cannot be assessed quantitatively without more data on the concentration of other visibility-reducing compounds.

Transport by the Atmosphere

The atmosphere moves emitted sulfur from the emission point to the receptor. As far as sulfur dioxide is concerned, the greater the transport distance, the greater the dilution. High stacks have been adopted widely to increase the transport and, thus, to increase the dilution that occurs before contact is made with the ground. For sulfate compounds and other reaction products, however, concentrations in a plume can increase with transport and, because these products increased with time, the impact of a given source may be observed for long distances--hundreds or thousands of miles in some cases--downwind.

Because of our poor knowledge of the quantitative aspects of the conversion of sulfur dioxide to sulfate in the atmosphere, model calculations of downwind impact are unsatisfactory.

Transformations

The importance of atmospheric reactions in the sulfur compound air-pollution problem has already been noted. Important pollutant impacts from sulfate compounds and sulfuric acid are postulated; however, these compounds are formed in the atmosphere, presumably as a result of atmospheric chemical reactions based on sulfur dioxide emissions. Some particulate sulfur compounds would also be formed from hydrogen sulfide and other natural emission.

Two general mechanisms appear to be considered important atmospheric processes: a photochemical process involving hydrocarbons, nitrogen dioxide, and strong oxidants (such as ozone); and a liquid-droplet process involving fog or cloud droplets and ammonia. A third process proposed on the basis of laboratory observations is surface catalysis involving solid-particle surfaces.

Field studies have been carried out to determine the importance of various transformation mechanisms. In general, the rate of conversion of sulfur dioxide to a sulfate compound is a

few percent (1-5%) per hour in the daytime and less than 1%/h at night. These values emphasize the photochemical rates. Liquid-droplet conversion rates have not been as well quantified, but are probably about 1-5%/h.

Processes Removing Sulfur Compounds from the Atmosphere

Sulfur compounds are removed from the atmosphere by being deposited onto the earth's surface. The most important processes are the deposition of sulfur dioxide on the surface by turbulent motions (i.e., "dry deposition") and the entrainment and deposition of sulfur compound particles by precipitation (i.e., "wet deposition"). The other two apparent processes, wet deposition of sulfur dioxide and dry deposition of sulfate, are considered to be of secondary importance in most situations.

A considerable amount of experimental data has been obtained on these removal processes. In terms of their relative effectiveness, estimates of the importance of dry versus wet processes of sulfur removal range from a ratio of 60:40% to 40:60%. Thus, it might be estimated that about half the emitted sulfur dioxide is lost to the ground surface in the gaseous state by dry deposition and about half is converted in the atmosphere to a sulfur-compound aerosol and then carried to the earth by precipitation.

These conversion and removal processes for sulfur dioxide are relatively rapid, and it is generally estimated that the residence time of sulfur compounds is 2-4 days (from emission to surface deposition). However, considering transport mechanisms, this still provides for a travel distance of 1,000 miles (1,600 km) or more for important fractions of the emission or its reaction products.

Sulfur Budgets

"Budget," as used in discussing an air pollutant, is a mass balance of a pollutant in a prescribed air volume using approximations of the emission, atmospheric transformations and transport, scavenging, and removal of the pollutant. It can be calculated for geographic areas of a variety of sizes--from regional (e.g., the northeastern United States) to global. Budgets are usually used to evaluate the relative importance of various interrelated processes. They have been especially useful in considerations of sulfur-compound systems by permitting an estimate to be made of natural emission processes, on which few, if any, applicable field data have been available.

For conditions in the United States, regional budget considerations can be made to show the predominance of pollutant emission in the area east of the Mississippi River. Similarly, budget models can explore the relative importance of dry and wet deposition processes and transport across the Canadian border or over the Atlantic Ocean.

Budgets in general contain broad assumptions and variables averaged over large areas; and conclusions based on budget modeling will depend heavily on those assumptions and variables.

From the sulfur budget calculation for the eastern United States, two conclusions are evident. The emission of sulfur into the atmosphere is dominated by anthropogenic sources. Three processes remove sulfur from the atmosphere over the eastern United States: wet deposition, dry deposition, and export to the Canadian and Atlantic Ocean atmosphere. The three processes remove approximately equal amounts of sulfur.

EFFECTS ON AQUATIC ECOSYSTEMS

The largest noticeable effect of SO_x on aquatic ecosystems is the acidification of oligotrophic lakes and streams by acidic precipitation. Acidic precipitation is caused by sulfuric and nitric acids in about a 2:1 ratio. There may be a slight contribution by hydrochloric acid. Lake acidification causes substantial alterations in ecosystem structure and function. Whole populations are destroyed, most noticeably the fish populations. Hundreds of lakes in the northeastern United States have been acidified in part by sulfuric acid in acidic precipitation.

As lakes acidify, metals go into solution. The concentrations of some of these metals (lead, aluminum, and mercury) have increased enough to be toxic to fish and potentially hazardous to humans.

Lakes susceptible to acidification are found throughout the United States, primarily in areas whose soil is derived from granitic and metamorphic bedrock.

EFFECTS ON VEGETATION

In general, there appears to be no serious threat to terrestrial vegetation from atmospheric sulfates. Insofar as direct, adverse effects of sulfur oxides on vegetation are concerned, present evidence indicates that gaseous sulfur dioxide is of greater toxicity than sulfate in particulate form or in dilute aqueous solutions.

There have been conflicting research results and much confusion in the literature about sulfur dioxide dose-response relationships in plants. This may be due to inadequate observations and control of experimental conditions. Results of many studies have suggested that the relative significance of short-, mid-, and long-term average concentrations must be evaluated with reference to the kinds of exposures that occur and the kinds of effects that can result. The occurrence of sulfur dioxide above specified atmospheric concentrations for short periods (12 h or less) appears to pose a greater hazard than longer exposures to lower concentrations, with reference to direct, adverse, aesthetic, and economic effects on higher plants.

Foliar injury may occur on susceptible species and varieties of plants under some ambient conditions if a peak atmospheric sulfur dioxide concentration greater than 2,600-5,200 $\mu g/m^3$ (1.0-2.0 ppm) occurs for less than 1 h, the concentration exceeds 1,300-2,600 $\mu g/m^3$ (0.5-1.0 ppm) for 1 h, the 3-h maximal average concentration exceeds 780-1,300 $\mu g/m^3$ (0.3-0.5 ppm), or the 6- to 8-h maximal average concentration exceeds 520-780 $\mu g/m^3$ (0.2-0.3 ppm). Foliar injury on most species is unlikely if the atmospheric concentration of sulfur dioxide does not exceed 520 $\mu g/m^3$ (0.2 ppm).

Adverse effects on the growth and yield of agricultural and forest species of plants generally can occur in the absence of foliar lesions at long-term mean concentrations of 130 $\mu g/m^3$ (0.05 ppm), but increases in growth and yield of the same plants and of other species can also occur at mean concentrations of 50-200 $\mu g/m^3$ (0.02-0.08 ppm).

Long-term, and perhaps indirect, adverse effects of sulfur dioxide on lichens and epiphytes have been reported in areas with annual means of 13-260 $\mu g/m^3$ (0.005-0.1 ppm).

The indirect effects of ambient sulfur dioxide on biotic relationships (plant-pathogen, -soil, or -insect interactions) may have long-term significance and deserve further study.

Interactive effects of sulfur dioxide and other gaseous and particulate atmospheric contaminants have been found. The interaction of sulfur dioxide and nitrogen dioxide generally elicits a response in plants (usually an adverse effect) that is greater than additive and suggests synergism between these gases. The nature of plant response to mixtures of sulfur dioxide and ozone is neither well understood nor consistent. Depending on plant species, experimental atmospheric conditions, gas ratios, tissue age, etc., mixtures of sulfur dioxide and ozone have caused additive, less-than-additive, and greater-than-additive plant responses. These two compounds are considered the two most important gaseous pollutants in the United States relative to

their abundance, distribution, and phytotoxicity, so more research is needed to clarify the nature and importance of their combined influence on vegetation.

Present evidence is inadequate to establish exposure-response relationships for the effects of sulfate aerosols on vegetation.

Research has indicated that simulated rainfall, acidified with sulfuric acid, can have direct adverse effects on plants and soils, but an unequivocal relationship between increased acidity of precipitation and decreased growth of crops or forests has not yet been demonstrated. Much more research is needed on frequency, duration, intensity, and temporal changes in composition, as well as the contribution of sulfate in acidic precipitation and their relationships to direct or indirect effects on vegetation that could be of a cumulative or irreversible nature.

TOXIC EFFECTS

With the exception of one study, acute exposure to sulfur dioxide at 1 ppm has been unassociated with pulmonary functional changes in animals. Concentrations many times higher are generally required to elicit functional changes by acute exposure. Prolonged exposure of animals to sulfur dioxide alone at 1 ppm has had no adverse cumulative effect on conventional tests of function or on lung structure. There is some evidence that the clearance of insoluble particles from the lung may be affected by sulfur dioxide administered at 1 ppm for several weeks (see page 141).

The results of studies of the effects of sulfur dioxide on healthy volunteers have suggested that 0.5 ppm elicits no functional change. Over a period of hours, 1 ppm may impede the flow of nasal mucus and depress maximal ventilatory performance. Continuous exposure may depress dynamic compliance measured at 120 breaths/min after 24-48 h, but the effect is less significant after 72-120 h. Dynamic compliance measured at lower frequencies is unaffected. Functional changes are more likely to occur when exposure is combined with exercise than at rest. Persons with a diagnosis of either asthma or early obstructive lung disease have reacted essentially the same as healthy persons during laboratory exposures to sulfur dioxide at 0.5-3.0 ppm. An occasional person has had an asthmatic attack at 1 ppm. Toxicologic evidence indicates that brief exposure to high concentrations of sulfur dioxide may cause a greater response than prolonged exposure to low concentrations, both in animals and in man.

Recent studies involving exposure of animals to a wide variety of sulfate-containing aerosols have adduced few changes in conventional tests of pulmonary function at concentrations ranging

from 100 $\mu g/m^3$ to several thousand micrograms per cubic meter. Impairment of tracheobronchial clearance has been noted in donkeys after exposure to sulfuric acid at 194 $\mu g/m^3$ and higher.

Chronic exposure to sulfuric acid alone at approximately 100 $\mu g/m^3$ has been unassociated with changes in pulmonary function or structure. Histologic evidence of damage to the airways has been noted at approximately 1,000 $\mu g/m^3$, in association with equivocal functional evidence of airway narrowing.

Healthy volunteers exposed for brief periods to various sulfate aerosols, including sulfuric acid, in concentrations of 10-1,000 $\mu g/m^3$ have experienced no symptoms of discomfort or functional aberrations. Subjects with asthma and allergies have been unaffected by ammonium sulfate administered over a 2-h period. The subjects were at rest.

The relatively high concentrations of ammonia in the upper airways, especially the mouth, may afford protection against atmospheric acid particles.

Few studies have incorporated a mixture of reactive pollutants. One report indicated that low concentrations of sulfur dioxide and ozone act synergistically to reduce maximal ventilatory performance in healthy subjects. A later study provided evidence that the synergism may have been attributable to particulate matter either drawn into the chamber from contaminated outside air or formed by the mixing of the two gases at high concentrations. When the entry and formation of particles were reduced to a minimum, the synergism was only marginal.

EPIDEMIOLOGIC STUDIES OF HEALTH EFFECTS

The epidemiologic evidence on the health effects of sulfur dioxide gathered since the previous criteria documents were published in 1969 and the several reviews that have appeared in the early 1970s have been studied. The important points stressed are related to both the usefulness of the measures of exposure for epidemiologic studies and the determination of health effects of both acute (24-h) and chronic (annual) exposure. In each case, there is relatively little new evidence available that stands up to rigorous critical assessment, and one is left with the following conclusions.

Sulfur Dioxide

There have been relatively few epidemiologic studies on the effects of short-term (24-h) high concentrations of sulfur dioxide. To the extent that the effect of sulfur dioxide can be separated

from the effects of particles in the data reviewed, the present 24-h primary standard for sulfur dioxide of 365 $\mu g/m^3$ is reasonable. Population exposures to this concentration are associated with a slight increase in asthmatic attacks and reversible changes in pulmonary function. More data are needed to support a change in the present standard.

There have been more epidemiologic studies with respect to effects of long-term chronic exposures. Here, too, it has been difficult to separate out the relative contributions of sulfur dioxide and particles. On the basis of the studies presented, there is no justification for changing the present annual average of 80 $\mu g/m^3$. There is a need for studies that will allow the separation of the effects of sulfur dioxide and particles--e.g., in areas with high sulfur dioxide and low particle concentrations, and vice versa.

There are no epidemiologic data that definitely incriminate sulfur dioxide as a carcinogen or cocarcinogen. The only study that raised this question involved heavy concomitant exposure to a known carcinogen.

There are no data that will allow one to predict accurately the differences in effects between an annual mean value with little day-to-day variation and a similar mean with a number of wide (high) excursions interspersed with very low concentrations. Studies need to be developed to try to answer this question.

More effort is needed to determine the actual exposures of populations, rather than relying on the small number of monitoring sites that have usually been selected for the purpose of regulation.

The effects of spending relatively long periods indoors and a short period outdoors need evaluation.

Sulfur Trioxide

There are no epidemiologic data with which to draw conclusions about the effects of sulfur trioxide.

Sulfates

There are not sufficient epidemiologic data to establish a standard for sulfates. When such a standard is to be developed, it must take into account the type of sulfate--e.g., sulfuric acid or "acid" sulfates--because the associated cations are likely to be more important than the sulfate radical.

3 POLICY ISSUES

The Committee, in preparing this review of scientific data on sulfur oxides, has attempted to delineate the concentrations that have effects and where those effects occur, in spite of conflicting and insufficient data. There are, however, matters on which decisions cannot be made only on the basis of scientific knowledge and judgment. These are matters that involve conflicting requirements and great uncertainties. In view of the enormous sums of money that may be involved in such decisions, this chapter attempts to outline some of these matters that require political and social decisions to be made on the basis of scientific judgment, but biased by national or societal goals. It does not attempt to recommend specific decisions, but only to call the subjects to the attention of the political and social decision-makers.

The order of subjects in this chapter does not indicate priority, but rather follows in general the order in which related material appears elsewhere in the text.

The evaluation of the physical characteristics and atmospheric processes of emitted sulfur and of their environmental impact brings to the surface a number of problems that either cannot yet be resolved technically because of a lack of data or, although technically definable, require a political decision as part of the control strategy adopted. These are listed briefly below:

- Sulfur oxides pollution comes from an increasing number of tall point sources in nonurban areas. This change can affect local and regional concentration patterns and may be important to consider when comparing observed concentration trends with emission trends.
- The increased number of tall stacks with large plume rise favors long-distance transport of emitted sulfur dioxide. Some consideration could be given to ways to reduce plume height to an

optimum in an attempt to reduce the impact of long-distance transport. Too much reduction would increase ground concentrations beyond this optimum.

- The seasonal cycle of emission seems to have shifted: there is more summer emission, owing to demands for air conditioning. Because photochemical reaction processes that convert sulfur dioxide to sulfates and sulfuric acid can be at a maximum in warm months, seasonal weather factors may be important in understanding seasonal concentration patterns. Control and emission policies may be influenced by these seasonal factors.
- Because of the long-distance transport of sulfur dioxide reaction products--sulfates and sulfuric acid--control strategies will include the recognition that distances of 1,000 miles (1,600 km) or more may separate sources and receptors. Thus, control actions will extend over large regions.
- Much of the impact of sulfur dioxide emission results from the atmospheric formation of aerosol particles. The reactions involved are not well defined or quantified. A better understanding of these reactions might suggest optimal control strategies.
- Section 169A of the Clean Air Act of 1970, as amended, put forth "as a national goal the prevention of any future, and the remedying of any existing, impairment of visibility in mandatory class I Federal areas which impairment results from manmade air pollution." Particulate sulfur compounds constitute an important, if not the dominant, chemical species of visibility-reducing aerosol over the eastern United States. Therefore, the implementation of the Clean Air Act Amendments with respect to visibility must be closely linked with appropriate sulfate control strategies.
- The surface concentration of sulfur compounds depends on source configuration (location and emission height). Therefore, time trends of concentrations and emissions may not match in a simple manner.
- Judgments about air quality are based typically on air-sampling data gathered over an extended period. Many aspects of the location and design of a sampling station affect the quality of the data from the station. The EPA is strongly encouraging better station design, and it is likely that significant amounts of older data can be challenged on the basis of station design and siting. This should be recognized when air-quality data are used to support controversial air-quality control strategy.
- It has been difficult to assess changes in atmospheric deposition of sulfur due to fossil-fuel combustion, because of the lack of a historical data base. A national atmospheric deposition network is necessary to alleviate this problem. Such a network will provide the data necessary for the determination of the effect of control strategies on sulfur emission.

- Fossil-fuel emission of sulfur into the atmosphere of the United States causes acidified precipitation in Canada. Atmospheric sulfate is also transported from Canada to the United States. Best estimates indicate that U.S. exports exceed the Canadian exports. This phenomenon will concern both U.S. and Canadian regulatory agencies.

Lake acidification by sulfuric acid in precipitation is a regional phenomenon. It occurs in areas remote from emission sources of sulfur dioxide. Therefore, control strategies for the reduction of sulfur dioxide emission will be regional in scope and allow for the fact that sulfur emitted in Ohio acidifies lakes in New York, Canada, and so on.

The increase in metal concentrations in drinking water from acidified reservoirs has the potential of being a regional phenomenon. The considerations related to solutions and control strategies that are mentioned above are applicable here.

It is difficult to assess the risk to human health and welfare from lake acidification. The problem is compounded because, with the exception of increased metal concentrations, the effects are welfare-oriented. However, we know so little about the long-term effects of ecosystem acidification in our environment that it is necessary to proceed cautiously, with respect to increasing the input of SO_x into the atmosphere of the United States.

Lake acidification is the result of sulfuric acid and nitric acid, both derived from fossil-fuel combustion. The elimination of only sulfuric acid from the atmosphere will reduce the extent of lake acidification, but will not prevent it, owing to the contribution from the nitric acid.

Our present knowledge of the effects of SO_x on vegetation and terrestrial ecosystems raises the question of the proper use and allocation of land, fuel, and energy in this country. Environmental trade-offs are inevitable when alternatives are developed and used.

In any attempt to regulate, or at least limit, SO_x emission into the atmosphere, a trade-off for energy availability will have to be considered. The forms of energy used and their applications will become increasingly important in the years ahead. For example, it is not inconceivable to suggest that more SO_x be tolerated in ambient air if the end result or benefit derived is the use of the increased amount of electricity produced for mass-transit systems. This might lower the concentrations of NO_x in ambient air and later the concentration of ozone, which is the most important phytotoxic air pollutant in the United States.

If a conscientious effort were made, in land-use policy, to locate stationary sources of SO_x (such as coal-fired electric

generating plants) properly, more U.S.-based energy reserves could be used less expensively, without causing intolerable interferences with plant growth and development.

Use and commodity priorities must be established. That means that various comparisons must be addressed, including the following:

- Crop economics versus landscape aesthetics.
- Crop wholesomeness versus crop appearance.
- Crop availability versus emission-source or energy-production economics.
- Emission-source economics versus landscape aesthetics.
- Emission-source economics versus crop wholesomeness.

The establishment of an SO_x standard, be it fixed or flexible, should accommodate the land-use priority in the area affected by SO_x sources. Some thought should be given to the protection of agriculture through land-use planning, as well as by standards for air quality, especially around metropolitan areas.

No single determinant controls the injury sustained by vegetation owing to SO_x. Genetic, environmental, developmental, and use factors must be considered together, with respect to the influence on injury at a given time or in a given location. Spatial and temporal differences can be quite important in the United States. Climate, soils, use patterns, topography, and frequency of meteorologic events differ substantially from North to South and from East to West in the United States. These factors might be superimposed on the spatial and temporal factors that determine the plant population at risk. Because the temporal pattern of dispersion, as well as the magnitude, of emission determines risk, proper siting can afford additional protection to what is gained by flue-gas desulfurization.

Because coal is increasingly replacing oil and will be the predominant source of additional energy, continuing and properly supported research into the longer-term and more widespread consequences of power generation should be ensured for the near- and mid-term periods, so that one can more adequately determine the marginal effects of additional sources of power.

To propose a standard for one pollutant that will protect the entire population is illusory. There are people who--perhaps owing to age, heredity, or underlying illness--will react at some time or other to mere traces of the pollutant. The dilemma is magnified if, as is customary, other pollutants are also present in the air. Different elements may interact and reinforce each other in their impact on the body, in ways that are virtually impossible to predict or to simulate in the laboratory. Thus,

mixtures of pollutants could be hazardous even if their individual components satisfied the standards. Furthermore, there is good evidence that the effects of pollutants are subject to influences as diverse as weather and socioeconomic standing. Indoor air pollution may pose a hazard equal to or greater than that of outdoor pollution. This is especially true in proximity to cigarette-smoking, in kitchens, and where some inefficient home-heating systems are used increasingly during cold weather. There is a need to develop better estimates of exposures of populations by placing more monitors where exposures are more likely and to take into account the fact that people spend most of their time indoors.

Legal and ethical constraints on clinical research are increasing. The problem of what constitutes "informed consent," in combination with the ethical dilemma and legal risks in exposing volunteers to pollutants, is making clinical research more difficult. This is much more of a problem in the study of "impaired" persons (persons with respiratory or cardiovascular disease). These impaired persons are the very group most likely to suffer damage from ambient air pollution. Such legal and ethical constraints would deprive society of valuable information.

Legislation and control measures should acknowledge these realities. Legal language that is rigid and categorical serves little useful purpose, in the face of the scientific uncertainty and ambiguity. The concept of "reasonable safety" or "acceptable risk" needs to be considered as a replacement for "no adverse health effect" in the assessment of air pollutants.

What constitutes an "adverse" effect needs to be defined. Should a change that is readily reversible, that is unassociated with impairment of any integrated function, and that may be undetected by the individual be considered "adverse"? In many such instances, there are insufficient data to make an objective decision. Inherent in this is the need to define what is an acceptable risk.

Because sulfur dioxide and particles often have a common source and appear to have some degree of interaction, consideration should be given to the use of an air-pollution index that could permit control of one to be relaxed if control of the other were more stringent.

Data are needed to permit a standard to be set for fine particles, up to several micrometers in diameter, in addition to total suspended particles.

There is a need to develop better dose-response relationships for both acute (short-term) and chronic (long-term) exposures and to determine the relative contributions of sulfur dioxide, sulfate and its cation, and particles.

The question of whether sulfur dioxide is a surrogate and/or an active component associated with health effects needs resolution. If sulfur dioxide is a surrogate, is it a surrogate for something quite different, or is it a surrogate for related compounds, such as sulfates? Continuing effort must be directed toward the difficult task of determining to what extent sulfur dioxide affects health directly or is a surrogate for other air pollutants or other factors.

4 SULFUR OXIDES IN THE ATMOSPHERE

As air pollutants, sulfur oxides and other sulfur compounds undergo several processes during their residence time in the atmosphere--i.e., from emission to arrival at a receptor. Some portions of this chapter describe those processes, which affect the characteristics of the pollutants when they reach receptors. Other sections present factual discussions of emission, measurement, and atmospheric sulfur budgets.

Much of the material in this chapter emphasizes the sulfate aspects of the sulfur-compound pollutant issue, rather than those related to sulfur dioxide, because of our belief that the sulfate aspects are less well known and pose more important problems in the design of control strategy than does sulfur dioxide.

SOURCES OF SULFUR POLLUTANTS

Anthropogenic Sulfur Dioxide Emission

Sulfur dioxide was emitted from man-made sources in the United States at an estimated rate of 30 Tg/yr* in 1973.[52] Fuel combustion exclusive of transportation accounted for 78%, industrial processes (primary-metal industry, petroleum industry, chemical manufacturing, etc.) for 20%, and transportation for 2% (Figure 1). Of the fuels used by utilities and industry, about 65% of the national anthropogenic emission of sulfur dioxide came from coal combustion and 13% from oil combustion (Figure 1).

*One teragram (Tg) = 10^{12} grams (g) = 10^{9} kilograms (kg) = 10^{6} metric tons (tonnes, t).

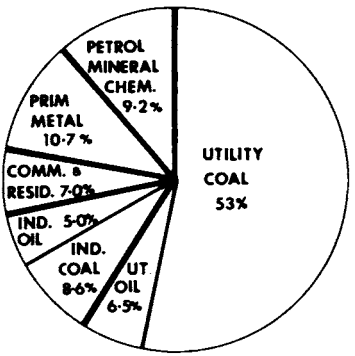


FIGURE 1 Sources of sulfur dioxide emitted in United States, 1973. Data from U.S. EPA.[52]

Some 75% of the sulfur dioxide emitted was emitted east of the Mississippi River, with the highest emission density in the vicinity of the Ohio River valley (Ohio, Pennsylvania, and Indiana); fuel combustion contributed 92% of the total sulfur dioxide (Figure 2). Of the 25% emitted west of the Mississippi River, fuel combustion contributed only 38%, and industrial and mining processes 62%.

Natural Emission of Sulfur Compounds

Natural emission of sulfur in the United States has these sources: marine (coastal) biogenic production of hydrogen sulfide, terrestrial (soils, wetlands, and lakes) biogenic production of hydrogen sulfide and a number of organic sulfur compounds, and geothermal emission of hydrogen sulfide and sulfur dioxide. Of these processes, the first is generally considered the most important,[21] but there are practically no experimental or monitoring data on which an evaluation of natural emission can be based directly. Natural emission of sulfur in the United States is estimated to be less than 2 Tg/yr.[21] The anthropogenic emission of sulfur in the United States is 15.7 Tg/yr.

The anthropogenic emission of sulfur dioxide is not evenly distributed throughout the United States. Indeed, 75% of anthropogenic sulfur is emitted east of the Mississippi River. The ratio of anthropogenic emission to natural emission is even greater in this region than in the total United States as a whole.

Sulfur Dioxide Emission Trends

In the period 1970-1974, there was a downward trend in national emission of sulfur dioxide, from 34.3 to 31.4 Tg/yr, or

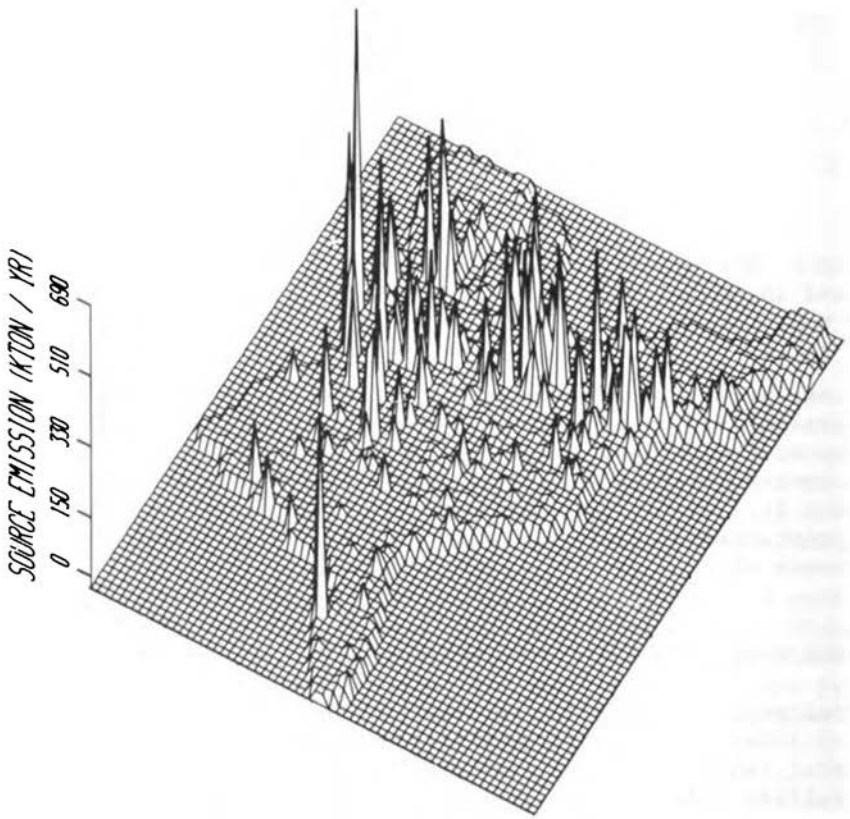
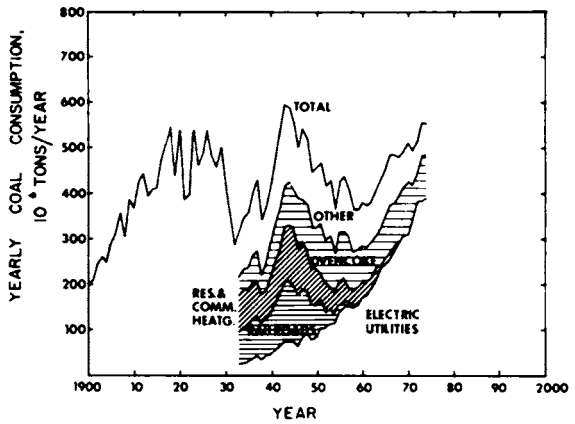
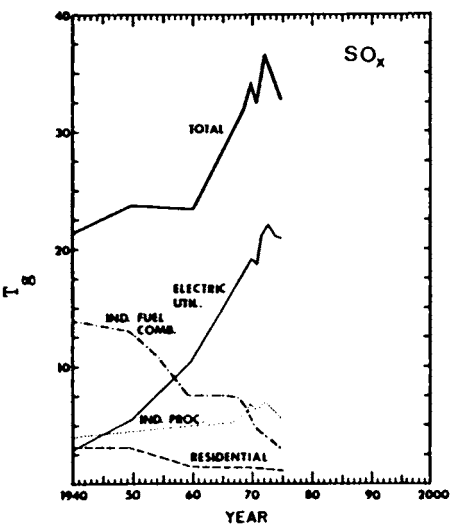


FIGURE 2 Sulfur dioxide emitted east of Mississippi River, United States. Source inventory for all area and point sources; 1973 EPA emission data. At 34.5°N, grid size is 32 km/side of squares. Unpublished data from R. E. Meyers, R. T. Cederwall, and J. A. Storch, Brookhaven National Laboratory, 1977.

approximately a 2%/yr reduction.[52] In the 1960s, however, there was an appreciable increase, from about 24 to 34 Tg/yr. The upward trend in the 1960s was due primarily to the increase in the utility coal combustion (Figure 3). EPA emission estimates for 1940, 1950, and 1960 indicate roughly constant emission, at about 23 Tg/yr.

Because coal-burning contributed a substantial portion of the sulfur dioxide emission in the past, it is instructive to observe the readily available[51] coal-use data for the last 75 yr. The





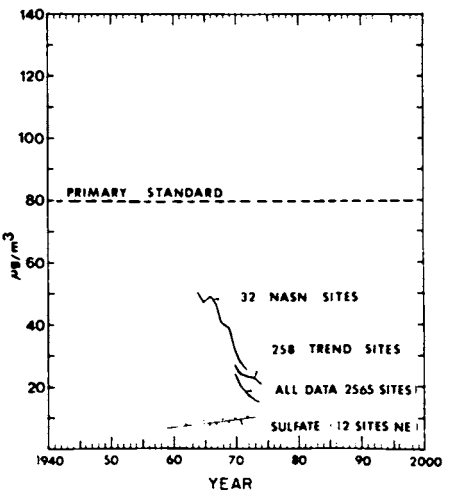


FIGURE 3 U.S. trends in (top) coal use, (bottom left) sulfur oxides emission, and (bottom right) sulfur dioxide and nonurban sulfate ground-level concentrations. Data from U.S. Bureau of Mines (top)[51] and U.S. EPA (bottom).[53]

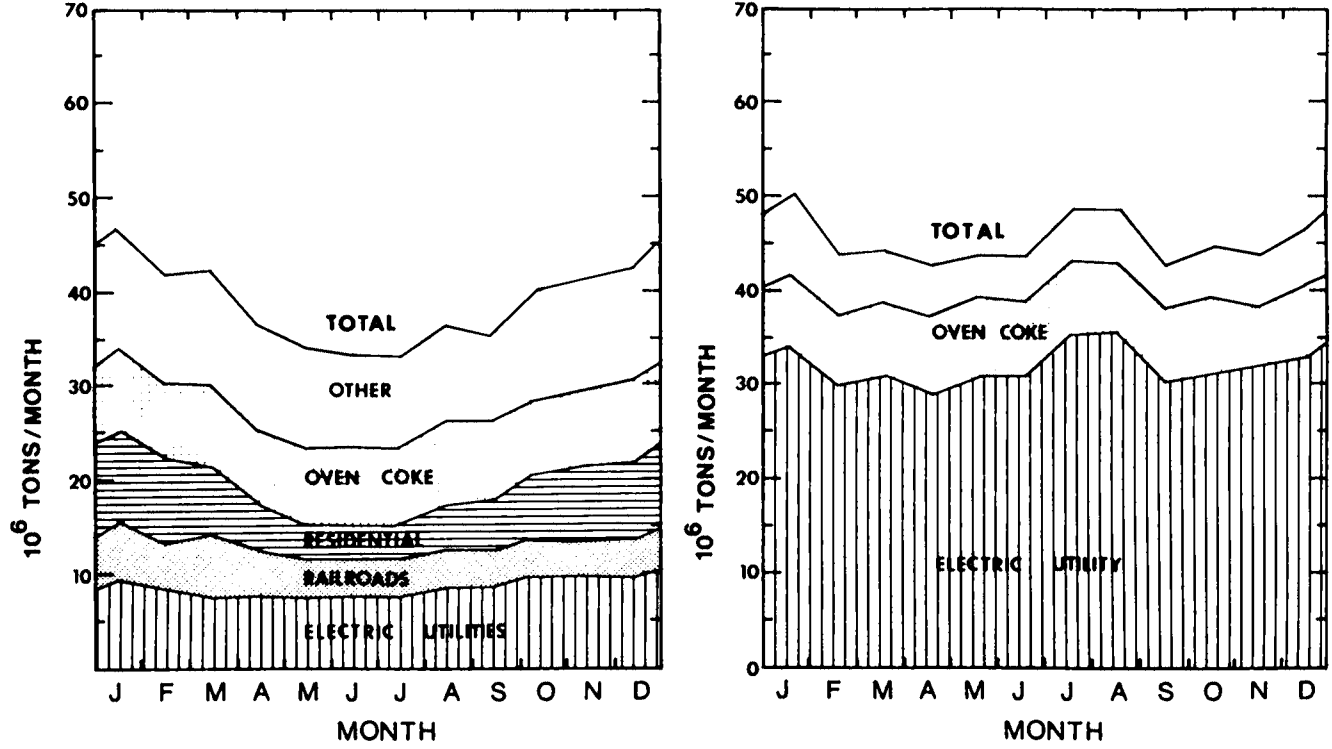


FIGURE 4 Seasonal pattern of U.S. coal use. Left, 1951; right, 1974. Data from U.S. Bureau of Mines.[51]

current use is approximately 600 × 10^6 t/yr, and it has been increasing by about 4.5%/yr since 1960. The current trend is driven by the electric utility use (Figure 3). Coal consumption rates were similar to the current use during 1941-1945 and during 1918-1930. However, there has recently been a shift in coal use away from railroads and residential heating and toward electric utilities, which now dominate the coal consumption. The national plan of the coal industry, as well as of the government, is to increase coal production to about 10^9 t/yr by 1985. The shift in use toward utility combustion has also meant a shift toward higher effective stack heights for the atmospheric release of sulfur dioxide. The higher stacks--over 1,000 ft (305 m) in some cases--have been installed to provide stack-gas dilution sufficient to meet the adopted sulfur dioxide air-quality standards.

Between 1950 and 1974, there was also a shift in the seasonal pattern of coal use (Figure 4). In the 1940s and 1950s, the maximum was during the winter, owing to the winter peak (Figure 4) of residential coal use. Since 1960, the summer coal consumption has increased, compared with winter consumption, owing to the increased summer use of coal by electric utilities.

Discussion

A number of features of the present state of SO_x emission should be considered with regard to their possible impact on an air-quality criteria document and on SO_x control strategies:

- Sulfur dioxide pollutant sources are now dominated by large point sources that are increasingly frequent in nonurban areas. This may be important when long-term data on concentrations or other SO_x impacts are considered.
- Sulfur dioxide emission is identified with increasingly taller stacks and effective plume dispersion heights. This can have an important bearing on the transport characteristics of the SO_x plume.
- The seasonal cycle of SO_x emission seems to have changed from a weak winter maximum to a weak summer maximum. This may affect the importance assigned to the several atmospheric chemical transformation mechanisms, e.g., $SO_2 \rightarrow H_2SO_4$ and $SO_2 \rightarrow (NH_4)_2 SO_4$, etc.

ATMOSPHERIC CONCENTRATIONS OF SULFUR COMPOUNDS

There is a good historical data base for sulfur dioxide concentrations in urbanized areas, and it shows a decline from an annual

average of 38 μg/m^3 in 1970 to 26 μg/m^3 in 1974.[53] This represents an overall decrease of 32%, or approximately 9%/yr (Figure 3). During this time, the national sulfur dioxide emission decreased by 8%, or about 2%/yr.

In 1974, the annual mean sulfur dioxide standard of 80 μg/m^3 was exceeded at only 3% of the monitoring stations (31 of 1,030), compared with 16% in 1970. The 24-h sulfur dioxide standard (365 μg/m^3) was exceeded at 4.4% of the reporting stations (99 of 2,241) in 1974, compared with 11% in 1970. The trend of sulfur dioxide concentration for 258 selected "trend sites" is shown in Figure 5,

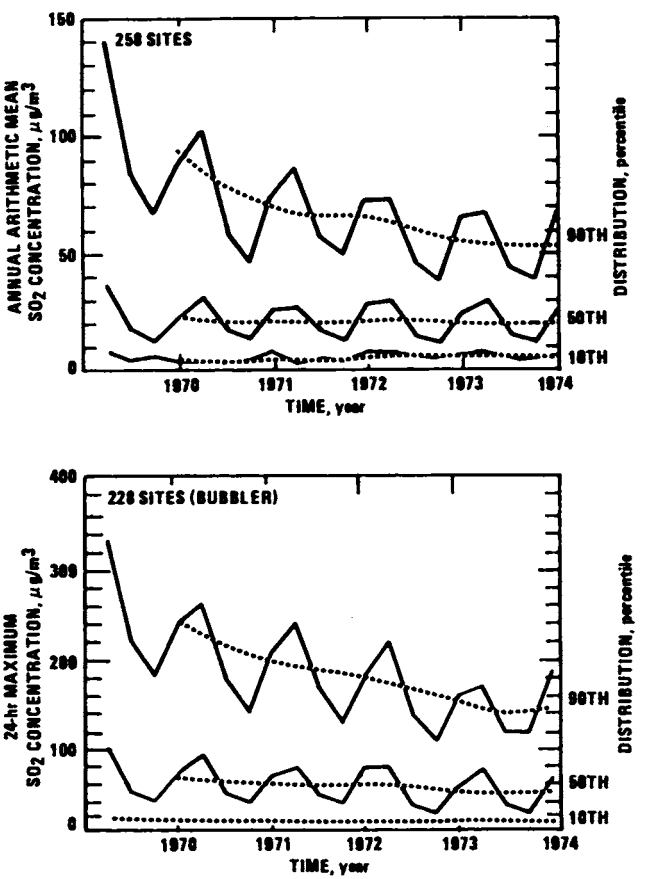


FIGURE 5 National trends in sulfur dioxide: 10th, 50th, and 90th percentiles for (top) annual mean and (bottom) 24-h maximum. Data from U.S. EPA.[53]

which displays the 10th, 50th, and 90th percentiles of the quarterly averages. The 10th and 50th percentiles have been fairly stable; the 90th percentile has improved appreciably at the sites with higher values. In the past, the high sulfur dioxide concentrations were recorded in large urbanized areas, and those showed the strongest decline. In smaller cities (population less than 250,000), the concentrations remained essentially constant, at about 18 $\mu g/m^3$.[53]

Over 90% of the National Air Surveillance Networks (NASN) monitoring sites are in urbanized areas, although emission shifted away from center-city and came from higher stacks in 1974 than in 1970. Thus, the overall decline is likely to be a combined result of reduced emission, redistribution of sources, and increased emission height.

The historical data base for sulfate concentrations in the United States is weak. Careful inspection of the existing data,[55] however, reveals an upward trend of nonurban sulfate concentrations in the Northeast-Midwest (Figure 3, "12 sites NE"). The spatial distribution of sulfates for 1974 is shown in Figure 6. The contour of the area with concentrations above 15 $\mu g/m^3$ corresponds roughly to the highest sulfur dioxide emission densities (Figure 7).

In assessing changes in air-pollutant concentrations and especially correlations between pollutants, it is important to know that meteorologic factors play a dominant role in determining most urban pollutant concentrations. Thus, it can generally be expected that, in a given urban area, there will be a high degree of correlation between observed concentrations of different pollutants--e.g., between sulfur dioxide and total suspended particles (TSP)--because the general concentrations of both pollutants are controlled primarily by wind speed, boundary-layer stability, and other components of weather. This dependence of concentration patterns on weather has some obvious implications for relating changes in the concentration of a specific pollutant, such as sulfate particles, to an adverse impact, such as respiratory complaints. Perhaps the most obvious is the fact that in an urban area most of the other components of the air-pollutant mixture will have the same type of concentration pattern, and it will be difficult to identify causative candidates that can be uniquely related to the impact. This has been pointed out by a number of investigators; but, in many older studies, health impacts were suspected for an easily measured pollutant, such as sulfur dioxide, because there was a simple correlation with the severity of the complaints. What was lacking in many such assessments was the recognition that the concentration of the single pollutant was a good index of the atmospheric concentrations of a wide variety of pollutants.

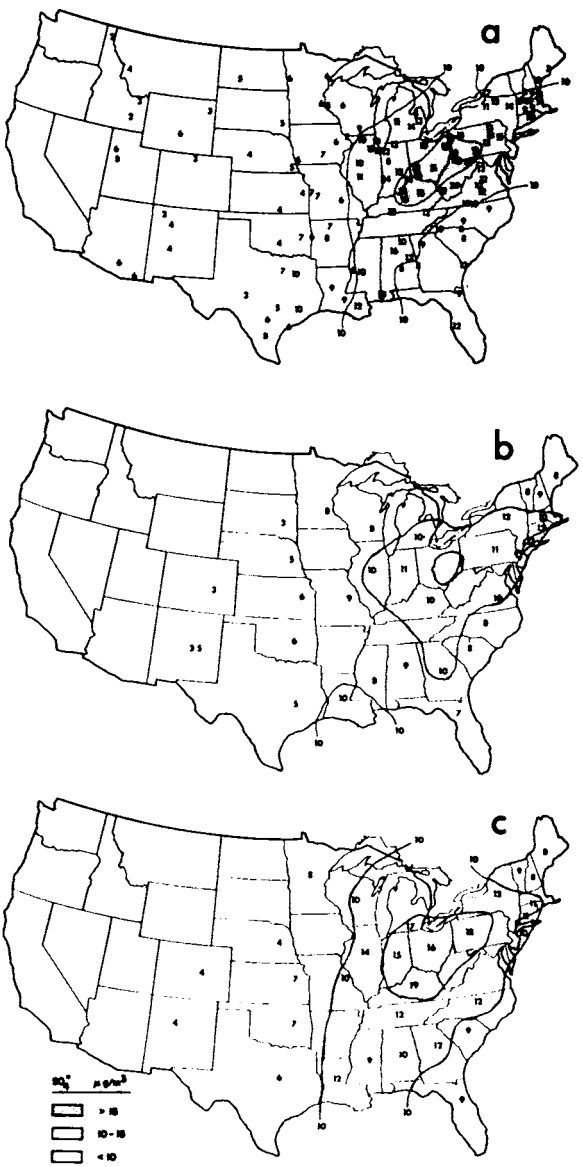


FIGURE 6 Contour maps of sulfate concentrations, $\mu g/m^3$, 1974. a, annual average; b, winter average; c, summer average. Data from U.S. EPA.[55]

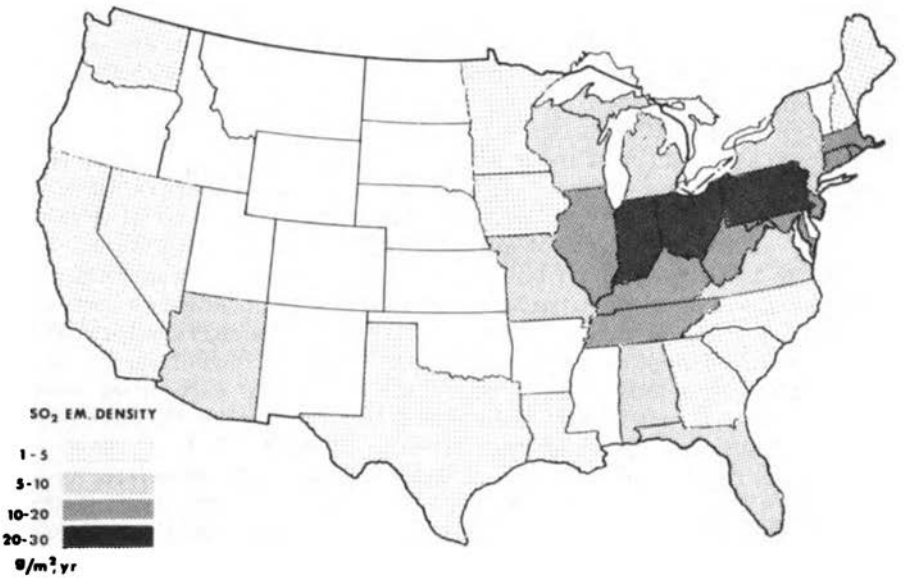


FIGURE 7 Sulfur dioxide emission density, by state. Data from U.S. EPA.[54]

Another meteorologic question with a bearing on pollutant concentrations is whether our knowledge is sufficient for us to model the likely exposures of population groups to a given pollutant, given the sources of the pollutant. Of the various sulfur compounds, it appears that modeling techniques for sulfur dioxide have reached a reasonable and useful stage of development. This has been shown especially by the modeling studies carried out in Europe in connection with the investigation of long-range transport of sulfur dioxide and sulfate into Scandinavia.[43] It thus seems likely that long-term average exposures to sulfur dioxide can be modeled reasonably well. Short-term exposures relatively close to a source can probably also be modeled with acceptable accuracy with available plume models.

However, models of sulfate concentrations in the ambient air are much less developed than the sulfur dioxide models. The principal reason is that the mechanisms responsible for forming sulfate from sulfur dioxide in the atmosphere are poorly understood. Thus, models must be based on the subjective extrapolation of individual experiments. This limits the reliance that can be placed on sulfate exposure models. However, some success has been obtained with this empirical approach in some areas.

For other sulfur compounds--such as sulfuric acid, ammonium sulfate, and hydrogen sulfide--model predictions of exposures are not possible, because of a lack of satisfactory chemical formation models and a lack of measurements of ambient air by which to verify proposed models.

Essentially all the data available represent ambient atmospheric conditions outside of buildings. For reactive gases (such as sulfur dioxide and the other sulfur gases) and to a lesser extent for aerosols, average concentrations inside buildings would generally be expected to be lower than outside concentrations. A few studies have been made to assess the differences between inside and outside concentrations, but no generally applicable model relating exposures encountered inside a building has been developed. It seems likely that, until indoor exposures are well documented, there will be considerable scatter in the data comparing impacts on man and ambient-air concentrations.

An aspect of atmospheric concentrations that seems to have been given less attention than is desirable is the distribution of concentrations about the long-term average. Much attention is being given to the annual average, with some further consideration to the maximal short-term value reached in a year. It seems reasonable to expect that a more complete description of the concentration frequency would improve knowledge of actual air-pollutant hazards. This appears to be especially true of a set of pollutants, such as the sulfur oxides, that seem to have little tendency to accumulate in biologic systems and whose impacts thus depend heavily on concentration, exposure, and exposure frequency. The annual mean is a relatively poor approximation of the exposure characteristics that are most important to the receptor community.

In summary, national concentrations of sulfur dioxide are decreasing, but this may not reflect national emission trends. There are a number of interacting factors related to source relocation, changes in the observed concentration ratio of sulfur dioxide to sulfates, and time-trend differences between fuels and sulfur dioxide emission that influence the concentrations. One must face a number of policy issues in reconciling these factors. For example, to what extent is the change in the sulfur dioxide: sulfate concentration ratio due to source relocation? Should the location of sources be used to control sulfur dioxide and sulfate concentrations? Should one minimize sulfur dioxide or sulfate aerosol? How can the observed reduced concentrations be equated with the known increases in sulfur dioxide emission?

VISIBILITY REDUCTION AND SULFATE

Light-scattering and absorption by aerosols can cause substantial deterioration of the optical environment; aerosols can also perturb the transfer of radiative energy in the atmosphere. Of the total atmospheric aerosol population, fine particles 0.2-1.0 μm in diameter are known to be the most efficient light-scatterers per unit mass. The mass distribution of sulfates is generally confined to the optical subrange of 0.2-1.0 μm; hence, they constitute the key component of the light-scattering aerosol population.

Section 169A of the Clean Air Act of 1970, as amended, put forth "as a national goal the prevention of any future, and the remedying of any existing, impairment of visibility in mandatory class I Federal areas which impairment results from manmade air pollution." A rational approach to that goal requires knowledge of visibility-reducing primary and secondary aerosol species, gaseous precursors of visibility-reducing secondary aerosol species, the sources of gaseous precursors and primary fine particles, and source-control techniques for reducing primary and precursor emission. This section discusses the role of sulfates as they are related to the perturbation of atmospheric transfer of radiative energy, including visibility and turbidity.

Atmospheric aerosols interact with both solar (short-wave) and terrestrial (long-wave) radiation. The efficiency of light-scattering per unit mass or volume depends strongly on particle size and less on refractive index. The aerosol diameter with the greatest light-scattering efficiency roughly equals the wavelength of scattered radiation. For solar radiation, for instance, the peak light-scattering diameter is about 0.5 μm (Figure 8).[16] For terrestrial radiation, the most efficient scattering aerosols are in the size range of 5-15 μm. The common atmospheric particulate sulfur compounds--ammonium sulfate, $(NH_4)_2SO_4$; ammonium bisulfate, NH_4HSO_4; and sulfuric acid--are essentially pure scatterers of solar radiation, owing to their small imaginary component of the refractive index. In the infrared region, however, these species are absorbents[44] (and emitters) and contribute to the trapping of the terrestrial radiation (greenhouse effect). The current understanding is insufficient to assess reliably the importance of aerosols in the transfer of infrared radiative energy. It is anticipated, however, that current research will answer the remaining questions. We are confined here to the discussion of radiative effects involving solar radiation.

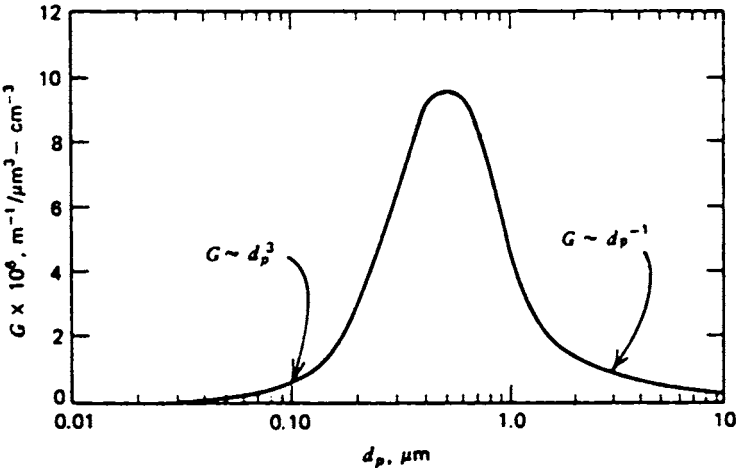


FIGURE 8 Light-scattering per unit volume of aerosol material as function of particle size, integrated over all wavelengths for refractive index, $m = 1.5$. Incident radiation is assumed to have standard distribution of solar radiation at sea level. Limits of integration on wavelength were 0.36-0.680 μm. Limits of visible light are approximately 0.350-0.700 μm. Reprinted with permission from Friedlander.[16]

Size Distribution of Sulfates

The concentration of particulate pollutants in a given size range can be determined from impactor-segregated samples. The distribution with respect to particle size of key species measured in the vicinity of New York is shown in Figure 9.[45] The normalized mass distribution plots in Figure 9 show clearly that sulfates, ammonium, lead, and some nitrates are confined to the fine-particle range. Soil-dust constituents like iron and magnesium, however, are found almost entirely among coarse particles. The size separation of these species is directly attributable to their sources and mechanisms of formation.

It is evident that the size range of atmospheric sulfates closely coincides with the particle-size window of most efficient light-scattering. Accordingly, sulfate at 1 $\mu g/m^3$ will scatter more than the same mass of species that are either larger (e.g., soil-dust particles) or smaller (e.g., lead halide particles).

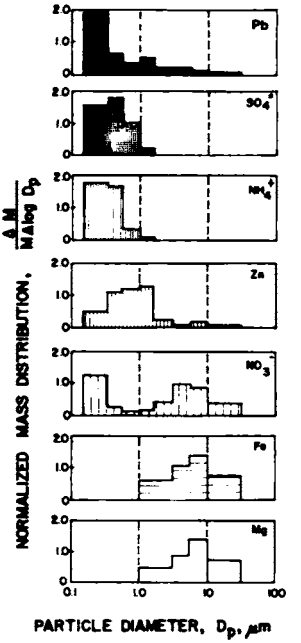


FIGURE 9 Normalized mass distribution functions of some species found in New York City aerosol. Data from Patterson and Wagman.[45]

Chemical Composition and Refractive Index

The optical properties of sulfur compounds depend on their chemical form, as well as on the amount of absorbed water, which in turn depends on the relative humidity.

The value of the refractive index for dry atmospheric aerosol particles ranges from 1.4 to 1.6. For water, the value is 1.33. For a hygroscopic or deliquescent particle, the refractive index will approach that of water as the particle grows at high humidities. Because the growth of particles with humidity is known for only a few pure substances, the humidity dependence of refractive index of atmospheric aerosols is not predictable on theoretical grounds. Barnhardt and Streete[1] quoted an empirical formula:

$$n = 1.54 + 0.03 \ln (1 - RH/100).$$

Hanel[23] proposed a linear interpolation between the dry-particle refractive index and water, based on the volume fraction of the dissolved matter.

The available data show that the particulate sulfur in most polluted areas is in the form of sulfate ion.[5,48] It has also

been shown that the cations may be either NH_4^+ or H^+, depending on the history of the air mass in which the sulfates reside.[5,8] The frequency of occurrence of the various sulfur compounds as a function of time and space is not well established.

Contribution of Sulfates to Total Light-Scattering

The role of sulfates in atmospheric light-scattering depends on their light-scattering efficiency, $(b_{scat} \times 10^{-4}\ m^{-1})/(\mu g\ of\ SO_4^{2-}/m^3)$, or m^2/g, as well as their relative contribution to the fine-particle (FP) mass concentration, $(\mu g\ of\ SO_4^{2-}/m^3)/(\mu g\ of\ FP/m^3)$. In principle, the contribution of sulfates to the light-scattering can be determined from fundamental physical-chemical analysis or from statistical multivariant correlations between b_{ext} (proportional to the inverse of visibility) and the chemical compounds in the aerosol.

The statistical approach has been used by White[58] to estimate the role of sulfates in visibility reduction in the Los Angeles basin. He correlated the measured light-scattering coefficient with the concentrations of sulfate aerosol and nonsulfate aerosol (NSA) and found that 90% of the observed variance in the scattering coefficient could be accounted for by the following least-squar fit:

$$b_{scat} = 7.6\ m^2g^{-1}[SO_4^{2-}] + 2.4\ m^2g^{-1}\ [NSA] \pm 1.0 \times 10^{-4}\ m^{-1},$$

where NSA = total aerosol - 1.3, the calculated concentration of nonsulfate aerosol with 1.3 representing the mass ratio of sulfate compound (e.g., ammonium sulfate, ammonium bisulfate, and sulfuric acid) to sulfate ion. From the statistical analysis, White concluded that the light-scattering efficiency of sulfate ($7.6\ m^2/g$) is higher than the efficiency of the nonsulfate aerosol ($2.4\ m^2/g$). Similar statistical analysis of sulfate and visibility relationship in Los Angeles was conducted by Cass,[7] whose conclusions supported White's analysis.

A high correlation ($r = 0.89$) between 24-h average sulfate concentration and light-scattering coefficient data was reported from the New York Summer Aerosol Study (NYSAS),[28] as shown in Figure 10. The light-scattering per unit sulfate ranged between 11 and 14 m^2/g. It is apparent that simple correlations of sulfates with b_{scat} or visibility without a chemical mass balance and without size-distribution data for fine particles can be used only as a qualitative measure of the role of sulfates in visibility reduction.

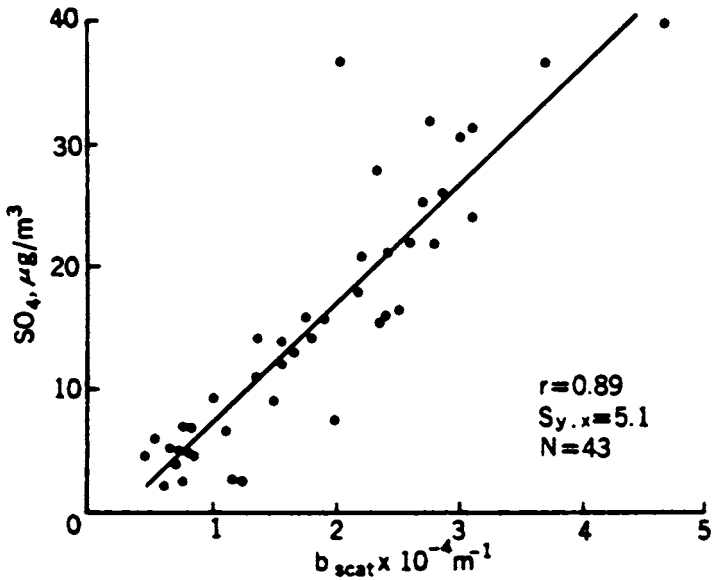


FIGURE 10 Correlation between total water-soluble sulfates as measured from 24-h high-volume samples and 24-h average scattering coefficients for visible light ($b_{scat} \times 10^{-4}$ m^{-1}) observed in New York City during the New York Summer Aerosol Study, 1976. Reprinted with permission from Leaderer *et al.*[28]

In St. Louis, as part of the Regional Air Pollution Study (RAPS), it was reported that particulate sulfur constitutes approximately 10% of the fine-particle mass concentration.[13,33,37] This corresponds to 30-40% of the fine-particle mass, depending on whether the chemical form is sulfuric acid or ammonium sulfate. Hence, if the light-scattering efficiency of sulfur compounds is taken to be the same as that of the rest of the fine particulate matter, their contribution would be 30-40% of the total light-scattering. It is likely, however, that sulfates are more efficient light-scatterers, and they are more hygroscopic than the rest of the fine particulate matter. Hence, 30-40% may be a lower bound for their relative contribution to light-scattering in the St. Louis region.

The relationship between aerosol size distribution and visibility (or extinction coefficient) is obscured by the hygroscopicity of aerosols, which causes particle growth by water uptake

at higher humidities (higher water vapor pressure). Charlson and co-workers[9,12] have demonstrated empirically the strong humidity dependence of light-scattering for laboratory-generated pure sulfur compounds, as well as for ambient aerosol. Detailed measurements of laboratory-generated aerosols of pure substances by Tang and Munkelwitz[49] showed that the hygroscopicity can be predicted by the theory of solution equilibria (Figure 11).

Regional-Scale Visibility Pattern

The spatial distribution and temporal variation of visibility over the eastern United States have been examined recently by contour plotting of the daily noon values.[34] It was noted that the noon visibility contours can reveal the evolution and motion of hazy air masses with characteristic scales of 1,000 km or more.[22,24] For a regional-scale air-pollution episode between June 23 and July 5, 1975, Husar *et al.*[27] compared the visibility contours and the sulfate contours for 2 days, on the basis of data reported by the NASN. In the beginning of the episode (Figure 12), the

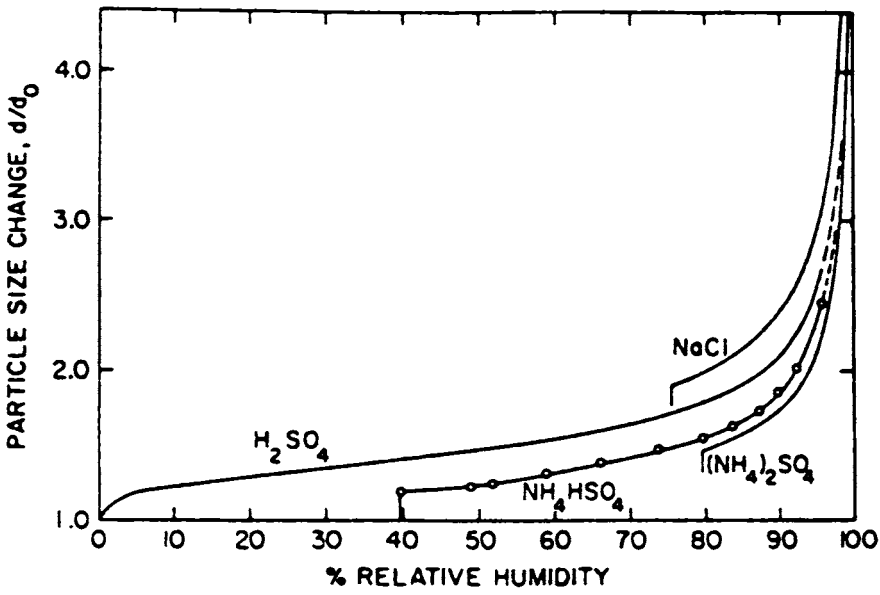


FIGURE 11 Theoretical growth curves for solution droplets of sulfuric acid and other inorganic salts of interest at 25°C. Reprinted with permission from Tang and Munkelwitz.[49]

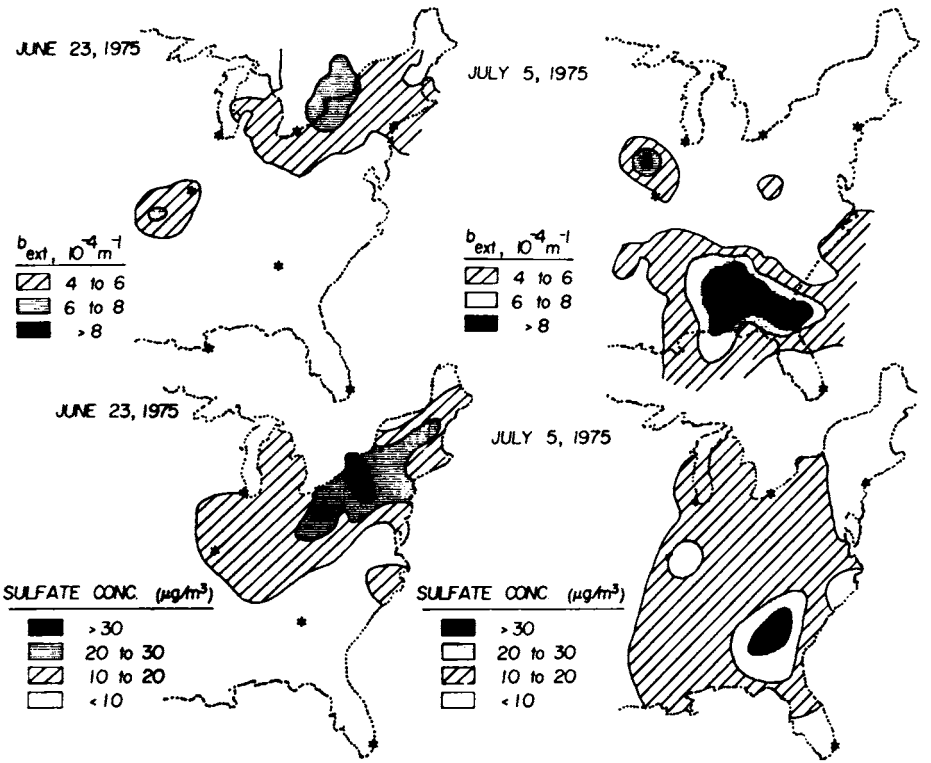


FIGURE 12 Comparison of contour plots of noon visibility reduction (b_{ext}, 10^{-4} m^{-1}) and sulfate concentration for June 23 and July 5, 1975. Data from Husar *et al.*[27]

hazy air mass (visibility, less than 6 miles, or 9.6 km) was south of the Great Lakes, corresponding to the region with sulfate at over 20 $\mu g/m^3$. After a 12-day residence time, the hazy air mass meandered over the eastern United States to the southeastern states of Alabama, Georgia, and Florida. The low visibility contours on July 5, 1975, also corresponded with the region of highest sulfate concentration. These data indicate the presence of sulfate in hazy air masses, but do not reveal their relative contribution to the visibility degradation. Such a quantitative estimate would require data on the size distribution and chemical mass balance for the aerosol in the optical subrange.

The June-July 1975 episode has also been observed on the visible spectrum images of the synchronous meteorologic satellite (SMS).[35] On June 30, 1975, the hazy air mass was over Missouri and Iowa (Figure 13). The grayish appearance of the

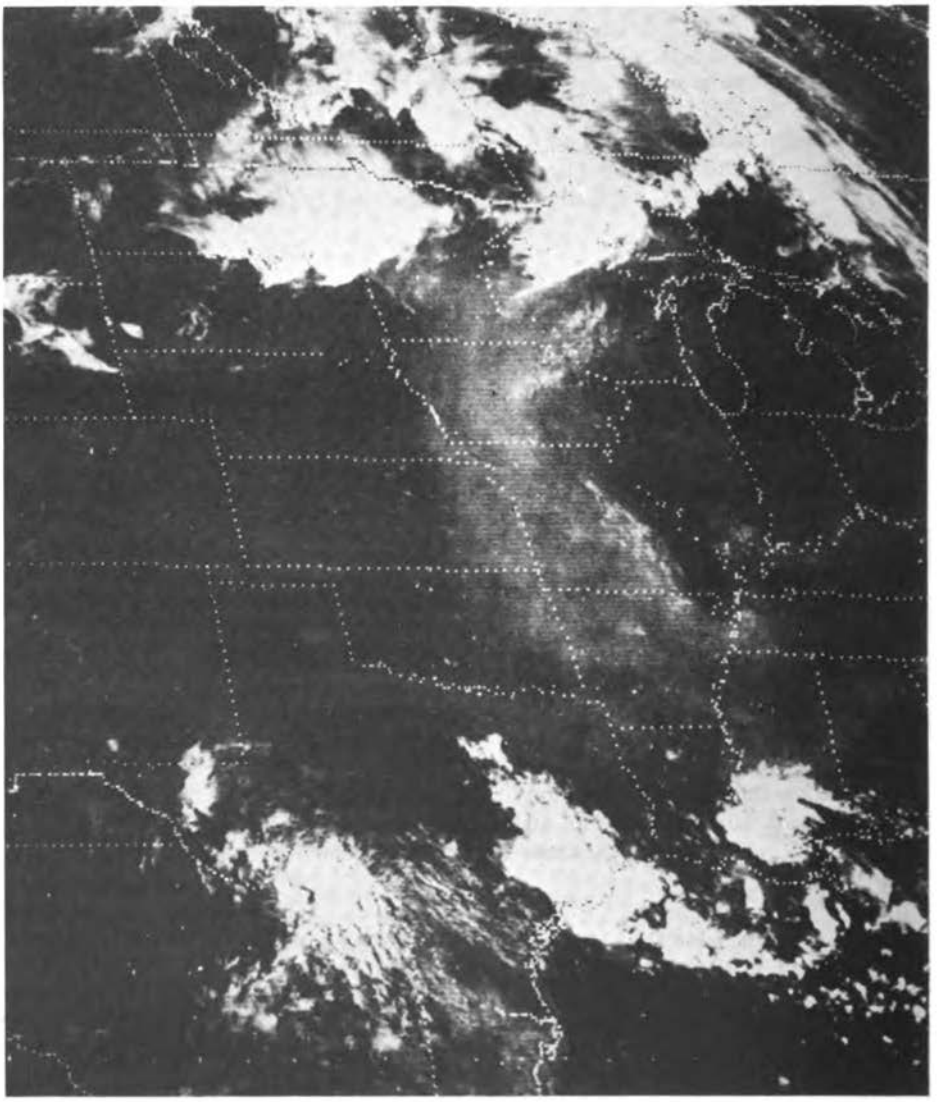


FIGURE 13 Satellite photo (SMS/GOES) of June 30, 1975, showing hazy air mass of geographic extent similar to that in Figure 12. Change in surface albedo is due to back-scattering by aerosols. Reprinted with permission of the American Meteorological Society from Lyons and Husar.[35]

hazy air mass compared with the surrounding darker background is evidence of the change in albedo (reflectance) due to the haze layer, composed of sulfate and other particles.

The seasonally averaged visibility contours over the United States (R. B. Husar, personal communication) for the relative humidity range (60-70%) are shown in Figure 14. It is evident that the visibility for the eastern half of the United States is appreciably less than that for the western half, with the exception of California's south coast air basin. Over the eastern United States, the worst visibility is recorded over the Ohio River valley, including parts of Indiana, Ohio, Pennsylvania, Kentucky, and West Virginia. Seasonally, the worst visibility over the eastern United States is during the summer months, when the Ohio River valley visibility is less than 6 miles at a relative humidity of 60-70%. It is worth comparing the summer average visibility contour map with the summer average sulfate contour map shown in Figure 6. Both the visibility and the sulfate concentrations are worse in the Ohio River valley region. However, the relative contribution of sulfate to the visibility reduction is not established, owing to lack of information on other visibility-reducing aerosol species.

Summary

Sulfates constitute an important, if not the dominant, chemical species of visibility-reducing aerosol population. This is due to their relative abundance, which is between 30 and 40% of the fine-particle mass, as well as to the coincidence of their mean size with the range of most efficient light-scattering per unit mass. Furthermore, particulate sulfur compounds in the atmosphere are hygroscopic or deliquescent; this enhances their role in light-scattering. The coincidence of visibility degradation and sulfates has been documented via correlations at fixed locations and by comparing geographic regions of reduced visibility and increased sulfate concentration. However, the relative contribution of sulfates to the total visibility degradation cannot be assessed quantitatively without more data on the concentration of the other visibility-reducing compounds.

TRANSPORT OF SULFATE COMPOUNDS

In contrast with sulfur dioxide transport, which can occur in well-defined plumes because of concentrated emission from large sources, the transport of sulfate compounds, such as ammonium

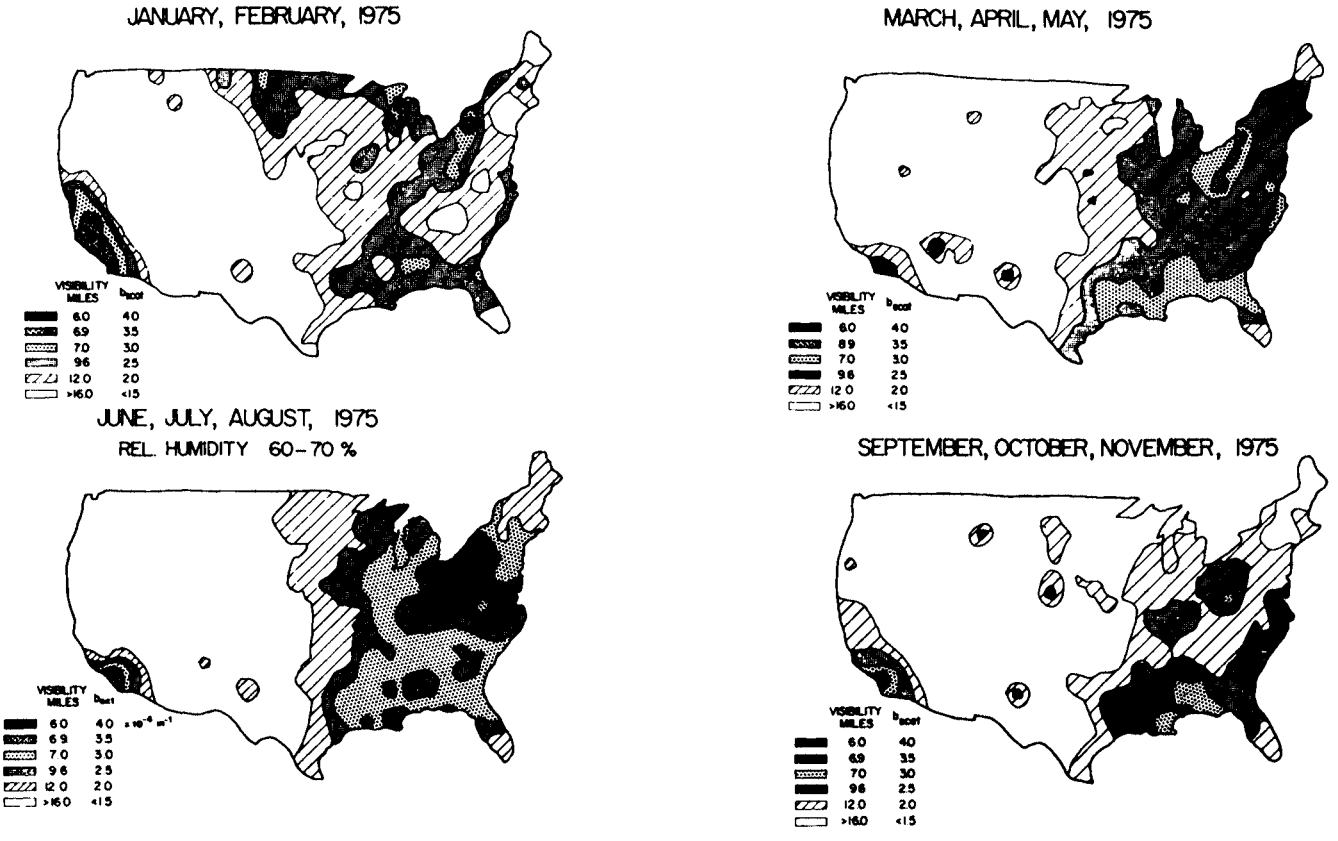


FIGURE 14 Worst visibility over eastern United States (with relative humidity 60-70%) occurs in summer. From R. B. Husar, personal communication.

sulfate and sulfuric acid, occurs in less-defined plumes. The reason for a much more uniform sulfate pattern is that the sulfate compounds form as a result of reactions in the plume (as described later) and at a lower rate than that of the normal dilution or dispersing processes in the atmosphere. Thus, much of the sulfate compound is formed after the emitted sulfur dioxide has lost its identity in a plume, and sulfate pollutants assume regional or large-area concentration characteristics.

Sulfur dioxide oxidation processes are accompanied by gas-particle conversion resulting in the formation of a fine-particle aerosol. In this physical form, scavenging or removal processes act relatively slowly. As a result, the sulfate aerosol remains in the atmosphere for 3-5 days, during which it becomes more dispersed and spreads over an increasingly wide area at a rate of about 500 km/day.

The meteorologic system whose characteristics favor the accumulation of sulfate compounds, along with other pollutants, is the slow-moving, warm, high-pressure system. Such a system is typical of summer and early fall and favors an increase in pollutant concentrations, because its overall motion is slow, inversions are common in the lower atmospheric layers, clear skies favor photochemical smog-forming processes, and an absence of rain reduces the likelihood of precipitation scavenging.

Because of the regional size characteristics of sulfate pollution episodes and their persistence over a number of days, sulfur dioxide emitted from a source will be added to prior days' pollutants and more or less evenly distributed across a relatively large regional pollutant mass. This will create a situation characterized by "hot spots," or high concentration areas, in the areawide sulfate pollutant region, and on succeeding days dispersion will tend to average out the pollutant concentration. Where the pollutant mass passes over another source area, a new, subregional hot spot can develop.

With respect to control strategies and air-quality criteria, the regional characteristics of sulfate pollutants (e.g., sulfuric acid and ammonium sulfate) indicate that the sources of the high concentrations of these materials in a given area may not be local activities. The impact of sulfate pollutants can extend over 1,000 miles (1,600 km) or more from the original sulfur dioxide source. Thus, the regional SO_x impact area is much larger than currently used air-quality control regions, and in most cases impacts can be postulated across most state boundaries in the northeastern United States. Such transport across state (national) boundaries has been demonstrated in the European (OECD) study of long-range transport.[43]

This regional impact of sulfates extending over 1,000 km or more requires control strategies that recognize the transport

conditions. Present controls are organized around local impacts; thus, a considerable need for new approaches is now evident.

MEASUREMENT OF SULFUR COMPOUNDS

Methods of measuring the concentration of sulfur dioxide (especially in areas affected by air pollution) are better developed than those for particulate sulfur compounds. This section therefore focuses on the measurement of particulate sulfur species, such as sulfuric acid and ammonium sulfate.

There have been numerous measurements over the years of the total sulfate concentration in the atmosphere determined on the basis of the amount of sulfate ion measured with high-volume filter samplers. It was generally assumed that this represented the sulfate content of the total suspended particles (TSP) in the atmosphere. More recently, and especially since the possible health effects of sulfates have been reported, there has been considerable concern over errors that can occur in high-volume sampling for sulfates in TSP. The most common source of error is probably the formation or neutralization of sulfate ion on the high-volume filter surface as a result of the reactions between sulfur dioxide or sulfate particles in the atmosphere and either the filter matrix or the already deposited atmospheric particles. A number of studies have attempted to determine the seriousness of the sulfate conversion problem. Answers are not yet consistent, and more research is needed.

With regard to the development by EPA of a revised air-quality criteria (AQC) document, it will be necessary for EPA to reach some supportable decision on the historical sulfate data and how they can be used to determine the trend of ambient sulfate concentrations. New techniques of sampling and analysis have already yielded some data on current sulfate exposures. However, it may not be possible to extrapolate from data being obtained now to earlier times and to different geographic areas in a way that will be satisfactory for developing correlations between sulfate and various adverse effects. We cannot yet assume that correlations between apparent and real sulfate concentrations are the same in all areas or are constant over time at a given location.

The identification of sulfate compounds in the TSP is important, particularly the fraction that is composed of sulfuric acid. Various water-soluble sulfates have been identified in TSP samples, but these are still being determined by expensive and time-consuming techniques, so data are limited. Thus, for an AQC document, any conclusions will have to be based on research data and probably no long-term monitoring data for specific particulate sulfur compounds.

It is generally assumed that the sulfate ion species, including sulfuric acid, are present in the atmosphere as particles. In some cases, there is evidence that sulfur compounds are present in the atmosphere mainly as particles of relatively pure compounds; at other times, the particles may be heterogeneous mixtures of many atmospheric compounds. Thus, when the sulfate aerosol is described as having a given size distribution, this may mean that the sulfate particles had this size pattern or that the sulfate was present as only one component in the particles of the stated size. Whether the sulfur compound was present as a generally pure particle or as part of a mixture could be important in estimating adverse effects.

TRANSFORMATIONS OF SULFUR DIOXIDE

Sulfur dioxide, a primary pollutant, undergoes chemical reactions in the atmosphere that lead to a change in its oxidation state, most commonly to SO_4^{2-}. The change is accompanied by a gas-to-particle conversion process having particulate sulfur, a secondary pollutant, as an end product.

Evidence is accumulating that the major effects of sulfur oxides (those on health, terrestrial and aquatic ecosystems, visibility, and weather and climate) are associated more with the reaction products than with sulfur dioxide itself. For this reason, an appreciable fraction of current sulfur research is focused on the sulfur dioxide transformation. The questions of main concern pertain to the mechanism and rate of conversion, the fraction of sulfur dioxide transformed, and the chemical and physical properties of the particulate sulfur compounds.

It is currently held that the oxidation of sulfur dioxide in the absence of promoting compounds is slow, compared with the observed or inferred atmospheric conversion. Hence, one challenge of atmospheric chemistry is to determine which substances and which environmental or emission characteristics promote or inhibit sulfur dioxide oxidation in the atmosphere.

From the point of view of effective controls, the specific questions are as follows:

- *Is the rate of aerosol formation linearly proportional to sulfur dioxide concentration*? If so, "linear-rollback" control strategies will work as expected, and a reduction in sulfur dioxide emission will lead to a proportional reduction in sulfate concentration. It is conceivable, however, that the conversion rate is dominated by external influences and depends only weakly on sulfur dioxide. In that case, a large reduction in sulfur

dioxide would yield only marginal improvement in sulfate concentration.

- *Are the agents that oxidize sulfur dioxide man-made and thus controllable*? If the sulfur dioxide oxidation is promoted by man-made oxidizing agents (as is now suspected), then the specific role of those substances (e.g., the HO radical) should be established and the means of controlling them should be explored. Although the HO radical is present in the natural atmosphere, its formation rate is increased in the photochemically active atmosphere.
- *Do natural (e.g., meteorologic) phenomena influence sulfur dioxide conversion*? Temperature, humidity, solar radiation, and other natural phenomena may influence the conversion rate, and they may offer a possibility of alternative controls.
- *What is the chemical composition of the particulate sulfur*? Acidic aerosol is believed to be environmentally more harmful than neutral aerosol. The conditions that favor formation of acidic aerosol should be established.

To answer those questions, it is necessary to understand the sulfur dioxide conversion mechanisms.

Mechanisms of Oxidation of Sulfur Dioxide

Four mechanisms are believed to be important in atmospheric sulfur dioxide conversion. The first, indirect photooxidation, is "homogeneous"--i.e., the key step in the sulfur dioxide oxidation occurs in the gas phase. The other three are "heterogeneous"--the reactions occur in liquid particles or on particle surfaces. As noted earlier, direct photooxidation of sulfur dioxide in pure air or sulfur dioxide oxidation in pure water droplets is believed to be negligibly small.[2,6,14]

Indirect photooxidation is a major route for conversion of sulfur dioxide to sulfate in the troposphere. The sulfur dioxide is oxidized after gas-phase collision with strong oxidizing radicals, such as HO, HO_2, and CH_3O_2. The source of these radicals in the polluted troposphere is hydrocarbon-NO_x emission, which in the process of daytime photooxidation produces oxidizing radicals as intermediate products. The sulfur dioxide oxidation step is therefore indirectly linked to photochemistry. The chemical kinetics of this mechanism has been formulated in models that use measured rate constants.[6] The modeling results were consistent with laboratory tests of sulfur dioxide conversion in the presence of photochemically reacting hydrocarbon-NO_x mixtures. An unambiguous confirmation of the homogeneous conversion mechanism

would require the direct observation of the reactive transients (such as HO, HO_2, and CH_3O_2 radicals) under a variety of atmospheric conditions. Such data are not available. Numerical simulations of chemical kinetics for typical urban mixtures (Figure 15) indicate 2-4%/h for a sunny summer day.[6] Eggleton and Cox,[14] in a summary of European results, concluded that, in the western European summer, sulfur dioxide oxidation rates due to gas-phase radical reactions in sunlight are expected to be between 0.5 and 5%/h, depending on the degree of pollution of the atmosphere. The lower figure refers to cleaner troposphere. In the winter, owing to the reduced sunlight intensity and duration, the conversion rates are expected to be lower by a factor of 2-5 (and perhaps an even greater factor).

Smog-chamber measurements occasionally show higher conversion rates.[38] It is likely that the homogeneous conversion rate will depend on the absolute concentration, as well as on the initial ratio of hydrocarbons to NO_x.

The specific roles of temperature, dewpoint, solar radiation intensity, etc., on the indirect photooxidation require systematic study. The current understanding is sufficient, however,

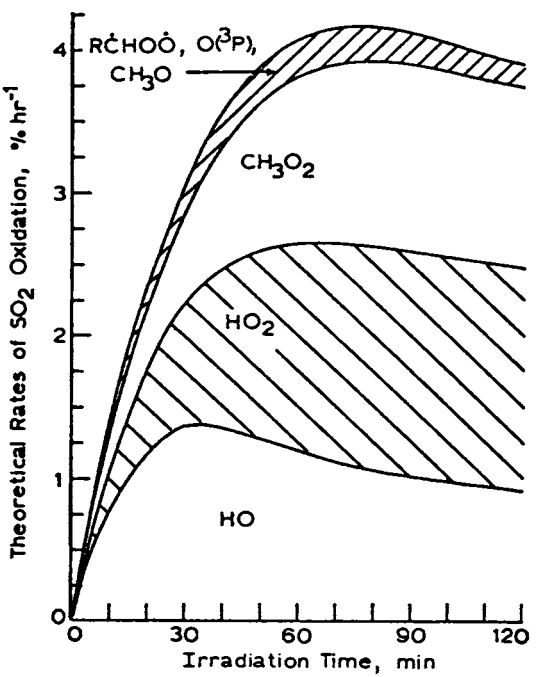


FIGURE 15 Theoretical rate of attack of various free-radical species on sulfur dioxide (%/h) for a simulated sunlight-irradiated (solar zenith angle, 40°), polluted atmosphere. Initial concentrations: $[SO_2]$ = 0.05 ppm, [NO] = 0.15 ppm, $[NO_2]$ = 0.05 ppm, [CO] = 10 ppm, $[CH_4]$ = 1.5 ppm, $[CH_2O]$ = 0 ppm, $[CH_3CHO]$ = 0 ppm. Relative humidity, 50% (25°C). Reprinted with permission from Calvert *et al.*[6]

to incorporate gas-phase chemistry into large-scale reactive plume models.

Catalytic sulfur dioxide oxidation in droplets has been studied extensively, but the results regarding its role in the atmosphere are less conclusive. The consensus reached at the International Symposium on Sulfur in the Atmosphere (ISSA) in Dubrovnik, Yugoslavia, is as follows:[39]

> The catalyzed oxidation of SO_2 in solution by transition metals (e.g., Fe, Mn) is believed to be important in situations in which relatively high ($>10^{-5}$ M) molar concentrations of catalyst are present in the droplet and in which the total atmospheric concentrations of catalytic elements are also high. Such conditions can exist in urban areas and in stack plumes and perhaps in urban fogs. In cleaner rural air, this reaction would occur only in clouds. However, unless the pH and metal concentrations are substantially different from those in rain water, this process is unlikely to be of significance. Both laboratory and field results of such reactions are necessary.

Oxidation in the liquid phase by strong oxidants has recently been receiving increasing attention.[2,14] Ozone and hydrogen peroxide absorbed in liquid droplets can promote the rate of oxidation to be comparable with or exceed the rate of indirect photooxidation. However, the current oxidation rate data vary by a factor of around 100; this prohibits an assessment of its importance in the atmosphere. The ozone and hydrogen peroxide in polluted atmospheres originate from the gas-phase photooxidation of hydrocarbon-NO_x mixtures. In clouds or fogs, such gases are absorbed into the water droplets within seconds. Measurements of hydrogen peroxide in polluted and clean atmospheres are necessary, as well as chamber studies to resolve the discrepancy of existing laboratory data.

Surface-catalyzed oxidation of sulfur dioxide on collision with solid particles has been demonstrated in the laboratory. Elemental carbon (soot) appears to be particularly effective in this regard.[42] However, because the existing data refer to sulfur dioxide oxidation on filters containing soot, the importance of this mechanism for suspended catalytic aerosols cannot be assessed.

A common feature of these major sulfur dioxide conversion mechanisms is that the rate-controlling species can be identified, they may in principle be controlled independently of sulfur dioxide, and their source is not necessarily that of the sulfur dioxide. It is regrettable that only the indirect-photooxidation mechanism can now yield sulfur dioxide oxidation rates and that

one therefore cannot evaluate the relative importance of each mechanism. A major difficulty in the interpretation of laboratory liquid-phase reactions is that in the atmosphere that reaction probably occurs sporadically (in clouds), rather than continuously.

Field Observations on Sulfur Dioxide Oxidation

The burden of establishing the actual conversion mechanisms and rates in the atmosphere rests with the field experiment. In recent years, a variety of approaches have been used for this purpose.

Large-Scale Monitoring and Modeling In large-scale monitoring and modeling, an emission inventory over a region and meteorologic transport conditions are used as the input data for regional-scale (about 1,000-km) transport models. The models also incorporate the rates of sulfur dioxide conversion and removal. The actual rate constants are unknowns, but they can be extracted from a best-fit comparison between calculated and observed values. In the OECD study,[43] the trajectory models were tuned to monitoring data obtained daily at about 70 stations. The measured daily concentration data for sulfur dioxide, SO_4^{2-}, and SO_4^{2-} in precipitation were compared with calculations, and the rate constants for transformations and dry and wet removal were adjusted until a best fit was obtained. The key model values for the OECD study are listed in Table 1.

The year-round average conversion rate of 1-2%/h and the overall average dry removal rate of about 3-4%/h were key new results of the OECD study. Studies similar in scope and objective to the OECD study are being conducted in the United States. The Sulfate Regional Experiment[46] of the Electric Power Research Institute, the Multistate Atmospheric Power Production Pollutant Study (MAP3S)[36] of the Department of Energy, and the Sulfur Transport and Transformations in the Environment (STATE) study of EPA are examples. A close coordination of these major projects appears to be highly desirable.

The main utility of the regional approach is that the obtained rate constants are inherently averages over all sources and spatial-temporal scales of interest. It is recognized, however, that the rate constants for removal and transformations are actually variables that may depend on source configuration, meteorologic conditions, and the presence of external (nonsulfur) species.

Plume Studies The average rate constants can be obtained from the regional monitoring and modeling efforts, but the specific

TABLE 1 Values Applied in the Calculations with the Model in the OECD Project[a]

Characteristic	Value
Fraction of emitted sulfur deposited locally	0.15
Fraction of emitted sulfur transformed directly to sulfate	0.05
Decay rate of sulfur dioxide	
Rain	$4 \cdot 10^{-5}$/s (14.4%/h)
Dry	$1 \cdot 10^{-5}$/s (3.6%/h)
Transformation rate $SO_2 \rightarrow SO_4$	$3.5 \cdot 10^{-6}$/s (1.26%/h)
Loss rate of SO_4^{2-}	$4 \cdot 10^{-6}$/s (1.44%/h)
Mixing height	1,000 m

[a]Data from OECD.[43]

dependence of the rates on the underlying chemical and physical processes has to be studied on a smaller scale. The gap between regional (1,000-km) scale and laboratory simulation can be bridged by mesoscale studies of sulfur transport, transformations, and removal (transmission). These are generally referred to as plume studies. Inherently, quantitative single-plume studies are limited to a spatial scale of less than 500 km and a plume age of less than 12 h.

The results of a 4-yr plume mapping study--Midwest Interstate Sulfur Transformation and Transport, or MISTT[59]--conducted in the St. Louis, Missouri, area show that the transport, transformation, and removal processes in power-plant plumes all have diurnal cycles (Figure 16). The daytime conversion rate was observed to be quite variable, between 1 and 4%/h, whereas the nighttime values were consistently below 0.5%/h.[26] Hence, in the midwestern United States during summer, the conversion rate was associated with the time of day. The data were insufficient to conclude which mechanism controlled the daytime conversion, because the observed variations were consistent with indirect photooxidation, as well as with liquid-phase oxidation in clouds. Observations of aerosol size dynamics in plumes[57] have shown, however, that homogeneous nucleation occurred consistently. Gillani *et al.*[19] noted that the aerosol formation in a given plume is frequently accompanied by ozone formation in the plume. Both these observations would support homogeneous indirect photooxidation. However, in summer in the St. Louis region, the plume material is transferred

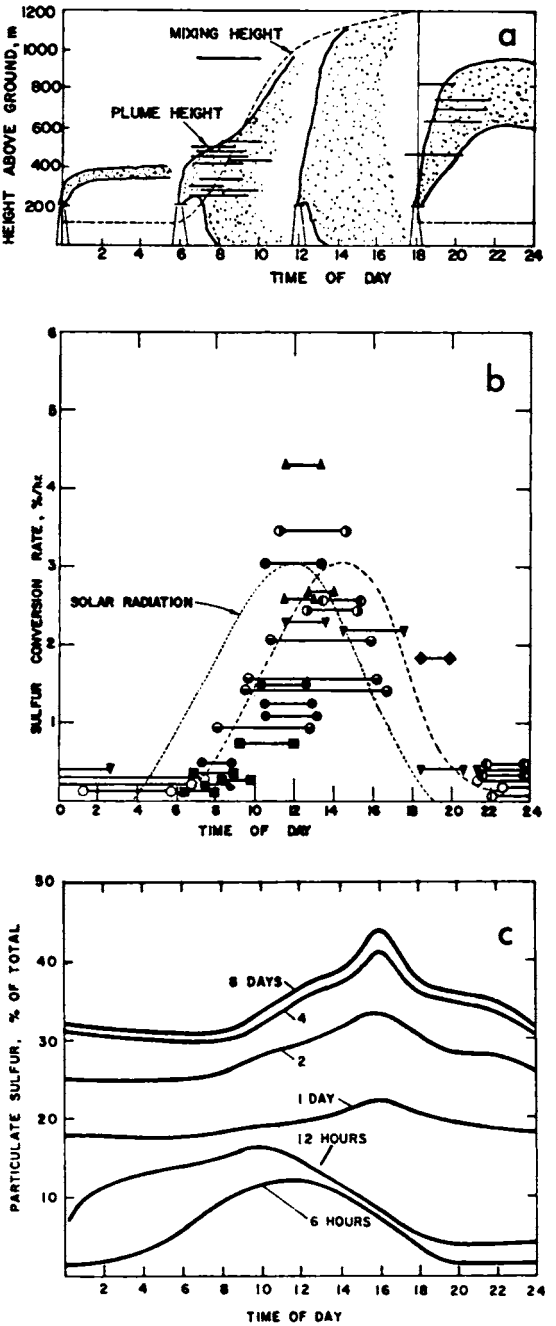


FIGURE 16 Diurnal pattern of (a) plume dispersion, (b) conversion rate, and (c) fraction of sulfur converted to aerosol in a midwestern power plant. Reprinted with permission from Husar *et al.*[26]

through clouds at least once on most days. Hence, estimation of the relative contributions of homogeneous and heterogeneous chemistry is not yet possible.

Outdoor Smog-Chamber Studies Ambient air irradiated by solar radiation but confined to a transparent chamber can be observed in a way similar to that in ordinary smog-chamber studies. Clark *et al.*[10] used such a system in Los Angeles, where they added sulfur dioxide to the hydrocarbon-NO_x mixture of the ambient air. Their observations showed that aerosol formation is linearly proportional to both sulfur dioxide (Figure 17) and the concentration of nonmethane hydrocarbons (Figure 18). These and similar observations reviewed by Eggleton and Cox[14] give strong support to the notion

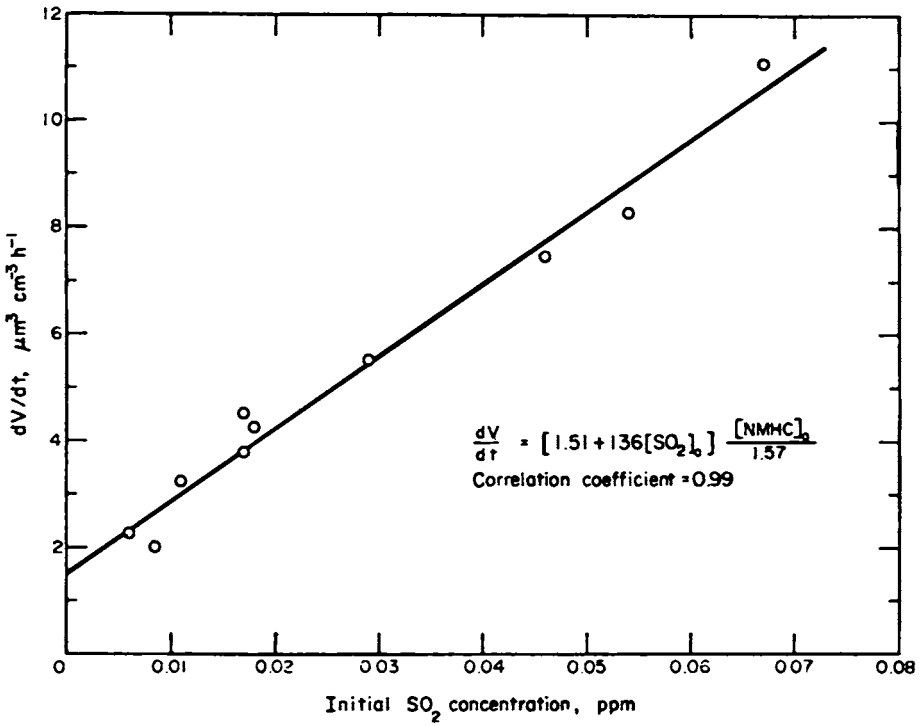


FIGURE 17 Rate of aerosol volume formation versus initial sulfur dioxide concentration for ultraviolet light intensity of 3.5 W/m^2 and a nonmethane hydrocarbon (NMHC) concentration of 1.57 ppm. Reprinted with permission from Clark *et al.*[10]

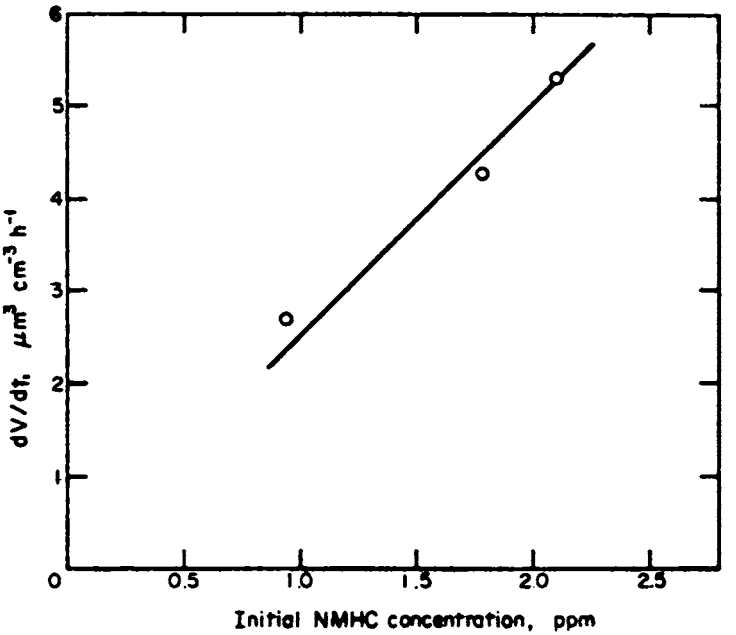


FIGURE 18 Rate of aerosol volume formation versus initial nonmethane hydrocarbon (NMHC) concentration for sulfur dioxide concentration of 0.017 ppm and ultraviolet light intensity of 30.5 W/m^2. Reprinted with permission from Clark *et al.*[10]

that the indirect oxidation of sulfur dioxide is an important, if not the major, mechanism of sulfur dioxide oxidation in the polluted atmosphere.

Summary

The average oxidation rate over the lifetime of sulfur dioxide is about 1-2%/h, as determined by fitting the rate constants in regional-scale models to European monitoring data. In plumes over a midwestern U.S. power plant, the daytime conversion rate was measured at 1-4%/h and the nighttime rate at 0.5%/h. Laboratory simulations and chemical kinetic model calculations of gas-phase controlled sulfur dioxide conversion in the presence of oxidizing radicals also indicated a 1-2%/h daily average conversion rate for summer conditions. The contribution of liquid-phase oxidation is not well established, but it is thought to be important.

REMOVAL OF SULFUR COMPOUNDS FROM THE ATMOSPHERE

The residence time and the transport distance of atmospheric sulfur are determined by the overall removal rate of sulfur compounds from the atmosphere. Overall removal has four major components: dry removal of sulfur dioxide, wet removal of sulfur dioxide, dry removal of SO_4^{2-}, and wet removal of SO_4^{2-}. Dry removal of sulfur dioxide and wet removal of SO_4^{2-} appear to be the two major components.

Dry Deposition

Dry removal of sulfur dioxide is a mass-transfer process whereby sulfur dioxide is first transported to a surface by turbulent and molecular diffusion and then removed by adsorption or absorption at the surface. The overall mass-transfer rate can be characterized by a mass-transfer coefficient (v_d) and the difference between the bulk and surface concentrations. Because the unit of v_d is length per time, it is called "deposition velocity." Conceptually, it is also convenient to use the overall resistance to mass transfer ($r = 1/v_d$), which is the sum of several, largely independent resistances.

The surface resistance (r_s) incorporates adsorption and absorption. In the case of vegetation, r_s is believed to be dominated by the size of the stomatal openings. The aerodynamic resistance (r_a) is due to turbulent diffusion in the atmospheric surface layer and controls the rate of dry deposition during stable conditions (inversions).

The range of deposition velocities was summarized at the International Symposium on Sulfur in the Atmosphere, Dubrovnik, and is shown in Tables 2 and 3.

Wet Deposition

Wet deposition of sulfur compounds proceeds through a combination of in-cloud and below-cloud scavenging by precipitation (rain and snow). The rate of wet deposition can be calculated from the sulfur concentration of precipitation and the precipitation rate. Sulfur deposition rates are compiled here for a number of different areas that vary in climate and industrial activity (Table 4). The anthropogenic contribution to sulfur deposition is difficult to assess, because of the lack of historical data. However, evidence from ice cores from Greenland[3,56] indicates that sulfur deposition has increased by a factor of about 3 over the last 100

TABLE 2 Sulfur Dioxide Deposition Velocities Over Vegetation[a]

Vegetation			Deposition Velocity (v_d), cm/s	
Height	Example	Height, m	Range	Typical[b]
Short	Grass	0.1	0.1-0.8	0.5
Medium	Crops	1.0	0.2-1.5	0.7
Tall	Forest	10.0	0.2-2.0	Uncertain

[a]Data from Moore *et al.*[39]

[b]Values were obtained in a humid climate; much smaller values are likely in arid climates.

TABLE 3 Sulfur Dioxide Deposition Velocities Over Soil[a]

Acidity (pH)	State	Deposition Velocity (v_d), cm/s	
		Range	Typical[b]
Calcareous ($\geq$ 7)	Dry	0.3-1.0	0.8
Calcareous ($\geq$ 7)	Wet	0.3-1.0	0.8
Acid (~4)	Dry	0.1-0.5	0.4
Acid (~4)	Wet	0.1-0.8	0.6

[a]Data from Moore *et al.*[39] No information is available to assess v_d on desert sand or lateritic soils.

yr in this remote area. On the basis of the meteorologic considerations, the source of the increased sulfur has to be North America, and it is certainly linked to the increased combustion of fossil fuels.

Unfortunately, we do not have similar data for the United States, and it is therefore difficult to assess the anthropogenic contribution. However, it is apparent from the available data that a large portion of the sulfur found in precipitation of the United States is anthropogenic (Figure 19).

It is certain that the sulfur concentration of precipitation in the eastern United States has increased because of fossil-fuel combustion. Similarly, because the oxidation product of sulfur dioxide is sulfuric acid, the hydrogen ion concentration of precipitation has also increased.

TABLE 4 Representative Annual Average Rates of Wet and Dry Deposition of Sulfur[a]

Location	Excess[b] Precipitation Sulfate Concentration (as Sulfur), mg/liter	Wet Deposition Rate of Sulfur, $g/m^2 \cdot yr$	Dry Deposition Rate of Sulfur, $g/m^2 \cdot yr$
Heavily industrialized areas			
North America	3-?	0.1[c]-3	?
Europe	3-20	2-4	3-15
Rural			
North America	0.5-2	0.1-2	0.2-2.6
Europe	0.5-3	0.2-2	0.5-5.0
Remote			
North Atlantic	0.2-0.6	1-3	0.04-0.4
Other oceans	0.04	0.01[c]-0.2	<0.1
Continents	0.1	0.01[c]-0.5	0.4

[a]Data from Moore *et al.*[39]

[b]Excess over concentration due to sea salt.

[c]Low deposition rates result from low precipitation.

This increased concentration of hydrogen ion has resulted in acid precipitation, defined as precipitation having a pH lower than 5.6.[30] The pH of precipitation in the eastern United States has steadily decreased (increased acidity) over a 17-yr period (1955-1972) for which data exist, so that precipitation currently falling on most of the eastern United States is 10-500 times more acidic than it was before today's rate of combustion of fossil fuels (Figure 20).[30] It is clear that the pH of precipitation in the eastern United States is decreasing as a function of time and that this is related to increases in fossil-fuel combustion. What is less clear is the degree to which sulfuric acid (derived from sulfur dioxide) has caused the observed pH decreases. Acid precipitation is not due solely to acid-sulfate aerosols. Increases in nitric acid in the atmosphere due to fossil-fuel combustion are also partially responsible.[40] Recent estimates of the relative contribution of acid sulfates and acid nitrates to the acidification of precipitation are about 60 and 40%, respectively,

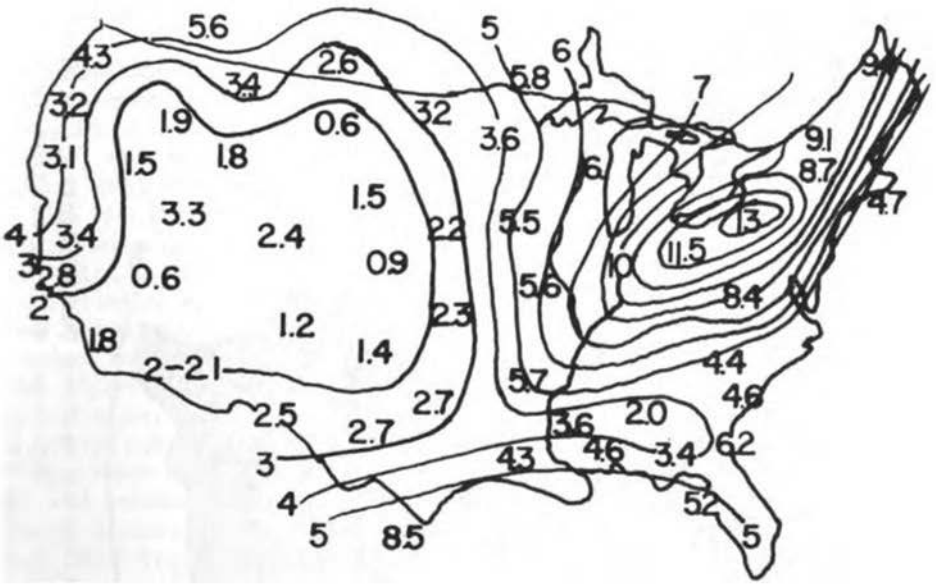


FIGURE 19 Excess sulfur in precipitation over United States in kilograms per hectare per year. Reprinted with permission from Eriksson.[15]

on an annual basis.[11,18,30] However, there is some evidence that nitric acid has played an increasingly important role relative to precipitation acidity in the last decade[17] and that recent increases in precipitation acidity may be due primarily to nitric acid, as opposed to sulfuric acid. The exact magnitude cannot yet be established, and this is definitely an important subject for future research.

In summary, increased emission of sulfur dioxide in the eastern United States has resulted in increased deposition of sulfur dioxide and sulfate aerosols (sulfuric acid, ammonium bisulfate, and ammonium sulfate). Owing to the acidic properties of sulfate aerosols (and nitric acid), the acidity of precipitation has increased by a factor of 10-500 over natural conditions. Acid precipitation is not peculiar to the eastern United States. Canada and northern Europe, especially Scandinavia, have also experienced increased acidity of precipitation, owing to increases in emission of sulfur dioxide.[4,21]

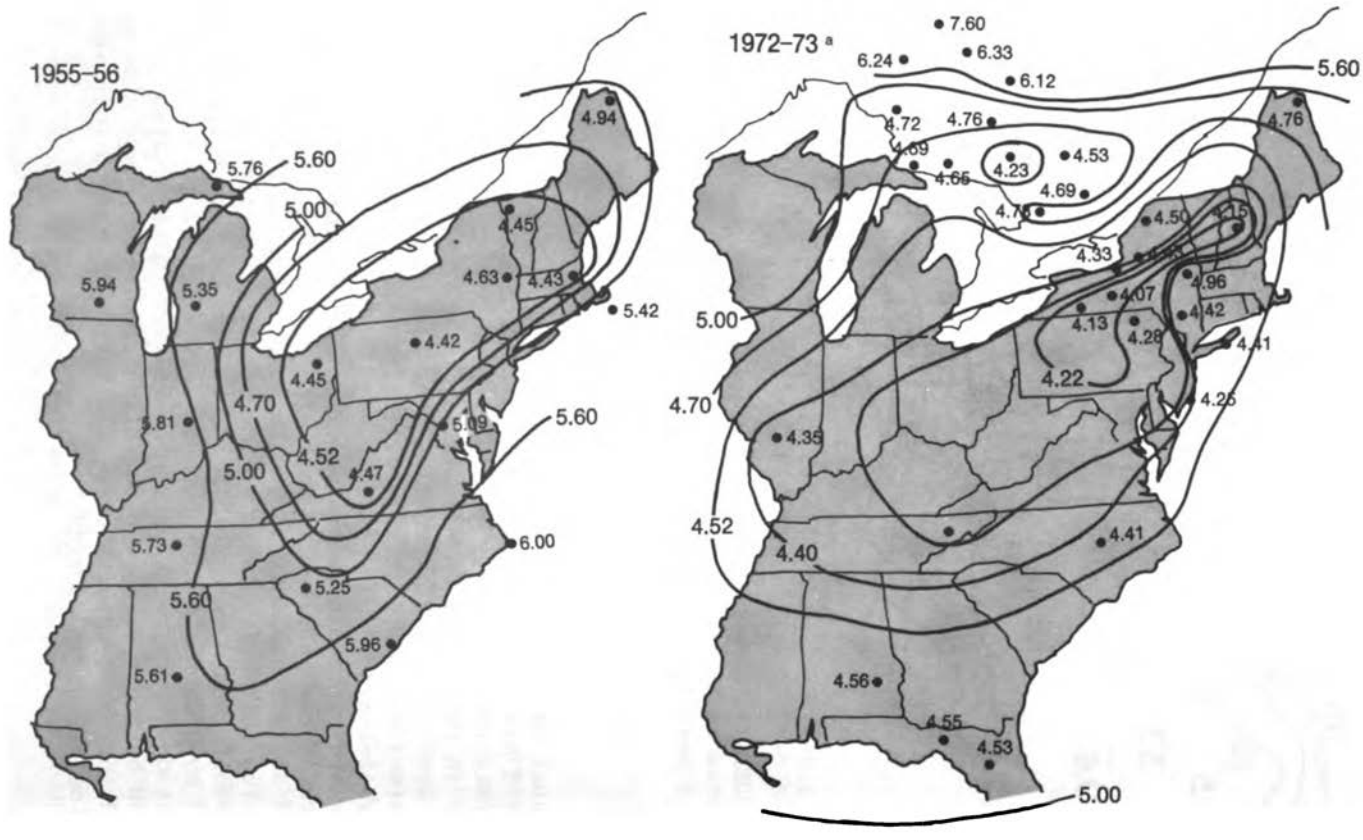


FIGURE 20 Weighted annual average of pH of precipitation in eastern United States in 1955-1956 and 1972-1973. Shading indicates pH less than 4.52. Reprinted with permission from Likens.[29] Source: *Chemical and Engineering News*, November 1976.

Dry and Wet Deposition

To understand sulfur deposition, rates of both wet and dry deposition must be measured. On a regional scale, this has been done only by the OECD study in northern Europe, although a similar study, the Multistate Atmospheric Power Production Pollution Study (MAP3S) is currently under way in the United States.

In the OECD study, overall dry and wet removal rates were estimated by comparing monitoring data with appropriately tuned model calculations. The rate constants that were extracted from these comparisons are given in Table 1. The study concluded that, of the total emission of 20 Tg of sulfur oxides per year, dry deposition accounts for 11 Tg, or about 55%; wet deposition accounts for about 6 Tg, or 30%; and the balance is exported out of the study area.

Although regional information is lacking for the United States, there have been intensive investigations on the relative magnitude of wet versus dry deposition for plumes,[20] urban areas,[25] and rural areas.[31] The results of these, coupled with the results of the OECD study, indicate that, near sources (stack and urban areas), dry deposition is more important as a removal mechanism than wet deposition. In areas removed from local sources, wet deposition is more important.[31] For the purposes of constructing sulfur budgets for a large area (such as the eastern United States), it is safe to assume that the rates of wet and dry deposition of sulfur are comparable.

Because of the paucity of historical data, quantification of past trends in precipitation composition is difficult. This is entirely due to the lack of a continuous national data base on precipitation composition. This deficiency of adequate data on a global contamination phenomenon has spurred the formation of a national atmospheric deposition program devoted to the determination of trends and the elucidation of physical, biologic, and chemical effects of precipitation contamination over long periods (decades). This program, scheduled to begin in the spring of 1978, is sponsored by the state agriculture experiment stations with financial support from the U.S. Departments of Agriculture and the Interior and participation by scientists in other federal agencies. This program will enable the establishment of a sound data base to determine trends and identify effects of the contamination of precipitation due to increased emission of sulfur dioxide.

Residence Time

The residence time of sulfur dioxide is determined by the competing rates of transformation to sulfate and by removal of sulfur dioxide and SO_4^{2-}. Using a conversion rate of 1-2%/h and an overall removal rate of 2-4%/h leads to a characteristic residence time of 14-33 h or about 1 day for sulfur dioxide. The residence time of sulfur dioxide in single plumes was estimated from aircraft sampling data and combined with simple models (Figure 21).

The residence time of sulfate is the sum of the formation and removal times. According to the current estimates,[39] the sulfate residence time is 3-5 days.

ATMOSPHERIC SULFUR BUDGETS

To assess the risk attending increases of SO_x in the environment, the magnitude of the increases over natural concentrations must be known for a number of scales of space and time. The construction of regional budgets is informative in this regard, for it indicates the degree of alteration of natural systems. This section considers the anthropogenic alteration of the sulfur cycle on a regional scale (the eastern United States).

Sulfur Budget for the Eastern United States

Because our concern is with the anthropogenic alteration of atmospheric SO_x cycles and its effects, we can consider only the eastern United States. About 75% of anthropogenic SO_x emission

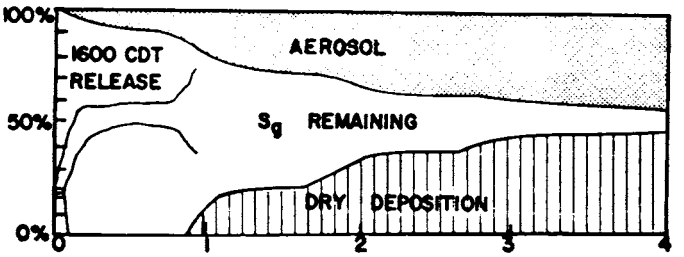


FIGURE 21 Estimated sulfur budget for a power-plant plume over a 4-day period. Reprinted with permission from Husar *et al.*[26]

occurs east of the Mississippi River. This, coupled with the fact that the prevailing winds are from west to east, means that most U.S. SO_x emission is kept east of the Mississippi River.

Four processes contribute sulfur to the atmosphere: combustion of fossil fuels, sea-salt aerosols, marine bacterial decay of organic matter, and terrestrial bacterial decay of organic matter. The last three processes constitute the natural-emission component of the sulfur cycle. Although various estimates have indicated that their contribution was sizable relative to anthropogenic emission globally, in the eastern United States this is not the case. In this region, on the basis of recent research from both the United States and Europe, terrestrial emission contributes an estimated 0.05 Tg/yr (after Granat *et al.*[21]), marine processes in coastal zones about 1 Tg/yr, and sea-salt advection about 0.3 Tg/yr (after Lodge *et al.*[32]). Thus, the total for the three natural processes is about 1.4 Tg/yr, which is about 10% of the 13.2 Tg/yr estimated for the eastern U.S. anthropogenic emission. This is similar to the conclusions reached for Europe on the basis of considerable recent study.

Sinks

Sulfur in the atmosphere of the United States is lost in three ways: wet deposition, dry deposition, and export.

Wet deposition of sulfur amounts to about 4.5 Tg/yr, extrapolated from the long-term data (5-15 yr) from Hubbard Brook Experimental Forest and other areas of the United States[31,47] and short-term data from the MAP3S program. This deposition represents an increase of about a factor of 10 over natural values (Table 4). In the light of previous discussion of dry and wet removal, dry deposition of sulfur is assumed to be equal to wet deposition (4.5 Tg/yr).

The export (to the North and East) of sulfur from the eastern United States is 5-8 Tg/yr. This is supported by the National Research Council of Canada,[41] which estimated that 3.4 Tg/yr is imported to Canada from the central and northeastern United States.

Summary

This budget is based on data and estimates that are weak at best; however, even given the inadequacies in the data and the possible errors of the estimates, it seems reasonable to state that anthropogenic emission of sulfur is substantially greater than natural emission in the eastern United States.

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5 EFFECTS OF SULFUR OXIDES ON AQUATIC ECOSYSTEMS

Materials deposited from the atmosphere enter biogeochemical cycles of terrestrial and aquatic ecosystems.[19,43]

Over the last several decades, the deposition of energy-related pollutants from the atmosphere has increased substantially.[17,36,37] This deposition is the major source of supply of some materials to fresh water,[22] and the amounts of anthropogenic materials now being deposited in southeastern Canada, the northeastern United States, and southern Scandinavia are great enough to cause considerable alterations in aquatic ecosystems. The energy-related materials primarily responsible for aquatic ecosystem changes are the acid sulfates and nitric acid. In addition, heavy metals derived from fossil-fuel combustion have been observed to reach deleterious concentrations at sites distant from the points of combustion (according to Hagen and Langeland[25] and J. N. Galloway and G. E. Likens, unpublished data).

The affected aquatic ecosystems are for the most part in oligotrophic waters in regions with thin, poorly buffered soils of granitic origin, and they are in both lakes and rivers. Because of their dilute nature, oligotrophic waters are more sensitive to chemical alterations and therefore to biologic damage. Temporary ponds or puddles, even in more highly buffered locations, are also affected, with consequent destruction of amphibian animals.[47]

A number of reviews and symposium volumes have been published recently on particular aspects of the effects of energy-related pollutants on aquatic ecosystems.[8,9,14,16,27,36,50] This chapter is not intended to constitute another comprehensive review, but rather to state the alterations known to occur as a result of the deposition of energy-related pollutants and to illustrate them with specific examples and evaluate their impact on human society. In the last century, the atmospheric deposition rate of sulfur has increased by an order of magnitude in some areas

of the United States, owing to anthropogenic activity. Because the effect of this increased deposition depends on the chemical form of sulfur deposited, the discussion that follows is divided according to chemical form.

EFFECTS OF SULFATE

Sulfur enters aquatic ecosystems in the form of sulfate, or as sulfur dioxide that soon becomes oxidized to sulfate. Sulfate itself is generally innocuous in concentrations of less than 1,000 mg/L. In systems dominated by atmospheric sources of sulfate, concentrations are not likely to exceed 10 mg/L.

EFFECTS OF HYDROGEN SULFIDE

In the presence of suitable organic substrates under anaerobic conditions--e.g., in the hypolimnia of mesotrophic or eutrophic lakes, in lake sediments, and in bogs--sulfur compounds (including sulfate) are reduced to hydrogen sulfide,[18] which is toxic to many forms of aquatic life. The toxicity of hydrogen sulfide has been observed to increase as pH decreases.[39] Hydrogen sulfide has been associated with reduced biomass of benthic invertebrates and with oxygen depletion in the hypolimnia of deep lakes as a consequence of its oxidation to sulfate.[52]

EFFECTS OF ACID SULFATES

The greatest anthropogenic alteration of the natural sulfur cycle is caused by the emission of sulfur dioxide into the atmosphere from the combusion of fossil fuels. Once in the atmosphere, sulfur dioxide is oxidized to sulfuric acid. Increasing atmospheric concentrations of sulfuric acid and nitric acid, another fossil-fuel atmospheric contaminant,[42] have caused the acidification of precipitation (rain and snow). Currently, precipitation over most of the eastern United States is 10-500 times more acidic than natural because of sulfuric and nitric acid.[36,38] According to stoichiometry, on an annual basis, approximately 60-70% of the increased precipitation acidity is due to sulfuric acid, and 30-40% to nitric acid.[11,20] Therefore, the increased emission of sulfur dioxide to the atmosphere has resulted in increased deposition of sulfuric acid by precipitation. This increased deposition of acid sulfates can cause acidification of fresh-water ecosystems.

Regions of North America that are potentially sensitive to acidification, as determined on the basis of bedrock geology and alkalinity of surface water, are shown in Figure 22.[19] Although the effects of acidification are currently demonstrable only on a regional basis, the problem of acid precipitation is of continental scope, owing to long-range transport of atmospheric pollutants (Chapter 4).

Regions in the United States that we know have lakes acidified (i.e., current pH values are lower than those of 30-40 yr ago) by acid precipitation are the Adirondack State Park in New York[50] and Maine.[13]

Microbiota

Lake acidification causes a reduction in microbial activity. Therefore, decomposition processes decrease, and organic matter accumulates in aquatic ecosystems. An abnormal accumulation of coarse organic detritus has been observed on the bottoms of six Swedish lakes where the pH decreased by 1.4-1.7 units in the last 3-4 decades.[24] Bacterial activity apparently decreased, and in some of the lakes the sediment surfaces over large areas were made up of dense felts of fungal hyphae. In Gårdsjön, 85% of the bottom in the zone 0-2 m deep was covered with a thick felt of fungus. Lime treatment caused a rapid decomposition of organic litter and great reductions of the fungal felt;[2] this indicated that bacterial activity had been inhibited at low pH. Similar neutralization of acidified lakes in Canada resulted in a significant increase in aerobic heterotrophic bacteria in the water column.[49] Results from field and laboratory experiments with litterbags in Norway[27] also indicated reduced weight loss of leaves in acidic water.

Accumulations of organic debris and extensive mats of fungal hyphae, as observed in the Swedish lakes,[24] both seal off the mineral sediments from interactions with the overlying water and hold organically bound nutrients that would otherwise become available if normal decomposition occurred. The reduction in nutrient availability can be expected to have a negative feedback effect on the organism, further inhibiting their activities. The reduction of nutrient supplies to the water column from the sediments, because of the physical covering and from reduced mineralization of organic materials in the water itself, will lead to reduced phytoplankton productivity. These ideas have been formulated into the hypothesis of "self-accelerating oligotrophication" by Grahn *et al.*[24]

FIGURE 22 Regions in North America with lakes that are sensitive to acidification by acid precipitation. Reprinted with permission from Galloway and Cowling.[19]

Reduction of microdecomposer activities may have a direct effect on invertebrates. Although some benthic invertebrates appear to feed directly on the allochthonous detritus material, it seems that "conditioned" material (that colonized by microorganisms) is preferred and that the nutritive value of the detritus is highly increased by conditioning.[5] Bacteria may also be a food source to filter-feeding zooplankton, if they are sufficiently aggregated to be removed by the filtering apparatus of such organisms as the Calanoida. An inhibition of the microbiota or a reduction in microbial decomposition processes would therefore have a direct impact on the animal communities in lakes.

Primary Producers

In water affected by acid precipitation, major changes occur in plant communities.

• *Macrophytes*: In laboratory tests, the growth and productivity of the rooted macrophyte *Lobelia* was reduced by 75% at a pH of 4, compared with the control (pH, 4.3-5.5), and the period of flowering was delayed by 10 days at the low pH.[33] In five lakes of the Swedish west coast, a region severely affected by acid precipitation, Grahn[23] reported that in the last 3-5 decades the macrophyte communities dominated by *Lobelia* and *Isoetes* have regressed, whereas communities dominated by *Sphagnum* have expanded. In the sheltered and shaded locality of Lake Örvattnet, in the zone 0-2 m deep, the bottom area covered by *Sphagnum* increased from 8% in 1967 to 63% in 1974. In the zone 4-6 m deep, the increase was from 4% to 30%. At the same time, the pH in Örvattnet decreased 0.8 units to about 4.8. At the pH of these acid lakes, essentially all the available inorganic carbon is in the form of carbon dioxide or carbonic acid. Conditions are more favorable for *Sphagnum*, an acidophile that is not able to utilize the carbonate ion, as do many other aquatic plants. Similar growths of *Sphagnum* occur in Norwegian lakes. The moss appears simply to outgrow the flowering plants under acid conditions.

Grahn *et al.*[24] hypothesized that lake acidification causes lakes to become progressively more oligotrophic, owing to decreased nutrient cycling. In developing their hypothesis on oligotrophication, they stressed two biologically important consequences of this *Sphagnum* expansion. First, the ion-exchange capacity of *Sphagnum* results in the withdrawal of base ions, such as Ca^{2+}, from solution, thus reducing their availability to other organisms. Second, dense growths of *Sphagnum* form a distinct biotope that is unsuitable for many members of the bottom fauna.

• *Attached Algae*: Under some acid conditions, unusual accumulations of both epiphytic and epilithic algae may occur. In the Swedish lakes, Grahn *et al.*[24] reported that *Mougeotia* and *Batrachospermum* become important components of the benthos. In Lake Oggevatn (pH, 4.6), a clear-water lake in southern Norway, not only is *Sphagnum* beginning to choke out *Lobelia dortmana* and *Isoetes lacustris*, but these macrophytes have been observed to be festooned with filamentous algae.

Heavy growths of filamentous algae and mosses not only occur in acidified lakes, but also have been reported in Norwegian streams affected by acidification. In experiments in artificial stream channels in which water and the naturally seeded algae from an acidified brook (pH, 4.3-5.5) were used, increasing the

acidity to a pH of 4 by addition of sulfuric acid led to an increased accumulation of algae, compared with that in an unmodified control.[26] The flora was dominated by *Binuclearia tatrana, Mougeotia* spp., *Eunotia lunaris, Tabellaria flocculosa,* and *Dinobryon* spp., each accounting for at least 20% of the flora at one time or another. The rate of radioactive carbon uptake per unit of chlorophyll in the channels was found to be lower in the acid channel by about 30%; this suggested greater algal accumulation at low pH, despite lower productivity.

- *Phytoplankton:* In the Swedish west coast region, 115 lakes were investigated with regard to phytoplankton.[1] Lakes with pH lower than 5 had a homogeneous and limited composition consisting of about 10 species. The greatest changes in species composition were found in the pH interval 5-6. Similar phenomena were observed in a regional survey of 55 lakes in southern Norway[28] and in a study of four lakes in Ontario, Canada.[12] Phytoplankton biomass was low in these acid lakes (< 1 mg/liter) and was correlated with the concentration of phosphorus, which generally decreased at lower pH. In the Ontario lakes, phytoplankton biomass at pH values near 4.5 was only one-ninth to one-third as much as near a pH of 6.5. Phytoplankton production per unit volume of water was reduced in lakes below a pH of 5.5 in the Sudbury area.[32]

In summary, simplification of the plant communities in lakes and streams reduces the variety of food available to the next higher trophic level, and reduction of phytoplankton production decreases the food supply to herbivorous zooplankton. In some cases, biotopes are radically altered, and that will certainly affect animal habitats. Finally, the nutrient supply of the water column is probably reduced as a consequence of these changes in plant communities.

Invertebrates

Zooplankton analyzed from net samples collected from 84 lakes in Sweden showed that acidification caused limitation of many species and led to simplification of zooplankton communities.[1] Crustacean zooplankton were sampled in 57 lakes during a Norwegian lake survey in 1974,[28] and the number of species observed was found to be related to the pH. The distributions and associations of crustacean zooplankton in 47 lakes of a region of Ontario affected by acid precipitation were strongly related to the pH and to the number of fish species in the lakes. However, fish and zooplankton were each correlated with the same limnologic

variables, especially pH.[53] Zooplankton communities become less complex, with fewer species present, as acidity increases. Food supply, feeding habits, and grazing of zooplankton will probably be altered after acidification, as a consequence of decreased biomass and species composition of planktonic algae and bacteria.

Surveys at many sites in Norway, Sweden, and North America[2,6,12,28] have shown that water affected by acid precipitation has fewer species of benthic invertebrates than water that is less acid. In 832 lakes, J. Økland[44] found no snails where the pH was below 5.2; snails were rare at a pH of 5.2-5.8, and they occurred less frequently at a pH of 5.8-6.6 than in more neutral or alkaline water. The amphipod *Gammarus lacustris*, an important element in the diet of trout in Norwegian lakes where it occurs, is not found in lakes with a pH less than 6.0.[45] Experimental investigations have shown that the adults of this species cannot tolerate 2 days of exposure to a pH of 5.0.[7]

In the River Duddon in England, acid from precipitation is the overriding factor that prevents permanent colonization of the upper acidified reaches of the river by a number of species of benthic invertebrates, primarily herbivores.[54] In the more acidic tributaries (pH <5.7), the epiphytic algal flora was reduced (in contrast with increases noted in Norway), and leaf litter decomposition was retarded. The food supply of the herbivores was apparently decreased, and this may have played a role in the simplification of the benthic fauna. Quantitative data concerning the effects of low pH on the benthic fauna are also available for some acid Norwegian lakes,[27] where notably low-standing crops have been observed.

Macrophyte communities of *Lobelia* and *Isoetes* in some acidified Swedish and Norwegian lakes[23] are being choked out by dense mats of *Sphagnum* and are heavily overgrown with filamentous algae, despite the oligotrophic nature of the lake water. Under these conditions, benthic invertebrate populations will be affected by starvation, evacuation, or extinction, owing to the loss of preferred habitat. Chironomids[46] and other benthic invertebrates, in many situations, will be affected by altered decomposition cycles and variations in available foods caused by increased acidification.

The tolerance of aquatic invertebrates to low pH varies over their life cycles, and the emergence of adult insects seems to constitute a period particularly sensitive to low pH. Bell[4] and Moss,[41] in similar studies with Trichoptera and Ephemeroptera, found emergence patterns to be affected at pH values higher than the 30-day survival limits. Many species of aquatic insects

emerge early in the spring, even through cracks in the ice and snow cover. Owing to the contamination of spring meltwater by atmospheric pollutants,[25,29-31] the early emergers must, in many cases, be exposed to the least desirable water conditions.

Damage to invertebrate communities will influence other components of food chains. Benthic invertebrates assist with the essential function of removing dead organic material. In litterbag experiments, the effects of invertebrates on leaf decomposition were much more evident at higher pH than at low pH.[27] A reduction of grazing by benthic invertebrates may also contribute to the accumulation of attached algae in acidified lakes and streams.

In unstressed lake ecosystems, there tends to be a continuous emergence of different insect species available to predators from spring to autumn. In acid-stressed ecosystems, the variety of prey is reduced, and periods may be expected to occur in which the amount of prey available to fish (and waterfowl) is diminished.

Fish

Acidification of dilute lakes and streams by sulfuric and nitric acid in precipitation has resulted in extensive depletion of fish stocks in Sweden, Norway, and parts of eastern North America.[3,14,35,50] Both commercial and sport fisheries have been affected in these areas. However, precise assessments of losses--in terms of population extinctions, reductions in yields, or economic and social impacts--either have not been attempted or are still in the process of evaluation. In Sweden, the number of lakes acidified to a pH of less than 6 has been estimated to be about 10,000.[14] Extensive surveys in southern Norway have suggested that fish populations have been affected by acidification in 20% of the area south of latitude 63°N.[35] The effects of acidification on fish populations in the Sudbury, Ontario, region are well documented,[3] but only recently have Canadian scientists discovered that the problem is widespread in eastern Canada and apparently related to the regional acid precipitation of eastern North America.[15] Fish populations have been severely affected by acidification in the Adirondack Mountains of New York,[14,51,55,56] one of the largest dilute-lake districts in the eastern United States. Potential damage to fish populations inhabiting other acid-sensitive aquatic ecosystems in New England, the Appalachians, and parts of the southeastern, north central, and northwestern United States has not yet been assessed.

Field surveys in acidified regions (C. L. Schofield, unpublished data, and Wright and Snekvik[58]) have indicated that most fish species disappear from acidified lakes when the pH drops to below 5. Reproductive inhibition has been demonstrated for some species at a pH between 5 and 6.[3,40,55,56] Both inhibition of gonad maturation[3] and mortality of eggs and larvae[55,56,58] can contribute to recruitment failure in populations inhabiting acidified water.[14,58] Physiologic stress resulting from osmoregulatory dysfunction at low pH and low calcium concentration has been identified as a primary source of mortality in the very dilute acidified waters characteristic of southern Norway.[14,58] The mobilization of toxic metals (e.g., aluminum) at low pH may be of greater concern for fish survival in other regions, such as the Adirondack Mountains of New York.[51] Rates of change in water quality, particularly in the northern areas subject to sudden acid episodes during snowmelt, are critical to fish survival in stream systems.[35,51] Species differences in acid tolerance,[3,35] acclimation,[56] and genetic adaptation[14,21,48] are all important in determining the extent of acidification that fish populations will tolerate in various regions.

The risks associated with intensified or expanded acidification of streams and lakes caused by acid precipitation are in several categories. The widespread extinction of fish populations has already resulted in some reduction in genetic diversity at the species level; this has implications for the maintenance of species integrity, but perhaps more important and of more immediate concern is the problem of species reestablishment in acidified regions. Many of the salmonid populations eliminated from areas in Sweden, Norway, and North America, although not themselves endangered species, were strains or races uniquely adapted to these environments and in this sense are irreplaceable. The alterations in ecosystem structure and function that occur when fish are removed can, in conjunction with other perturbations associated with acidification, lead to the development of aquatic ecosystems that are difficult, if not impossible, to rehabilitate completely.[24] The economic and social impacts of losses to both commercial and sport fisheries have not yet been thoroughly examined for the existing extent of acidification; hence, predictions of expected risks of continued or expanded acidification are not possible. However, it is clear from the geographic distribution of acid-sensitive regions[19] that the major risk is to sport fisheries, rather than commercially developed fisheries, in the United States. An indirect effect of acidification that is of potentially direct concern to human health is the possible

contamination of edible fish by toxic metals. Studies in Sweden,[34] Canada,[10] and the United States (C. L. Schofield, unpublished data) have revealed high mercury concentrations in fish from acidified regions. It has been hypothesized that the increased mobility of mercury in these low-pH environments is the reason for the increased mercury concentration found in fish,[10,34] but further research is necessary for evaluation of this apparent relationship.

In addition to increased mercury concentrations in acidic lakes, the concentrations of zinc, manganese, iron, and aluminum increase as the lake acidity increases.[50] The concentrations of aluminum exceed the threshold that causes gill damage in trout.[51]

Humans

The ingestion by humans of metal-contaminated fish from acidic lakes has been mentioned previously. Another human-health aspect is the possibility that, as drinking-water reservoirs acidify, owing to acid precipitation, the increased concentrations of metals may exceed the public-health limits. The increased metal concentrations in drinking water are caused by increased watershed weathering and increased leaching of metals from household plumbing. Indeed, in New York State, water from the Hinckley Reservoir has acidified to such an extent that "lead concentrations in water in contact with household plumbing systems exceed the maximum levels for human use recommended by the New York State Department of Health."[57]

ASSESSMENT OF RISK

The acidification of aquatic ecosystems by acid precipitation causes severe stress on the ecosystems: species diversity decreases, fish populations are extinguished, and ecosystem productivity is decreased. However, it is not enough to state that these effects occur. It is also necessary to assess the damage that these effects will cause in our society and our environment. To do this, the population (number and location of aquatic ecosystems sensitive to acidification) at risk must be identified. The aquatic ecosystems that are sensitive to acidification are scattered throughout the United States (Figure 22). It is clear that lake acidification is not a local phenomenon or one that will affect only a small number of lakes. There are thousands

of lakes in the United States that have the potential to acidify (hundreds already have acidified).

Just as the number of sensitive lakes is large, so are the alterations caused by acidification of individual aquatic ecosystems. The destruction of biotic communities increases as the lakes become more acidic. The risk associated with these changes can be assessed from two viewpoints: ecologic and social. Ecologically, the risk is absolute for species or communities that are eliminated by acidification. In addition, the entire structure of the ecosystem is simplified; the numbers of species are reduced, and changes in the biomass of some groups of plants and animals have been observed. These effects can reduce the entire ecosystem's ability to protect itself from further impingement or stresses.

It is difficult to assess the social risk of acidification, because it is not likely to produce acute changes on a global scale, such as climate alteration. Rather, the local extinction of fish populations in acid-sensitive areas is a tangible indicator of environmental stress on a regional scale.

Societal views of and potential reactions to these expanding alterations of aquatic ecosystems have not yet been assessed. Values associated with the concept of an uncontaminated wilderness area, a national park, or a forest preserve are more likely to be expressed in political than in economic terms. People who will never visit the mountains and those who are frequent visitors may act together to influence legislation that will establish and preserve particular regions as parks or wilderness. The concept of protecting unpolluted areas from the effects of sulfur emission has been expressed as law in the Clean Air Act and amendments thereto (42 USC 7401 *et seq.* and PL 95-95, Aug. 7, 1977, 91 Stat. 685).

The economics of sport-fishery losses due to acidification should be evaluated to provide dollar estimates of damages in affected regions. But it is the intangible public perception of damage to sensitive ecosystems--especially in areas like the Adirondacks, which are remote from emission sources--that will constitute the greatest economic factor when that perception is conveyed through the legislative processes to the control of sulfur emission.

The difficulty of evaluating the actual damage or the perception of damage (such as fish kills and ecosystem simplification) does not decrease the significance of the fact that lake acidification will have effects at many levels of our society. To wit:

- Acidified lakes, many in wilderness areas, will no longer support recreational fish populations.
- Acidified reservoirs will experience an increase in metal concentrations that can exceed public-health limits for drinking water.
- Acidified lakes will become visually unattractive, owing to dense growths of sphagnum mosses and filamentous algae.
- Unique communities of populations are in danger of extinction.
- Individual species may be in danger of extinction.

In conclusion, lake acidification has the potential to occur in thousands of lakes throughout the United States. Acidification has ecologic, human-health, aesthetic, and recreational effects.

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6 EFFECTS OF ATMOSPHERIC SULFUR OXIDES AND RELATED COMPOUNDS ON VEGETATION

For more than a century, the actions of sulfur oxides on vegetation have been the subject of continuous scientific investigation. There have been many observations in the field and different kinds of experimental exposures under controlled conditions, predominantly with reference to the direct effects of sulfur dioxide on plants. Some attention has also been given to the effects of sulfates or sulfuric acid as aerosols or in dilute aqueous solutions and to the effects of sulfur oxides on soils. These studies have been most successful in their contributions to the diagnosis, estimation, and analysis of sulfur dioxide-induced effects, through the identification of foliar symptoms, the analysis of foliage for sulfur, and the measurement of changes in growth and yield. Research has also been successful in the identification of the manifold factors in receptors and their environments that determine the kind, occurrence, and degree of effect. Much less information is available on the mode and mechanism of action of sulfur oxides; the nature of long-term, cumulative, ecologic effects; and the quantitative relations between exposure and risk of adverse effects. Inasmuch as the last subject is the special concern of this review, others will be considered only as they are relevant to it, and references to reviews or representative publications will be cited.

Attempts to relate the occurrence of sulfur oxides to their effects on vegetation are most often undertaken to answer questions concerning environmental impact--"What is the risk of an effect, given an exposure to sulfur oxides that may or does occur?"--or concerning air-quality criteria--"For what exposure is the risk of an effect no greater than a particular value?" Answering either question is difficult because of the complexities of the response of vegetation to sulfur oxides and because information is incomplete. Accordingly, one should not

expect a well-defined dose-response relationship that will be generally applicable, but rather a consensual definition of areas in which exposures to sulfur dioxide cause or present a risk of adverse effects to vegetation.

The plan of this review is to discuss the effects of sulfur oxides with respect to their significance, relationships, and occurrence; the nature of exposure and the relationships of exposure to the risk of adverse effects; and the effects of the biologic and environmental determinants of susceptibility on the exposure-effect relationship.

NATURE OF EFFECTS

Several systems have been used to describe and analyze responses of plants to sulfur dioxide and other pollutants. Such systems deal most frequently with biologic changes where each can be ordered by degree, kind, and stratum of biologic organization at which it occurs.[60,85,158] The common feature of all such effects is a change in structure or function of the receptor, and one can term any change that interferes with or diminishes the intended use of the plant an "adverse effect." A convenient way to group these effects is with reference to three general functions of vegetation: aesthetic, economic, and ecologic.

Effects that diminish the aesthetic value of a plant or group of plants--effects on their appearance--most commonly occur when visible lesions of foliage or flowers are produced. Although an effect on plant growth may not commonly be reckoned as aesthetically objectionable, a pollutant-induced variation in growth within a group of the same or different species may be objectionable if uniformity or some other relationship in size or form is desired.

There are several different kinds of economic effects, which directly or indirectly reduce the value or increase the cost of products derived from plants. When the appearance of a plant or produce determines its commercial value, an aesthetic effect is also an economic one. Other direct effects are based on a reduction in the quantity or quality of the product (yield) of the plant, if normal cultural practices are followed and it is harvested at the normal time of maturity. Indirect effects occur where pollutant-induced effects increase the cost of production.

Ecologic effects are not completely separate from those already discussed. Aesthetic values are part of the enjoyment of natural areas, and economic values are part of the managed forest or rangeland. In addition, ecologic effects would

include an impaired ability of vegetation to provide habitats for wildlife, to control soil erosion and the water-retention capacity of watersheds, and to perform functions that are not readily apprehended. One should also note that forests offer considerable capacity for the removal of airborne pollutants.[161] The indirect effects of sulfur oxides in agriculture may become direct and significant in managed and natural plant communities and ecosystems. They include induced effects on plant tolerance to stress and resistance to biotic and abiotic factors.

Although the inherent susceptibility of vegetation varies with species and from variety to variety or individual to individual within a species, one species or variety may serve different functions within a geographic area. Because adverse effects are defined with respect to function, it is the combination of use and biologic susceptibility that will determine the populations at greatest risk.

INTERPRETATION OF EFFECTS

One problem in the interpretation of effects is the relationship of one that in itself may not be adverse to one that is. Perhaps the best example of this problem is the relation of the occurrence and degree of foliar injury to an effect on a plant's growth or reproduction. One should expect that foliar lesions, by their reducing the amount of photosynthetically active tissue, should be inversely related to yield, and such relations have been found.[22,33,142] Nevertheless, it has also been found that the relationship depends on the stage of development at which injury occurs and the environmental conditions under which the plant is grown.[155] It is also true that reductions in yield occur without associated foliar lesions.[5,95] Thus, foliar injury is not always an indicator of an effect on yield, and whatever relationships exist are not invariant, but determined by the interaction of species, time, and environment.

There is even difficulty in the interpretation of the occurrence of foliar lesions, because the receptors often occur as specimen trees at individual residences. Thus, the risk of effects should be evaluated not with reference to a mean or median of population, but with reference to individuals lowest in tolerance and to the probability that any individual will be affected.

Many sulfur-dioxide-induced changes have been found in metabolic or physiologic processes and states of plants, such as changes in the sulfur content,[52,55-57] pH of the cellular milieu,

metabolites, activities of enzymes,[2,12,31,32,69,170] respiration, transpiration, and photosynthetic carbon dioxide fixation.[9,13,58,106,143] Although altered growth and yield are consequences of changes in the metabolism and physiology of the plant, the relations of these changes to adverse effects is very difficult to interpret, especially when modest exposures can result in increased yield.[29,46] Some estimates have been made with reference to the relation between a sulfur dioxide-induced effect on stomatal aperture and water utilization in the field,[9] effects on gaseous exchange and photosynthetic carbon fixation of alfalfa,[145] and physiologic changes and mortality of lichens.[106] The accumulation of sulfate itself can also be a measure of effect, but the interpretation of it depends on what is known about the effect of both rate of uptake and net accumulation, as well as species of plant and nutritional status.

Effects on the vigor, structure, and composition of the flora[53,155] and changes in the pH and sulfur content of soils and waters[113] of plant communities have been reported. But the progressive and cumulative nature of ecologic effects indicates that any change of a receptor or component ought to be interpreted with reference to the reciprocal relationships between plants and the biotic and abiotic factors of their environment.

Sulfur dioxide, as well as other relatively stable pollutant compounds, can cause changes in the pH, nutritional status, and microbe populations in various soils,[113] which may later influence the sensitivity of plants to sulfur dioxide. Because primary and secondary biomass producers and decomposer microbes exist with one another in a rather delicate equilibrium, a stress exerted at one point will almost certainly have an effect (of greater or smaller magnitude) elsewhere in the system. For example, not only are many cations made more available to higher plants via increased soil acidification, but significant changes in microbial populations and behavior also result. Nitrifying bacteria are more detrimentally affected than are ammonifiers at a low soil pH; and, if the pH falls below 5.7, organisms of the genus *Azotobacter*, nitrogen fixers, can be eliminated.[113]

There have been many reports that a change in the incidence or severity of a plant disease is associated with the presence of air pollution in the field (see review of Heagle[63]). There was more damage by *Armillaria mellea* in forests injured by air pollutants;[37] in young stands of spruce, more injury by *Lophodermium abietis* was associated with pollutant-induced injury.[89] The presence of sulfur dioxide resulted in more

severe symptoms of *Rhizosphaera kalkhoffii* on *Pinus densiflora*.[23] But circumstantial evidence from field surveys has suggested that sulfur dioxide can also reduce the infectivity of fungal pathogens.[86,94,109,117,127] In addition, sulfur dioxide at a concentration of 100 $\mu g/m^3$ for 2 days markedly reduced the infectivity of black spot *(Diplocarpon rosae)* on rose foliage;[114] and, in areas where sulfur dioxide concentration exceeded 100 $\mu g/m^3$, the disease was checked or eliminated.[77,115]

Several possible mechanisms have been suggested to account for the interactive effects of sulfur dioxide on diseases of plants. A direct effect on the growth and development of the organism was found in a systematic study (at very high concentrations) on cultures of eight organisms pathogenic to plants and two that infect animals.[104] More recently, it has been shown that reduction in germination of fungal spores and mycelial growth is proportional to sulfur dioxide concentration and duration of exposure.[27,28,54] Both preinoculation and postinoculation exposures of bean to sulfur dioxide resulted in a decrease in the incidence and severity of rust (*Uromyces phaseoli* [Pers.] Wint.) and in the size and percentage germination of uredospores.[160] Thus, it is possible that sulfur dioxide--through its effects on the structure, physiology, or metabolism of the host--indirectly affects the pathogen. It could also alter the suitability of the hosts's organs as habitats for the pathogen by affecting the physiology and microenvironment of the foliar surfaces.[115,116]

Although field surveys[90,119] and experimental exposures[14,125] have shown that sulfur dioxide can damage lichens, its effects on the inhibitory effect of *Peltergeria* on the growth of grasses indicates that allelopathy can be another ecologic effect of concern.[110]

Investigators in central Europe have noted an association between pollution-induced injury and the appearance of insect pests in forests for more than a century.[162] For the most part, these associations have been with reference to secondary pests--those which attack already damaged or weakened trees. Increased infestations of bark insects were found in forests where the stands had been thinned or weakened by pollutant-induced damage.[15,89,117] From their studies in Silesia, Schnaider and Sierpinski[118] concluded that secondary insect pests posed the greater economic threat to forests exposed to pollutants and distinguished between the species that attacked relatively dense stands and the ones that preferred the more open stands (the latter were termed "tertiary pests"). They also suggested that the thinning of stands or canopies by insects makes the trees more open to the effects of atmospheric pollutants.

Some infestations of primary invaders, such as the spruce

sawfly, do occur, and Wentzel and Ohnesorge[162] advanced four hypotheses to account for the phenomenon: the pollutant directly affects the insect; pollutant-induced changes in the trees make them more attractive (perhaps through pheromones) to insects; natural predators or parasites of the insects are inhibited; and pollutant-induced changes make the host tree a better habitat for the insect. Their observations, although providing no clear answer, favored the third and fourth hypotheses. Templin[140] also concluded that pollutant-induced changes in the water economy of the tree favored the development of pine-infesting insects and noted a decreased parasitization. However, Przybylski[109] reported that a spider mite was susceptible to sulfur dioxide exposures and an aphid was highly resistant; the population of the former decreased, and that of the latter increased around a source of sulfur dioxide emission.

Although experimental investigations tend to focus on changes in the median tolerance or susceptibility of plants to pathogens or insects, an effect on the heterogeneity of tolerances in a natural population could prove important. Similarly, experience in North America and central Europe has shown that natural populations have considerable intraspecific differences in tolerance to sulfur dioxide. Because frost and drought tolerance is associated with sulfur dioxide tolerance in some species, the selection against susceptible segments of the population may also select against other significant traits, increase homogeneity, and restrict the genetic pool.

RELATION OF EXPOSURE TO RESPONSE

Information on exposure-response relations for plants comes from two kinds of investigations. One consists of the controlled exposure of plants to sulfur dioxide; the gas is administered in an experimental facility, and control is exercised over the dosage and environmental conditions during the experimental period. The other consists of observations made at different sites in an area around a source of sulfur dioxide; the ambient concentration of the gas is monitored at sites where native plants are observed periodically or potted plants are set out and maintained for specified periods. For information from either kind of study to be adequate for the formulation of dose-response relationships, the atmospheric concentrations of sulfur dioxide must be known with reasonable accuracy and completeness, and some control or measurement of attendant environmental conditions must be available. These

criteria are more often fulfilled and exposures are more easily described in experimental work under controlled conditions. In field experiments, the statistics that are relevant to or descriptive of the exposure may often be incompletely reported.

There are more than 100 publications presenting the results of more than 1,000 exposures in which an effect can be associated with a defined exposure to sulfur dioxide. But so many species of plants, kinds of responses, and experimental conditions have been used to obtain these data that the collation of the results is difficult.

Foliar injury is the most commonly observed response of plants to sulfur dioxide. Table 5 summarizes the experimental exposures that have been associated with the occurence of any sulfur dioxide-induced foliar lesions. The results are arranged primarily according to the duration of the exposure and secondarily (for each duration) according to sulfur dioxide concentration. If the same duration of exposure was used more than once for the same species (in one publication or several), the lowest concentration is given. Table 6 summarizes the exposures that produced no foliar injury or that represent the threshold for the occurrence of foliar injury for different species of plants. Table 7 summarizes some of the physiologic responses that are induced by sulfur dioxide and that occur before or in the absence of any foliar lesions. A comparison of Tables 5 and 6 shows that for a given species there is no clear demarcation between injurious and noninjurious exposures, and this reflects the biotic and abiotic factors that affect a plant's susceptibility and vary from one experimental study to another.

Nevertheless, experimental exposures have been successful in determining at least four variables of exposure to sulfur dioxide that can affect a plant's response: concentration of sulfur dioxide, duration of exposure, number of exposures that occur, and interval between successive exposures. Although it is evident that the likelihood of an effect of a given magnitude increases with the atmospheric concentration of sulfur dioxide, the duration of exposure, and the frequency of exposure, the latter two variables have an effect apart from that on the total dose received by the receptor. An increase in the duration of exposure also increases the likelihood that periodic or transient changes in the environment and the plant will produce a period of greater susceptibility during the exposure. Similarly, an increase in the frequency of exposure not only increases the likelihood of exposure during a period of greater susceptibility, but also reduces the effects of

TABLE 5 Concentrations of SO_2 at Which Foliar Injury Has Been Found in Experimental Exposures of Plants

Duration of Exposure	SO_2 Concentration, mg/m^3	Plant	Reference
1.5 min	2,620	Tomato, tobacco	146
4 min	2,620	Buckwheat	146
8 min	165	Tomato	146
10 min	157	Scotch pine	157
	2,620	Chaparral species	108
12 min	22.3	Alfalfa	141
1 h	0.131	Eastern white pine	25
	0.655	Petunia	171
	1.57	Western larch	83
	1.72	Buckwheat	172
	2.10	Wheat, meadow fescue	172
	2.57	Swiss chard, Chinese cabbage	172
	2.83	Eggplant, endive	172
	10.5	Tomato, salvia, coleus	172
2 h	0.655	Eastern white pine, red pine, Scotch pine	8
	1.31	Desert species	65
	2.10	New Zeland spinach	172
		Barley	172
	2.57	Radish	172
	2.62	Desert species	65
	2.75	Turnip, cos lettuce	172
	4.10	Winter barley	55
	5.24	Desert species	65
		Chinese elm	139
	7.86	Norway maple	139
	10.5	Ginkgo	139
		Desert species	65
	13.1	Pin oak	139
	15.7	Desert species	65
	26.2	Desert species	65
3 h	1.42	Mountain ash	131
	1.57	Buckwheat	172
	1.73	Oats, rye	172
	2.15	Sweet clover	172
	2.16	Sweet pea	172

TABLE 5 Continued

Duration of Exposure	SO_2 Concentration, mg/m^3	Plant	Reference
3 h	2.8	Oat	56
	3.28	Alfalfa	81
	4.98	Blueberry	21
	10.48	Coleus, salvia	171
4 h	1.31	Tomato	18
		Pinto bean	128
	1.73	Sweet clover, barley	172
	1.97	Barley	81
	2.02	Cucumber	18
	2.57	Castor bean	172
	2.62	Tobacco	97
	2.78	Buckwheat	122
	3.46	Alfalfa	81
	5.24	Weed species	6
	7.86	Ginkgo	139
	10.5	Pin oak	139
5 h	1.73	Alfalfa, tomato	172
		Oat, barley, rye, sweet clover	171
	2.28	Buckwheat	122
	2.57	Salvia	172
	2.62	Castor bean, salvia, pepper	171
	5.24	Tobacco, tomato	172
		Sugar beet	73
6 h	0.066	Eastern white pine	72
	1.258	Apple, pear	131
	1.31	Buckwheat	171
		Anemone, ixia	130
	1.83	Rose	172
	1.89	Western larch, Douglas fir	83
	1.97	Turfgrass species	17
		Crocus species, sparaxis	130
	2.23	Turfgrass species	17
	2.62	Anemone fulgens, eranthis, *Chionodoxa*	130
	3.28	Squill, *Allium moll*, crown imperial	130

TABLE 5 Continued

Duration of Exposure	SO_2 Concentration mg/m^3	Plant	Reference
6 h	3.93	Siberian squill, grape hyacinth	130
	4.72	Turfgrass species	17
	5.24	Norway maple	139
		Checkered lily	130
	10.84	Pin oak	139
8 h	0.786	Western larch	83
	1.13	Douglas fir	83
	1.57	Barley	172
	2.15	Alfalfa	81
	4.00	Foxglove	57
	7.86	Pin oak	139
24 h	0.786	Begonia, dahlia, aster, zinnia, cucumber, violet, spiderwort	20
	1.31	Barley	81
	13.1	Lichens	111
8-24 h/day	0.393	Western larch	83
for 3 days	0.786	Tomato	18
	1.83	Pine	40
for 5 days	1.965	Chinese elm	139
	2.62	Douglas fir	82
for 6 days	1.97	Ponderosa pine	82
for 8 days	0.262	Alfalfa	81
for 14 days	1.31	Douglas fir	82
for 15 days	1.50	Sunflower	47
for 20 days	0.262	Eastern white pine	36
	1.50	Radish	47
for 21 days	1.97	Norway maple	139
for 30 days	1.97	Ginkgo	139

TABLE 6 Concentrations of SO_2 at Which No Foliar Injury or Threshold for Injury Has Been Reported in Plants

Duration of Exposure	SO_2 Concentration, mg/m^3	Plant	Reference
0.25 h	21.000	Rye	154
0.50 h	1.310	Soybean	33
	13.000	Rye	154
1 h	1.572	Buckwheat	172
	2.148	Sweet clover	172
	7.000	Rye	154
	26.206	Winter rape	30
2 h	1.310	Tobacco	67
	1.310	Desert species	65
	1.572	Buckwheat	172
	2.100	Crimson clover	55
	2.148	Sweet clover	172
	2.620	Desert species	65
	5.240	Desert species	65
	7.860	Ginkgo	139
	10.48	Desert species	65
	20.96	Pin oak	139
	26.20	Desert species	65
3 h	2.646	European beech	131
	2.800	Oat	55
	3.300	Rye	154
	3.668	Sycamore maple	131
	3.747	Mountain ash, European bird cherry	131
	12.838	Blueberry, high bush	21
4 h	1.050	Tomato	18
		Crimson clover	55
	1.153	Alfalfa	81
	1.310	Tobacco	67
		Moss	24
	1.467	Cucumber	18
	1.886	Western larch	83
	2.306	Barley	81
	2.777	Buckwheat	122
	5.240	Norway maple	139
5 h	1.415	Buckwheat	172
	3.013	Alfalfa	81
	11.266	Lily, orchard species	171

TABLE 6 Continued

Duration of Exposure	SO_2 Concentration, mg/m^3	Plant	Reference
6 h	1.205	Buckwheat	172
	1.310	Ponderosa pine, Douglas fir	83
		Moss	24
	2.000	Rye	154
	7.86	Pin oak	139
	9.17	Snowdrop	130
8 h	0.786	Douglas fir, lodgepole pine	83
	0.865	Western larch	83
	1.310	Jerusalem cherry, Stevia, ixora, sorghum, tulip	173
	2.279	Alfalfa	81
	2.620	Tobacco	97
	5.24	Ginkgo, pin oak	139
12 h	0.524	Tobacco	97
	1.310	Ponderosa pine, Douglas fir	82
	2.620	Broadbean	98
1 day	0.200	Bean	87
	0.786	Azalea, periwinkle, Swiss chard, pepper	19
	2.044	Barley	81
	2.469	Douglas fir	83
2 days	0.865	Buckwheat	122
		Ponderosa pine	83
	1.808	Douglas fir	83
3 days	0.393	Western larch	83
	1.00	Foxglove	57
	1.965	Douglas fir, ponderosa pine	82
4 days	0.200	Bushbean	87
5 days	0.498	Buckwheat	122
	1.965	Douglas fir, ponderosa pine	82
9 days	1.500	Tobacco	47
10 days	1.965	Pin oak	139
13 days	1.500	Corn	47
14 days	1.965	Ponderosa pine, Douglas fir	82
15 days	1.00	Sunflower	47
19 days	0.655	Ponderosa pine, Douglas fir	82
20 days	1.00	Radish	47

TABLE 6 Continued

Duration of Exposure	SO_2 Concentration, mg/m^3	Plant	Reference
21 days	1.310	Blueberry, petunia, pepper, coleus	21
42 days	1.310	Ponderosa pine, Douglas fir	82
77 days	0.208	Perennial ryegrass	95

regenerative or compensatory processes in the plant during pollutant-free periods.

Formulations of the Exposure-Response Relationship

Two kinds of formulations of the exposure-response relationship have been developed. One expresses the magnitude of an effect produced by sulfur dioxide as an explicit function of the variables of exposure, and it is common that, for some ranges of the exposure variables, no effect is present. The other kind of formulation defines the boundary for the occurrence of an effect with reference to one variable (usually concentration) as an implicit function of the other variables of exposure.

Equation 1 was originally proposed by O'Gara, but its exposition and development were due mainly to the efforts of M. D. Thomas and his co-workers:[142]

$$T(C - C_O) = K_R. \qquad (1)$$

The variables T and C are duration of exposure and concentration of sulfur dioxide, respectively. The parameters C_O and K_R assume values according to the inherent resistance of the plant (as determined by species, variety, and stage of development), the relative humidity, and the magnitude of effect concerned.

The equation was based on short-term exposures (mainly 0.5-4 h), and coefficients for the susceptibilities of different crops relative to alfalfa and corrections for relative humidity have been tabulated.[142] For example, K_R assumed values of 0.94, 2.1, and 3.2 ppm/h and C_O values of 0.24, 1.4, and 2.6

TABLE 7 Physiologic Effects of SO_2 on Plants

Concentration, mg/m^3	Duration of Exposure	Effect	Reference
0.070	10 min	Decreased stomatal resistance, broadbean	9
0.131	5 min	Decreased stomatal resistance, broadbean, corn	152
0.524	10 days	Decreased CO_2 fixation, alfalfa	141
1.31	30 min	Decreased $^{14}CO_2$-derived photosynthate, barley	129
	8 h	Decreased regeneration of leaves, moss	24
1.78	3 h	Threshold for effect on potassium-efflux, lichen	106
2.62	1 h	Decreased CO_2 fixation, European larch	156
	4 h	Decreased regeneration of leaves, moss	24
	5 h	Decreased CO_2 fixation, Norway spruce	11
	24 h	Breakdown of chlorophyll, bryophytes	135
3.80	30 min	Decreased CO_2 fixation, crimson clover	55
7.074	6 min	Decreased CO_2 fixation, Scotch pine	156
8.00	15 min	Inhibition of net CO_2 assimilation, mosses and lichens	14
13.1	5 h	Increased O_2 uptake, bryophytes	135

ppm for trace, 50%, and 100% leaf destruction, respectively, for alfalfa exposed at 100% relative humidity. When the equation is used for a threshold or incipient degree of foliar injury, C_O expresses a limiting or asymptotic concentration that can be endured indefinitely.

It is apparent from the model formulated by Equation 1 that, although the product of time and concentration remains constant, the effect of exposure may vary. However, it was the observation of Guderian *et al.*[60] that the relation of exposure to the injury threshold was more sensitive to changes in concentration than to changes in duration of exposure. Accordingly, they proposed, as an equation that could account for the effects of concentration more adequately than that of O'Gara, Equation 2:

$$T - T_O = K_V \exp - A_R(C - C_O). \qquad (2)$$

The variables T and C are the same as in Equation 1; T_O is the threshold (asymptotic) exposure time; C_O is the threshold (asymptotic) concentration; K_V is the length of the growing period or maximal length of time that vegetation would be sensitive; and A_R is a parameter based on effects of a complex of biologic factors that determine the resistance of a plant to sulfur dioxide. Time cannot be less than the period required for diffusion, absorption, and reaction of the gas or greater than the period in which the crop is susceptible to the gas.

Whereas both the O'Gara-Thomas and the Guderian *et al.* models are fitted empirically to data from controlled exposures and theoretically based on the factors of absorption and accumulation of sulfur dioxide in foliar tissue, the former may be viewed as emphasizing state-sensitive and the latter rate-sensitive processes in the plant. The authors of both models recognized that time-dependent changes occur in the susceptibility of a plant and that these could not be ignored in the application of their models.

A third model has been proposed,[168] on the grounds that it fits the experimentally derived thresholds better than the two formulations previously discussed. Equation 3 expresses the liminal duration of exposure as a function of concentration, and the equation $TC^2 = 2$ has been suggested as a simple and useful approximation for it:

$$T = K_1 P_1 \left(\frac{1 + 0.5C}{C(C - C_R)} \right) . \qquad (3)$$

K_1 is a parameter that expresses the effects of environmental conditions on the resistance of the plant to sulfur dioxide, with a mean value of 2.6 and a range of 1-4 (when C is in parts per million and T is in hours); P_1 is a parameter that expresses the effects of stage of development and inherent factors on resistance of the plant; and C_R is the value of the threshold concentration for a given response.

Zahn also derived a dose-response relationship (Equation 4) in which the response is expressed on a graded scale of injury; for a given species, conditions, and concentration of sulfur dioxide:

$$T = T_R \exp K_2 P_2 \left(\frac{S - S_R}{\sqrt{10C}} \right) \quad . \tag{4}$$

The variables S and T are, respectively, degree of foliar injury produced ($0.5 < S \leq 5.0$) and duration of exposure required to produce a degree of foliar injury equal to S; K_2 is a resistance parameter for the complex of environmental conditions; P_2 is a resistance parameter for the set of biologic conditions; C is the concentration of sulfur dioxide; S_R is the lowest degree of injury (= 0.5 on Zahn's scale); and T_R is the duration required to induce injury equal to S_R.

On the basis of this dose-response relationship, a means of comparison between continuous and intermittent exposure was formulated to account for the effects of the individual exposures and the recovery periods between them (Equation 5):

$$T' = T_R \left[\exp \left(K_2 P_2 \frac{S' - S_R}{\sqrt{10C}} \right) + F_r \right] , \tag{5}$$

in which S' and T' are, respectively, injury and duration in intermittent exposures (T' equals the sum of individual exposures); the parameters K_2, P_2, T_R, and S_R are the same as in Equation 4; and F is a recovery factor evaluated by Equation 6:

$$F_r = 2 \left[C \left(\ln \frac{T_R}{t_i} \right) \left(\ln \frac{t_e}{t_{eo}} \right) \right]^{1/2} , \tag{6}$$

in which t_{eo} is the minimal length of the period necessary for recovery; t_e is the duration of periods between exposures ($t_e \geq t_{eo}$); and t_i is the duration of an individual exposure period ($t_i \leq T_R$).

Further work by Zahn[169] on the effects of intermittent exposures has indicated that a subacute exposure may increase the resistance of some monocots and conifers to a later acute exposure. This phenomenon was viewed as mediated by some induced metabolic activity and not due to effects on stomata. He also indicated that this inductive effect decays with time, that its magnitude is proportional to the product of concentration and duration of exposure, and that this product must exceed a critical value for the effect to occur.

Insofar as short-term exposures and effects are concerned, the threshold surface (as a function of concentration, duration, and frequency) appears to have these characteristics: upward concavity, asymptotic values (thresholds), and nonadditivity, especially where subacute doses and the synergistic or antagonistic effects of successive exposures may be present. In most of these discussions of dose-response relationships, the asymptotic values for concentration of sulfur dioxide in the most susceptible species appear to be in the range of 260-600 $\mu g/m^3$ (cf. Thomas and Hendricks,[142] Guderian,[158] and Zahn[168]).

Characteristics of Ambient Exposures

Descriptions of ambient exposures are complex and have been based on theoretical models for atmospheric dispersion or on the examination of data from ambient air-monitoring systems. Generally, the exposures that occur during some extended period (e.g., a year or a growing season) can be represented by a surface in space defined by concentration, averaging time, and frequency (the number of times a mean value for a specified averaging period is greater than or equal to a specified concentration). The parameters that define this surface are based on the descriptive statistics derived from probability-density and spectral-density functions that fit or express the air-monitoring data.[124] A log-normal distribution function appears to represent the distributions reasonably well for a range of averaging times,[124] but the negative binomial has been proposed as a suitable distribution function for short averaging times (10 min to 1 h) when zero values are frequent. The distribution of values for air-monitoring data may be a compound one that reflects not only the intervention of meteorologic conditions and some variations in source strength, but also the distribution of sampling and analytic error (cf. Stratmann *et al.*[133]).

Two long-term studies have sought to determine the relation of ambient exposures to effects on plants.[38,59] In the first, groups of plants were stationed at different distances from a single source, and several measures of responses were determined (Table 8) for different species of plants. The reported air-monitoring data (Table 9) were censored; 10-min averages less than 0.1 ppm were not included, because it was believed by the investigators that these were subliminal exposures.

The results of a 4-yr study of the effects of ambient exposures on many species of plants are summarized in Table 10, which presents the statistics of exposures (1-, 2-, 4-, and 8-h means) whose minimums were associated with the occurrence of foliar injury.[38] These statistics are also based on censored data and represent only exposures that occurred during the day (sunrise to sunset) and during the growing season (May through October), because it was judged that biologic and environmental factors rendered the plants most susceptible during these periods. The investigators also judged that only short-term statistics (1- to 8-h means) were important and that long-term or annual means had no direct significance or efficiency in estimating the injury induced by an exposure. The relevance of an annual mean was problematic, in that sulfur dioxide was present at measurable concentrations only 21% of the time at the station where it was encountered most frequently. On the basis of these observations, the authors of the study concluded that one could be reasonably certain of avoiding foliar injury to vegetation in the study area if concentrations did not exceed 0.70, 0.40, 0.26, or 0.18 ppm as 1-, 2-, 4-, or 8-h means, respectively. In view of the results reported by others from controlled exposures and the results at other stations in the Sudbury area, the 4- and 8-h means specify a compound measure of lower concentrations during the period and the frequency with which 1-h peaks at higher concentrations may occur.

Characteristics of Response

Among the general characteristics of the response of a plant to sulfur dioxide that are of major importance with respect to exposure-effect relationships are the time-dependent characteristics of both, and matters are simplified if one divides the temporal scale into short-, mid-, and long-term ranges. Of the different kinds of effects, the occurrence of foliar injury may be regarded as typical of the short-term range, and exposures of 12 h or less may be of greatest consequence, owing to the effects of environment and stage of development on the

TABLE 8 Effects of Exposures to Ambient Sulfur Dioxide on Different Measures of Growth and Yield for Several Crops[a]

Crop and Response	Field Monitoring Station[b] I	II	III	IV	V
Winter rye (*Secale cereale* L.)					
Quality (as green fodder)	a	a	a		
Yield of grain	**	**	**		
Yield of straw	**	**			
Cold hardiness	a	a			
Winter wheat (*Triticum sativum* L.)					
Yield of grain	**	**	**	**	
Yield of straw	**	**			
Cold hardiness	a	a	a	a	
Spring wheat (*Triticum sativum* L.)					
Yield of grain	**	**	**		
Yield of straw	**	**	*		
Oats (*Avena sativa* L.)					
Quality (as fodder)	a	a	a		
Yield of grain	**	**	**		
Yield of straw	**	**	*		
Rape (*Brassica napus* L. var. *oleifera*)					
Quality (as fodder)	a	a	a		
Yield of seeds	**				
Alfalfa (*Medicago sativa* L.)					
Yield	**	**	**		
Quality	a	a	a		
Cold resistance	a	a	a		
Red clover (*Trifolium pratense* L.)					
Yield	**	**	**		
Quality	a	a	a		
Potato (*Solanum tuberosum* L.)					
Yield	**	**	**	**	
Quality	a	a			
Tomato (*Lycopersicon esculentum* L.)					
Yield	**				
Spinach (*Spinacia oleracea* L.)					
Yield	**	**			
Quality	a	a	a	a	
Beet (*Beta vulgaris* L.)					
Yield of roots	**	**	**		
Yield of foliage	**	**			
Quality of foliage	a	a			

TABLE 8 Continued

Crop and Response	Field Monitoring Station[b] I	II	III	IV	V
Carrot (*Daucus carota* L.)					
Yield	**	**			
Apple (*Malus communis* Mill cv Ellisons Orange)					
Yield		**	**	*	
Quality		a	a	a	
Shoot (elongation) growth		**			
Bole (radial) growth		**	**		
Sweet cherry (*Prunus avium* L. cv Primavera)					
Yield		**	b	b	b
Quality		a			
Shoot (elongation) growth		**			
Bole (radial) growth		**	**		
Sour cherry (*Prunus cerasus* L.)					
Quality		a	b	a	
Shoot (elongation) growth		**	**		
Bole (radial) growth		**	*		
Prune (*Prunus domestica* L.)					
Yield	*				
Quality		a			
Shoot (elongation) growth	*				
Bole (radial) growth		**	**		
Currant (*Ribes rubrum* L.)					
Yield		**	**	**	
Quality		a	a		
Shoot (elongation) growth		**	**	*	
Gooseberry (*Ribes uva-crispa* L.)					
Yield		**	**	**	**
Quality		a	a	a	
Shoot (elongation) growth		**	**	**	**
Larch (*Larix europaea* Lamet DC)					
Shoot (elongation) growth		**	**		
Bole (radial) growth		**	**	**	
Pine (*Pinus sylvestris* L.)					
Shoot (elongation) growth		**	*		
Bole (radial) growth		**	**	**	
Spruce (*Picea excelsa* Link.)					
Shoot (elongation) growth		**	**	*	
Bole (radial) growth		**	**	*	

TABLE 8 Continued

Crop and Response	Field Monitoring Station[b] I	II	III	IV	V
Oak (*Quercus pedunculata* Ehrh.)					
Shoot (elongation) growth		**	**		
Bole (radial) growth		**	**	**	
Bean (*Fagus sylvatica* L.)					
Shoot (elongation) growth		**	**	**	
Bole (radial) growth		**	**	**	

[a]Derived from Guderian and Stratmann.[59] Statistics that describe the exposures are given in Table 9.

[b]Empty space in column indicates no data (Station I) or no difference from control (Stations II-V). * = significantly different from control; $p = 0.05$. ** = significantly different from control; $p = 0.01$. a = lower than control. b = unknown.

susceptibility of a leaf.[38] Reductions in growth or yield may be viewed as representative of the mid-term effect and associated with the cumulative result of short-term effects, such as the reduction in photosynthetically active foliar tissue by lesions or the periodic reductions in photosynthesis. Nevertheless, the effects of continuous lower concentrations (0.100-0.400 $\mu g/m^3$) where they occur over a growing season should also be considered.[5,95,147] Short- and mid-term effects can ultimately be expressed over the long term (1 yr or more), but the indirect and systemic effects, including effects on epiphytes[90] by acidification of bark or the mineral substrate,[96] may also be associated with total flux, as estimated by an annual mean.

For each kind of adverse effect there is a roughly corresponding temporal scale for its occurrence or manifestation and for the exposure that produces it. One could expect aesthetic effects to be most closely associated with the shorter-term exposures to higher concentrations. Economic effects could be expected to be associated with the cumulative effects of exposure over a growing season for most horticultural and agronomic crops, as well as with the short-term exposures. For orchards, forests, and ecosystems, the time scale is lengthened and the cumulative effects of many seasons must be considered.

TABLE 9 Measures of Exposure to Ambient Sulfur Dioxide in Studies on Growth and Yield of Crops[a]

Measures of Exposure	Field Monitoring Station I	II	III	IV	V
In 1959:					
Mean concentration, ppm					
30-min maximum	5.4	3.7	2.5	1.4	0.9
During exposure[b]	0.570	0.373	0.377	0.229	0.205
Entire period	0.124	0.061	0.050	0.015	0.010
Number of hours					
Concentration greater than the mean during exposure	327	241	174	104	73
During exposure[b]	1,075	815	648	320	227
Entire period	4,955	4,979	4,927	4,999	4,884
In 1960:					
Mean concentration, ppm					
30-min maximum	6.3	6.5	2.2	2.1	1.8
During exposure[b]	0.603	0.488	0.311	0.277	0.236
Entire period	0.159	0.104	0.051	0.024	0.009
Number of hours					
Concentration greater than the mean during exposure	421	326	242	128	54
During exposure[b]	1,256	1,068	807	430	201
Entire period	4,759	5,007	4,960	4,968	5,006

[a]Derived from Guderian and Stratmann.[59]

[b]During 10-min intervals when concentrations of at least 0.10 ppm were registered.

FACTORS AFFECTING THE EXPOSURE-RESPONSE RELATIONSHIP

Three sets of characteristics define the population at risk: the effect produced, the inherent biologic susceptibility of the receptors, and the environmental factors (other than sulfur oxides) that influence the susceptibility of the receptors.

Genetic Factors

Among the many factors that can influence vegetation responses to sulfur oxides and related compounds are those which change

TABLE 10 Ambient Exposures to Sulfur Dioxide That Caused Injury to Vegetation[a]

Exposure Where Injured SO_2 Concentration, ppm, for Averaging Periods of:				
1 h	2 h	4 h	8 h	Plant
0.41	0.38	0.33	0.30	Willow
0.41	0.38	0.34	0.26	Larch
0.42	0.39	0.26	0.13	Quaking aspen
0.45	0.34	0.25	0.21	Bracken fern
0.45	0.35	0.25	0.21	White pine
0.46	0.38	0.28	0.21	White birch
0.46	0.45	0.43	0.21	Bean
0.46	0.43	0.43	0.21	Alder
0.52	0.44	0.29	0.20	Jack pine
0.56	0.39	0.26	0.15	Buckwheat
0.63	0.44	0.24	0.12	Barley
0.63	0.59	0.34	0.17	Oats, peas, rhubarb
0.64	0.56	0.43	0.38	Lettuce, tomato, potato
0.66	0.43	0.37	0.20	Large-toothed aspen
0.66	0.45	0.44	0.33	Austrian pine
0.66	0.54	0.40	0.21	Timothy
0.70	0.46	0.27	0.14	Red clover
0.74	0.63	0.53	0.39	Raspberry
0.76	0.54	0.29	0.14	Radish
0.78	0.69	0.44	0.30	Red pine
0.82	0.65	0.45	0.26	Balsam poplar
0.82	0.65	0.62	0.46	Sugar maple
0.87	0.74	0.55	0.29	Celery
0.87	0.79	0.70	0.50	White spruce
0.88	0.64	0.42	0.27	Swiss chard
0.89	0.82	0.61	0.41	Red oak
0.94	0.89	0.70	0.45	Cabbage
1.08	0.79	0.50	0.25	Carrot, cucumber
1.14	0.75	0.45	0.23	Witch hazel
1.31	0.77	0.45	0.23	Beet, turnip
1.34	0.91	0.50	0.34	Spinach

[a]Derived from Dreisinger and McGovern.[38]

slowly over time. The inherent susceptibility of plants, as governed by genetic factors, is one such stable influence. Whether a single plant, or a group of plants, is sensitive or tolerant to the effects of sulfur oxides will not change, unless there is hybridization or some other phenomenon (e.g., mutation) responsible for changes in genetic makeup. Plant sensitivity, which varies within a given plant population because of genetic diversity, is manifested as a function of morphologic and biochemical characteristics. Differences in sensitivity exist not only among higher taxa, but between and within species.[41,48,67]

In some ecosystems, species composition is strongly influenced by the sulfur dioxide selection pressure.[155] Some investigators have suggested, on the basis of bacterial DNA studies, that sulfur dioxide in the atmosphere can constitute a genetic hazard.[123] More work is certainly necessary on this before generalizations can be made relative to more complex organisms.

Plant sensitivity to air pollutants has been treated more or less singularly and as related to other phenomena as a predisposing, protective, or potentiating influence. Some information from central Europe indicates that gaseous diffusion into foliar tissue explains differences in tolerance between two species of larch.[157] Recent experiments have indicated that this mechanism does not account for differences in tolerance between two selections of perennial ryegrass.[5] Some characteristics of plants have been correlated with those plants' sulfur dioxide sensitivity. Larches with curled needles are reportedly more resistant to sulfur dioxide injury than those with straight needles.[61] Sulfur dioxide injury resistance in Norway spruce has been associated with chromatographic fluorescence patterns in sap.[10] Peroxidase activity in eastern white pine can be used to differentiate among sensitive and insensitive clones.[70,71]

Plants differ in their inherent capacity to convert the more toxic sulfites to the less harmful sulfates. Therefore, differential uptake of sulfur dioxide among plants can be related to injury via the ability of those plants to detoxify sulfites. Vascular plants absorb sulfur dioxide through the stomata, whose activity is governed by several external stimuli (discussed in greater detail later). Nonvascular plants (lichens and bryophytes) are known to be generally more sensitive to sulfur dioxide because gas absorption occurs over the entire surface and critical factors for photosynthesis and respiration are not as important as in vascular plants.[113]

One of the difficulties in the interpretation and practical use is the great lack of uniformity of plant materials. Owing to genetic diversity in most plant populations in nearly any geographic area in the United States, inherent susceptibility to sulfur dioxide varies sufficiently to place anywhere from only a few to nearly all individuals in a plant population at risk. Generally, there is less diversity in manipulated agricultural ecosystems, be they annual crops or artificially regenerated forests, but variation is present even within one seed source. For crop species, the median tolerances span a range of 10- to 20-fold for the same kind of effect and the same kind of exposure (usually the occurrence of foliar lesions and short-term exposures). Natural communities have a considerable range of tolerances in the different species that constitute them. For example, in desert species, at least a 20-fold difference in sulfur dioxide exposure was needed to injure both sensitive and tolerant species.[65]

Plant Development

Developmental characteristics of plants are similar to genetic factors in their degree of stability. Although there are significant morphologic and physiologic differences among the many different types of plants in the United States, each usually performs its diurnal and seasonal activities consistently. Plants may or may not be included in the population at risk simply because exposure occurs when they are in a stage of development that renders a given plant more or less sensitive to pollutant stress.

Annual crops are known for their variation in susceptibility during the earlier phenologic stages.[22,155] It has been reported[155] that seedling grains are quite resistant up to the second-leaf stage, increase to their maximal sensitivity when they have formed the third leaf, and then become more resistant. The resistance of grains increases until just before inflorescence, when leaf sensitivity increases again. Cereal grains in the tillering stage can sustain significant sulfur dioxide injury without later losses in yield; yields are reduced much more if injury occurs after culms form than before. Whether the plant in question is an annual grain, an ornamental, a vegetable, or a perennial tree, the general sensitivity of the whole plant is determined by leaf stage at any time.[155]

Foliage of plants is generally more sensitive to sulfur dioxide effects than reproductive parts (flowers), although there are reports that pollen sterility and pollen grain deformation

can result from exposure to sulfur dioxide. Many crop plants seem most sensitive to sulfur dioxide when the products of assimilation are being translocated to seeds, roots, tubers, etc.[113] It is likely that fruit trees would be similarly affected just after fruit is set in the spring or summer.

Deciduous trees are most sensitive to sulfur dioxide just after the leaves are fully expanded, not in either the juvenile or older stage. Deciduous trees, therefore, are less likely to sustain injury during the winter months than conifers and other evergreens, which display some photosynthetic activity all year. Conifers, unlike deciduous trees, cannot tolerate strong fumigations during the winter months, because needles remain sensitive and function as long as water is available.[155] However, conifers are much more sensitive in spring and early summer than during fall and winter. As the shoots of conifers are elongating, they can withstand sulfur dioxide fumigations strong enough to cause the previous year's needles to fall off.[155] But on full elongation, new needles reach maximal sensitivity and are much more easily injured than the previous year's needles, which were more sensitive only a few weeks earlier.

Growth characteristics have been associated with sulfur dioxide sensitivity. For example, it has been reported[155] that such plants as lettuce, celery, and beets, which develop with a rosette form, produce the most sensitive leaves toward the inside.

Environmental Factors

Unlike genetic and developmental characteristics, environmental influences to which vegetation is exposed are quite variable. Such factors are unstable, and it is probably not possible to assess the plant population at risk of sulfur dioxide injury with respect to homogeneity of the factors over the long term and in large georgraphic areas.

Temperature Temperature plays an important part not only in determining the metabolic rate of a plant, but in determining (with moisture, fertility, and light) the species diversity and richness in a given ecosystem. Temperature--like humidity, soil moisture availability, and light--exerts an influence on the guard cells that control stomatal opening and closing. In fact, nearly all the physical environmental influences on plant sensitivity can affect vegetation via stomatal behavior. In general, as long as increases in temperature cause increases in physiologic activity, the risk of plant injury from sulfur dioxide also increases.[113]

Several investigators[103,121] have noted greater resistance of conifers in the winter and attributed their findings to a lowered pace of physiologic activity. Plants are usually less sensitive to sulfur dioxide at temperatures below 4.4°C, but Setterstrom and Zimmerman[122] observed no differences in buckwheat sensitivity between 18.3 and 40.6°C. Buckwheat is not a winter-grown crop, but some plants--such as winter wheat, barley, and evergreens--remain physiologically active during the winter months, which are often characterized by intermittent air temperatures over 4.4°C. Katz[80] reported that a given concentration of sulfur dioxide administered near the end of the dormant period required a fumigation only 44% as long to cause the same amount of injury as an autumn fumigation with the same sulfur dioxide concentration. Spring and fall temperatures are no doubt similar, but the pre-existing physiologic state must be considered in relation to temperature.

Relative Humidity As humidity increases, so do stomatal openings and plant sensitivity to sulfur dioxide. Although sensitivity increases with relative humidity, it has been reported that, once above a relative humidity of 40%, changes of 20% or more are necessary to cause changes in plant sensitivity.[122] A change from 50 to 75% has little or no effect on sensitivity. Swain[134] substantiated this contention and indicated that an increase in relative humidity from 70 to 100% did not result in much increase in sensitivity. According to Zimmerman and Crocker,[172] although humidity is important in governing sensitivity and consequently the susceptible population, it is not as important as tissue turgidity. On the basis of studies of water relations in trees, Halbwachs[62] has rated plants as sensitive, intermediate, and tolerant at relative humidities of over 75, 50-75, and under 50%, respectively.

Light Light, another of the stomatal stimuli, is closely related to plant sensitivity. Plants are more resistant to sulfur dioxide injury when fumigated in darkness or held in the dark for a couple of hours before fumigation.[172] The relationship is not quite as simple as it might appear, however, inasmuch as injury is greater if a night exposure follows a daylight one. Setterstrom and Zimmerman[122] observed that buckwheat grown under heavy shade--at least a 65% decrease in light intensity--was more sensitive than when exposed to sulfur dioxide in full sunlight. A decrease in light intensity of up to 35% had no effect on sensitivity.

It is possible that shade could have a greater or smaller effect on sensitivity of given species, depending on their

normal demands for sunlight for photosynthetic efficiency (photoperiod). Other investigators found injury more severe when tomato stems and foliage were fumigated on clear, rather than cloudy, days. Apparently, an increase in light intensity is responsible for an increase in sensitivity to sulfur dioxide injury greater than the associated effect of light on stomatal opening. It has been reported[113,142] that plants seem more susceptible from midmorning to midafternoon, in spite of a high light intensity that might continue after midafternoon, although plants are more sensitive in the morning during good weather, but may increase in sensitivity if temperature and light increase in late afternoon.[155]

Regardless of the stomatal stimuli--temperature, humidity, and light--plants exhibit a definite diurnal change in sensitivity when exposed to sulfur dioxide under constant conditions in growth chambers. It has been postulated that depletion of photosynthetically derived carbohydrates in leaves during a dark period increases the susceptibility in a later light period.[58]

Edaphic Factors When determining the population at risk of sulfur dioxide injury on the basis of edaphic factors, one must consider both direct and indirect influences. Fertility, moisture, and physical characteristics of soils can directly influence the sensitivity of plants to sulfur dioxide injury.

Plants are most sensitive to sulfur dioxide when there is adequate soil moisture for normal growth.[153] Small changes in soil moisture have little or no effect on plant susceptibility, but a marked increase in resistance occurs when the wilting point is approached.[80,122,167,172] As long as plants are grown with an ample supply of water, they are much more sensitive to sulfur dioxide than plants grown with an inadequate supply, even though the moisture content of the soil is the same at the time of fumigation.[122] Therefore, sudden changes in soil moisture at particular growth stages will probably have little influence on susceptibility to sulfur dioxide injury, although withholding water from some crops during periods of high pollution risk has been suggested.[16] Water balance in the plant is very important in determining susceptibility, and, regardless of soil moisture conditions at the time of exposure, turgid foliage is generally more sensitive than that which is flaccid or near wilting.[122]

Brandt and Heck[16] reported that sensitivity is reduced when plants are grown in heavy soils, compared with sandy ones. This is no doubt related to moisture availability, although heavy soils retain water better than lighter sandy soils. Oxygen

tensions are lower in heavier soils, however, and resistance may be related to this influence.

The resistance of some plants increases in response to fertilization.[40,167] Others, such as Scotch pine, do not respond as well,[113] and results of greenhouse and field fertility experiments involving eastern white pine do not indicate a simple relationship. Increasing nitrogen, phosphorus, and potassium concentrations in the greenhouse increased resistance to needle necrosis in sensitive clones, but did not prevent chlorotic banding in the field.[26]

Nitrogen and sulfur deficiencies were correlated with increased resistance in tobacco and tomato.[92] Similarly, nitrogen and other elemental increases contributed to an increased sensitivity to sulfur dioxide in oats. Conversely, nutrient deficiencies increased sensitivity in alfalfa.[122] Setterstrom and Zimmerman[122] stated that low soil fertility was conducive to greater injury in buckwheat and that the sulfate content of the nutrient supply had no effect on injury. Sulfur dioxide, sulfur, and water have no effect on the nitrogen content of alfalfa. Fertilization of several dicots with a complete fertilizer has been effective in decreasing their sensitivity to sulfur dioxide, but similar treatment of monocots like oats and barley are ineffective.[155,167]

Differences in observed sulfur dioxide-injury responses of plants related to altered fertility can have various causes. There may, in fact, be physiologic differences between monocots and dicots regarding altered snesitivity, but the many conflicting published reports lack useful common denominators. Experimental procedures, treatments, constants, and variables differ among studies, but the results and conclusions of the same reports are often considered as a whole in literature reviews, even to the point of developing "relative susceptibility" rankings by combining results obtained under different conditions.

Other Air Pollutants

A great deal of published information about pollutant effects on plants concerns single compounds such as sulfur dioxide, ozone, and various fluorides, oxides of nitrogen, and hydrocarbons. However, at any given time and location, several recognized "pollutants" may be present, each possibly reacting with the other and acting in concert to exert combined stresses on living organisms. There are conflicting reports regarding the interactions of sulfur dioxide with other compounds, inasmuch as the same mixtures can cause different responses in different species

of plants and different ratios of combined gases can elicit different responses in a given species. Throughout the literature, numerous terms are used to designate exposure conditions, relationships of experimental conditions, and plant responses. Reinert *et al.*[112] referred to the various exposure combinations as follows: "simultaneous" (mixtures of pollutants), "sequential" (one pollutant followed by a second pollutant), and "intermittent" (with some period between sequential exposures). They also designated terms relating plant responses to pollutant combinations: "less-than-additive" (which might be identified as antagonism), "additive," and "greater-than-additive" (which might be considered synergism).

In general, sulfur dioxide combined with low concentrations of nitrogen dioxide (NO_2) causes greater-than-additive effects on plants. Tingey *et al.*[148] observed that foliar injury resulted in tobacco from lower concentrations of each of nitrogen dioxide and sulfur dioxide in combination than from higher concentrations of the gases singly. A similar synergistic effect was observed on enzyme activity in pea seedlings.[69] These same two gases synergistically inhibit the photosynthetic rate of alfalfa, according to White *et al.*[163] White *et al.* also confirmed the observation of Tingey *et al.*[148] that the degree of synergism decreases when the concentrations of the two gases exceed approximately 0.15 ppm. Dunning *et al.*[39] and Matsushima[102] observed greater leaf injury in several crop species due to an apparent synergistic action of sulfur dioxide and nitrogen dioxide than from exposures to the gases singly. The latter also demonstrated the importance of sequential exposures of these two pollutants. If nitrogen dioxide preceded sulfur dioxide, the resulting injury was similar to that from individual exposures to the gases; but if sulfur dioxide preceded nitrogen dioxide, the leaf injury was similar to that caused by synergism of the gases in combination.

Combinations of sulfur dioxide with ozone have produced plant responses ranging from less-than-additive to greater-than-additive. Different plant species do not necessarily respond similarly;[75] and plants of the same species, but in different stages of phenology, do not always respond to mixed pollutants in the same way. Different investigators have observed a greater-than-additive effect of sulfur dioxide and ozone, including Houston[70,71] and Jaeger and Banfield.[76] Needle mottling and early defoliation, associated with the chlorotic dwarf syndrome in eastern white pine, is attributed to a synergistic effect.[34] The earliest published report of sulfur dioxide-ozone synergism is that of Menser and Heggestad,[105] in which tobacco displayed ozone-like injury when exposed to mixtures of sulfur dioxide and

ozone at concentrations below which neither gas alone caused injury. Heagle *et al.*[64] reported that sulfur dioxide alone or combined with ozone (both at 0.10 ppm) had no significant effect on injury, growth, and yields of fumigated soybeans. However, mixtures of ozone and sulfur dioxide synergistically and significantly affected the shoot growth, foliar injury, and leaf abscission of Golden Delicious apple trees.[84] Synergistic effects have also been observed on leaves of quaking aspen, *Populus tremuloides* Michx.[79] Additive, greater-than-additive, and less-than-additive effects of combinations of sulfur dioxide and ozone were observed among 11 plant species.[149] There was additive inhibition of top growth, but less-than-additive inhibition of root growth. But other studies have shown that mixtures of sulfur dioxide and ozone caused greater-than-additive effects on root-growth inhibition in soybean, additive inhibition in tobacco, and less-than-additive inhibition in alfalfa.[147,150] Some have observed less-than-additive effects of sulfur dioxide and ozone mixtures on young, tender Scotch pine needles,[107] but greater-than-additive effects (including mottling and necrosis) on mature, hardened-off needles of dormant Scotch pine seedlings (T. C. Weidensaul and J. H. Brown, Jr., unpublished data).

Only a few reports have been published concerning sulfur dioxide-hydrogen fluoride (HF) interactions. Matsushima and Brewer[103] found additive effects of the two gases on linear growth and leaf area of Koethen orange, but found no synergistic effect of the two gases on chlorosis of Satsuma mandarin foliage. Other investigators studied the combined and singular effects of sulfur dioxide and hydrogen fluoride on several plant species.[66,101] They observed greater-than-additive effects on foliar injury in sweet corn and barley. A more recent review of sulfur dioxide-hydrogen fluoride interactions has been prepared by Weinstein.[159] In this paper, data are presented on foliar injury, growth characteristics, and elemental uptake. It is interesting to note that, in most species studied, fluoride accumulation in leaves is significantly less in the presence of sulfur dioxide. Similarly, sulfur accumulation is decreased in the presence of gaseous fluorides. Great variability was reported in responses among different species, gas concentrations, and other characteristics measured. Greater-than-additive effects have also been reported for sulfur dioxide and hydrogen chloride.[58]

Because stomata serve as the entry points of gases into plant leaves, it is possible that some gaseous compounds are indirectly responsible for the exclusion of others from inside higher plants. Carbon dioxide is known to stimulate stomatal closing. Majernik

and Mansfield[99] found that carbon dioxide continues to induce stomatal closure in the presence of sulfur dioxide. Even in ambient polluted atmospheres where carbon dioxide is mixed with sulfur dioxide and other materials, the carbon dioxide concentrations are sufficiently high to cause partial stomatal closure.

Very little work has been reported on the influence of sulfur dioxide on heavy-metal activity in plants. Krause[87] observed that sulfur dioxide intensified the phototoxicity of zinc and cadmium. When oxide dusts of cadmium, lead, copper, and manganese were applied to leaves, sulfur dioxide influenced neither uptake nor translocation of the cations, but foliar injury attributed to the metals increased, owing to sulfur dioxide.[88]

Two rather comprehensive reviews on pollutant interactions have been prepared.[51,112] It is intended not to duplicate those efforts in this report, but to point out some of the consistencies and inconsistencies apparent in the interactions of sulfur dioxide with other compounds. An understanding of the responses of plants to mixtures of pollutants is important in predictions of effects and particularly important in interpretations of field exposures where sulfur dioxide is a principal but not a sole component of atmospheric pollution.

Factors of Dispersion and Deposition

It is evident that the plant population at risk varies in both spatial and temporal dimensions. Natural and manipulated communities of plants may or may not be subjected to SO_x injury, depending on such spatial factors as climate, SO_x source, topography, and pattern of use. Temporal variability in the population at risk encompasses physiologic activity of vegetation (dormant, vegetative, or reproductive), climate, intensity of SO_x emission, and intended use of vegetation.

The frequency and severity of meteorologic events can certainly influence the population at risk, if for no other reason than by functioning as a collective selection pressure against particular species. Fog, dew, and frost also help to determine which plants are sensitive to SO_x and related compounds, inasmuch as the likelihood of frequent rains is linked to scrubbing of the atmosphere and soil acidification. Fog and dew serve as concentration factors related to aerosol formation and later plant injury.

Topography not only influences pollutant dispersion, but often determines local weather patterns responsible for changes in environmental factors that govern plant sensitivity. Closely related to topography is aspect, or the direction faced by a

slope; some plants and communities can develop normally only on particular aspects.

Some plants, by virtue of the density of stocking (in forests) or planting (of agronomic and horticultural crops), may shade or shield others in the group, thereby affording some protection against injury, because the growth habit alters the microenvironment. Understory vegetation in a forest community, although relatively sensitive to a sulfur dioxide stress, is often not in the population at risk only because it is protected by overstory vegetation. Such protection may be periodic for epiphytic flora in a deciduous forest where their exposure to sulfur dioxide can vary markedly with the season.

The combination of meteorologic and topographic factors that determine the inherent susceptibility of receptors, the exposures to sulfur dioxide, and the environments that affect the receptor's response will necessarily have an influence on the interpretation and prediction of effects. Flemming,[49] Holzworth,[68] and Benedict *et al.*[7] have presented methods and approaches to assess injury or categorize risks of it with reference to probability of emission toxic to plants, as related to frequency of emission sources and fuels consumed, and prediction of atmospheric pollution on the basis of probability of meteorologic events.[120]

Modeling[132] and experimentation[3] have indicated that attention to wind velocity and the existence of boundary layers must be used in the interpretation of experimental exposures. Similarly, field observations must take into account the orientation of monitors relative to receptors and the nature of concentration profiles within irregular canopies.[91]

SO_x AND PRECIPITATION

The interaction of sulfur oxides with precipitation has been studied in Scandinavia for several years. Only recently has research on this subject been emphasized in the United States. The chemistry of precipitation has been investigated far more than the effects of "acid precipitation" on terrestrial ecosystems. Investigators from around the world met in 1975 to address the subjects of atmospheric transport, chemistry, precipitation, and acidic precipitation with respect to aquatic ecosystems, forest soils, and forest vegetation.[35] Much of the discussion on vegetation and soils addressed potential or theoretical effects.

Although some investigators have adduced decreased forest productivity as a result of increased acidity of precipitation,[78]

others have not observed similar responses.[1] Tamm and Cowling[137] indicated that present knowledge of the effects of acidic precipitation on plants is wholly inadequate. Tamm[136] further pointed out that biologic processes are indeed sensitive to acid applications, but that effects of acidic rain are not easily isolated and are superimposed on a highly variable and complex pattern of plant responses to pollutants and other stresses. However, Tamm suggested that, although there is limited published information, it does appear that forest ecosystems, at least in Scandinavia, are affected by acidic rain in the direction of decreased productivity in the long run.

Wood and Bormann[166] actually observed a short-term increase in the productivity of white pine seedlings as the concentrations of sulfuric, nitric, and hydrochloric acids were increased in artifical rain. No differences in growth were induced by rain whose pH was 3.0-4.0. Some investigators have reported that sulfuric acid mist causes a decrease in needle length of pines,[45,93] but some[166] could not demonstrate this phenomenon experimentally.

Very few published accounts have reported on the influence of acidic precipitation on microorganisms or on the epidemiology of infectious plant diseases. Shriner[126] observed that misting simulated rain at a pH of 3.2 produced an 86% decrease in telia production of *Cronartium fusiforme*, a 66% decrease in the reproduction of the nematode *Meloidogyne hapla*, a 10% decrease in bean rust severity caused by *Uromyces phaseoli*, and a 73% decrease in *Rhizobium* nodulation of *Phaseolus vulgaris* and *Glycine max*. He also observed marked erosion of leaf surfaces of *Quercus phellos* and *Phaseolus vulgaris* due to the acidic nature of simulated rain.

Thomas *et al.*[144] reported necrotic spotting of plant foliage by sulfuric acid in concentrations of 30-65 ppm. Evans *et al.*[43,44] concluded that the adaxial leaf surface is most affected after exposure to simulated acidic rain. They observed that injury was first apparent near stomata and at the bases of trichomes of *Phaseolus vulgaris* and *Helianthus annuus* after exposure to a dilute sulfuric acid rain of low pH. Galls due to hyperplasia and hypertrophy of parenchymal cells have been attributed to simulated acidic rain (pH, 2.7-3.4) atomized onto hybrid poplars.[43] Lesions of different types were found on different clones. Very young and older leaves were not as severely affected as those in a stage just before maximal leaf enlargement.

In a study of *Pteridium aquilinum* sperm, Evans and Bozzone[42] detected a 50% decrease in sperm mortality within 2 min of exposure to sulfate (86 μM) in simulated acidic rain. Flagellar

movement was reduced at a pH below 5.8. Fertilization was reduced at a pH below 4.2.

A distinction between managed and unmanaged soils should be made in discussing the effects of acidic precipitation or deposition of sulfur oxides on soils. There appears to be general agreement that managed, agricultural soils are less susceptible to the influences of acidic rain than are unmanaged forest and rangeland soils, because fertilizers increase soil acidity much more than does precipitation. Similarly, liming tends to counter the acidic nature of soils, whether they are acidified by fertilizers or by precipitation.[50,100] Frink and Voigt[50] reported that acidity produced by biologic cycling of nitrogen and sulfur compounds in forest stands exceeds that found in rain and that, unless there is a substantial increase in acidity of precipitation, it should pose no threat to soils of the northeastern United States.

Malmer[100] emphasized that it is not likely that soils are all equally susceptible to changes induced by acidic precipitation. Natural soils with a high pH and base saturation would be most resistant to acidification; those most affected would be the acid soils with hydrated aluminum compounds present, because they have a low buffer capacity. The most adverse effects would be expected in soil types transitional between brown earths and podsols.[164,165]

Ulrich[151] reported that aluminum released by acidified soils could be phytotoxic if acidic rain continued for a long period. The degree of ion leaching increased with decreases in pH, but the amount of cations leached was far less than the amount of acid added.[1] Baker *et al.*[4] found that sulfur dioxide in precipitation increased the extractable acidity and aluminum and decreased the exchangeable bases, especially calcium and magnesium. Although dilute surfuric acid in sandy podsolic soils caused a significantly decreased pH of the leached material, the amount of acid applied (not more than twice the yearly airborne supply over southern Scandinavia) did not acidify soil as much as did nitrate fertilizer.[138] Hutchinson and Whitby[74] observed that acidic rainfall and heavy-metal particulate fallout have caused soils to become toxic to tree seedling establishment and survival near smelters in Canada.

As Tamm stated,[136] soil organisms are sensitive to acid applications. Such increases in acidity as have been discussed above may affect mycorrhizae, nitrogen-fixing bacteria, and other pathogenic organisms in the rhizosphere.

Most experimental research on specific effects of acidic rain on vegetation are based on "artificial rain," and much remains to be determined with reference to the effects of total

acidity and pH in rain on quite complex biologic systems that are influenced by various ions and ionic equilibria normally found in rain, as well as all the factors that affect the responses of plants to the dry deposition of sulfur oxides.

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7 INHALATION TOXICOLOGY: THE EFFECTS OF SULFUR OXIDES ON THE LUNG

This chapter considers recent research on the effects of sulfur oxides on animals, *in vitro* biologic preparations, and human volunteers studied in controlled laboratory settings. Material has been selected for comment with an eye to its potential significance for public health. Some of the material is sufficiently recent to have been presented only at a scientific forum or to have appeared only as an abstract. There is an admitted risk in citing work that may still be evolving and has not been subject to review by peers, as is required for publication by scientific journals. But work in this field is unfolding rapidly, and to impose such criteria would be to exclude important information. For more detailed and inclusive reviews of the subject, the reader is referred to several recent publications.[46,77-79]

A classical means of describing the response of an organism to air pollutants is in terms of dose-response relations. Epidemiologists, as well as toxicologists, use this convention. Ideally, a mathematical expression of dose-response relations is predictive. It permits estimates of the rate at which an effect, presumably adverse, will increase or regress as the dose changes, or estimates of the dose at which the effect will disappear or become so slight as to be deemed acceptable. Unfortunately, the problems inherent in establishing dose-response relations that can be applied with confidence to large diverse groups of individuals are enormous. Epidemiologists face inescapable difficulties in deciding which pollutants to measure, how to ensure that they will be measured adequately, and how to correct for widely different amounts of time spent outdoors, physical activity, or other hazards that may intrude. By contrast, the approaches of toxicologists and clinical investigators are often criticized for being too schematic. Until recently, few have had the resources to mimic community air pollution, even on a modest scale. The toxicologist has had limited success in replicating

models of human lung disease in animals so as to examine the response of more vulnerable elements of the population. Understandably, the clinical investigator must deal with social, ethical, and, of late, increasing legal constraints in attempting to study persons with underlying illness who might be expected to react excessively. Yet all three types of research are needed to develop a comprehensive and coherent view of the hazards posed by air pollution.

What determines dose? A summary answer is that dose is represented by the product of pollutant concentration and time (duration) of exposure--that is, $D = CT$. There is some evidence to suggest that, for a given total dose, high concentrations of sulfur oxides administered over short periods will have greater effect than low concentrations administered over long periods. The evidence is derived from two sources: studies with sulfur dioxide involving healthy subjects (Table 11) and studies of animals that were accidentally exposed to excessive concentrations of the gas

TABLE 11 Changes in Pulmonary Flow Resistance During Exposure to Sulfur Dioxide Alone and to Sulfur Dioxide Plus Sodium Chloride Aerosol[a]

Substance	Concentration (C), ppm	Duration (T), min	CT, ppm-min	Pulmonary Flow Resistance (R_L)[b]	
				Control, cm H_2O/L/s)	Exposure, % change
SO_2	1.0[c]	120	120	1.25 ± 0.50	+6 ± 29
	4.2[c]	30	126	1.09 ± 0.41	+27 ± 21
	15.8[d]	10	158	1.37 ± 0.34	+191 ± 217
SO_2 + Nacl[e]	1.0	120	120	1.45 ± 0.55	-6 ± 57
	5.2	30	156	1.43 ± 0.34	+10 ± 15
	14.8	10	148	1.73 ± 0.66	+118 ± 103

[a] Derived from Charles *et al.*[26]
Data compiled from two studies carried out in same laboratory to provide roughly similar total doses (CT). Number of subjects in each mode, 6.

[b] Mean ± SD.

[c] Data from Frank *et al.*[38]

[d] Data from Frank *et al.*[39]

[e] Aerosol administered as dry particle at about 50% relative humidity.

during the course of chronic exposure.[4] It is conceivable that for sulfur oxides, in contrast with pollutants that accumulate in the body, mean ambient concentrations are less significant as an index of hazard to health than the variations--or peak concentrations--that occur around the mean. This postulate can be tested experimentally. If shown to be true, it would underline the importance of short-term standards.

Biologic factors affect dose in several ways. For example, at a given ambient concentration of pollutant, the degree of exposure will vary with the degree of activity. A bicyclist or jogger is at greater risk than a seated person. The often strenuous activity of children may contribute to their vulnerability to air pollution.[37,64,68] With exercise, ventilation per unit time is increased. In addition, the sites and rates of transfer of the pollutant in the respiratory system are likely to change, owing to accelerated rates of air flow in the upper and central airways. Evidence has been adduced that the fractional uptake of such gases as sulfur dioxide by the upper airways decreases as inspiratory flow rate increases; penetration to the lower airways is augmented. Exercise might therefore be expected to initiate or aggravate the effects of sulfur oxides on the lung, as it does the effects of ozone.[17] These expectations are borne out in preliminary findings on healthy volunteers exposed to a mixture of sulfur dioxide and an aerosol of sodium chloride, both at rest and during moderate exercise.[73] Clinical studies combining exercise with exposure to sulfur oxides are under way in several laboratories. Few studies incorporating exercise or hyperpnea have been carried out on animals.

The structural and functional attributes of the respiratory system also determine dose. Variations in dimensions of the airways and parenchyma among subjects and among species may lead to distinct patterns of deposition of inhaled particles. The rate at which the parenchyma and airways of healthy people and animals are cleared of particles may vary.[79,102] The clearance rate varies considerably among, but not within, individuals; this implies consistent differences in the normal population in dose from retained particles.

In particular, airway or parenchymal disease is likely to affect the distribution of inhaled pollutants in the lung, as well as to affect the local rates of clearance of relatively insoluble particles. As a consequence, some regions may become "hot spots." The increased vulnerability of patients with asthma, bronchitis, or emphysema to air pollution may reflect in part the effect of intensified regional exposure on preexisting defects. Additional research into the biologic factors affecting dose in healthy and abnormal lungs is critical. The results should cast light on the

determinants of risk among individuals and might also be turned to use in prophylaxis.

Perhaps most physiologists would agree that the reflex bronchoconstriction caused by sulfur dioxide is a form of dysfunction or adverse effect. But the question may be asked whether an isolated change in ventilatory pattern during an exposure or a biochemical response that may also be elicited by a variety of nonspecific stimuli is to be judged adverse. The biologic significance of an effect should receive consideration. Some investigators may be inclined to devote more attention to the refinement of methods for detecting effects than to weighing their importance. Among the considerations that might receive focus are the following:

- Is a particular effect smaller than the normal variations of that measurement that occur daily, weekly, or seasonally?
- Is it perceived by the subject (not necessarily, of course, a test of importance)?
- Is it evoked at rest, with moderate activity, or only through extreme effort?
- Does it lead to secondary effects that may have important consequences, or is it an isolated phenomenon?
- Does it persist, increase, or diminish during continued exposure; how long does it persist after the end of exposure?
- Does it tend to recur with equal intensity, diminish, or worsen on repeated exposure?

Some attempt should be made by the investigator to assess the biologic importance of the changes produced experimentally, even though speculative and subject to revision. Whether all effects--or, more precisely, responses--are to be proscribed by government regulators will depend in great measure on judgments provided by scientists.

SULFUR DIOXIDE

Respiratory Uptake

The notion that ordinary concentrations of sulfur dioxide alone are not likely to injure the lung is commonplace. This is not to imply that functional changes may not be produced, inasmuch as evidence of airway narrowing has been found in a few subjects exposed to sulfur dioxide at 1 ppm or less[16,18,39,63] and in animals exposed to only 0.26 ppm.[11] Instead, this judgment is based on two strong lines of evidence:

- The gas is so soluble in the mucous lining of the airways that only a small fraction, less than a few percent of the inspired concentration, penetrates farther than the larynx, especially during quiet breathing.[16,41,94] (The nose is a more efficient scrubber of sulfur dioxide than the mouth. With increasing activity, as in exercise, a person switches from nasal to oral breathing and loses some of this protective sorption. Rodents, which are frequent subjects for these experiments, are said to be obligatory nose-breathers.)
- Long-term exposures of animals, including subhuman primates, have generally been unassociated with adverse effects when the concentrations ranged up to about 5 ppm.[3-5] A possible exception to this statement is found in a study of beagles exposed to sulfur dioxide at 5 ppm for 225 days (other groups of beagles were exposed to sulfuric acid or to the combined pollutants); the animals were reported to have higher pulmonary flow resistance and lower compliance than animals exposed to sulfuric acid alone at 755 ± 362 $\mu g/m^3$.[66] However, the report is marred by deficiencies in details of the functional measurements and the results, so the conclusions cannot be assessed properly.

A preliminary attempt at modeling the uptake of sulfur dioxide in the tracheobronchial system during a single breath suggested that removal of the gas from the airstream is virtually complete before the bronchioles and parenchyma are reached.[71] On the basis of the computer model, any sulfur dioxide entering the trachea might be expected to act principally on central and intermediate airways. Whether the mucous lining of the upper airways eventually becomes saturated with sulfur dioxide during frequent or continuous exposure is unknown. In studies of the fractional uptake of 25-50 ppm administered for 30 min at a time to the surgically isolated upper airways of dogs[41] and of 25 ppm administered for 6 h to human subjects breathing quietly by nose,[16] there was little or no change with time. A question that has not been investigated is whether a droplet aerosol that is mixed with sulfur dioxide in ambient air can alter the site(s) of transfer of the gas in the respiratory system. Among the factors affecting the solubility of sulfur dioxide in the droplet are temperature (solubility and temperature are inversely related), hydrogen ion concentration (solubility and hydrogen ion concentration are inversely related at pH values below neutrality), and ammonia, which is typically found in trace concentrations in ambient air and in significantly higher concentrations in the upper airways of human adults[60] (solubility and dissolved ammonia are directly related).

Biochemistry

Not all sulfur dioxide absorbed by the mucous lining is retained by the body. A small fraction, estimated at about 12%, is desorbed and eliminated with the next exhalation.

Within minutes of the onset of exposure of the surgically isolated upper airways of dogs to [^{35}S]sulfur dioxide, sulfur-35 is detectable in blood. A fraction of this sulfur-35 is physically dissolved gas that diffuses out of the pulmonary circulation into the parenchymal air spaces.[42] Thus, a mechanism exists for exposure of the periphery of the lung that is not ordinarily reached by the sulfur dioxide in inspired air. However, the amount of gas reaching the peripheral tissues from the pulmonary circulation is small, and its importance uncertain.

Information about the chemical fate of the retained gas is expanding. Sulfur dioxide reacts with water to form sulfurous acid, H_2SO_3, a weak acid that dissociates into hydrogen, H^+; sulfite, SO_3^{2-}; and bisulfite, HSO_3^-, ions. The relative concentrations of sulfite and bisulfite ions in aqueous solution depend on pH. The ratio of bisulfite to sulfite ions is about 10^6:1 at a pH of 1, about 10^3:1 at a pH of 4, and about 1:1 at neutrality.

Sulfites, whether ingested or formed from inhalation of sulfur dioxide, react with disulfide bonds (R—S—S—R) in plasma proteins to form thiosulfonates:[47]

$$\underset{\text{disulfide}}{R{-}S{-}S{-}R} + SO_3^{2-} \qquad R{-}S{-}SO_3^- + RS^-. \quad \underset{\text{thiosulfonate}}{}$$

An enzyme, sulfite oxidase, which has been identified in man and a variety of experimental animals,[48] catalyzes the oxidation of bisulfite to sulfate, SO_4^{2-}. Apparently, sulfate is freely diffusible and nontoxic. After exposure to radiolabeled [^{35}S]-sulfur dioxide, the kidney becomes a major avenue of excretion of sulfur-35, chiefly as inorganic sulfate.[103]

Sulfur dioxide sulfites react with a variety of alveolar constitutents.[82] (See section on mutagenesis and carcinogenesis.) Their reaction with and breakdown of thiamine in the cells of the respiratory tract may impair carbohydrate metabolism locally. The conversion of sulfites to sulfates probably acts to protect tissues and to confine the effects of inhaled sulfur dioxide to the respiratory system.

It has been shown that the rate at which sulfite is transformed varies among species, and it may be a factor determining risk.[48] Man appears to oxidize sulfite more rapidly than do rabbits.[49] There has been one report of a deficiency of sulfite

oxidase in a person, which led to neurologic disorder and death.[75] If rats are rendered deficient in sulfite oxidase, the lethal dose of intraperitoneally injected bisulfite is reduced, and survival after exposure to sulfur dioxide at 925 ppm or higher is shortened.[30]

It is speculative which ion is more hazardous, sulfite or bisulfite. Alarie[1] postulated that the sensory irritation and stimulation of nerve endings in the respiratory system are due to the reaction between sulfite or bisulfite ions and the disulfide bonds present in the receptor sites of the nerve endings. With coworkers, Alarie[6] compared the ventilatory response of mice to aerosols of sodium sulfite and sodium metabisulfite and concluded that the bisulfite ion formed in the slightly alkaline pH of the nasal mucosa was responsible for sensory irritation. Both sodium metabisulfite and sulfur dioxide caused a decrease in respiratory frequency, whereas sodium sulfite had no effect.

It has been suggested by Eatough and associates that stable and biologically potent sulfite complexes may form in aerosols containing Fe^{3+} or Cu^{2+}. They have developed a technique of thermometric titration to distinguish reduced metallic complexes (sulfur IV) from sulfates (sulfur VI) in samples obtained in the vicinity of copper and lead smelters, a steel mill, and urban regions considered to be unaffected by these industrial activities.[33,52,91] The concentrations of sulfite by weight were about 2% in the smelter plumes, about 1% in the steel-mill plume, and about 0.2% in a single sample obtained from New York City. These concentrations are low, compared with those used experimentally in mice,[6] but they probably exceed by several orders of magnitude the amounts of sulfite and bisulfite that are formed in droplet aerosols in the presence of low ambient concentrations of sulfur dioxide, as in the experiment of McJilton *et al.*[70] Additional toxicologic research on this family of compounds, and on the closely related role of hydrogen ion concentration, is needed.

Animal Toxicology

Acute Exposures If mice are exposed to sulfur dioxide at 17 ppm or higher, they respond with a reduction in respiratory frequency.[1] Despite continuing exposure, the response is limited to about 3-10 min, becoming more prolonged as the concentration increases. With repeated exposures, the response disappears entirely. The change in frequency has been attributed to irritant stimulation of the fifth cranial nerve endings in the upper airways. Mice are said to be virtually incapable of bronchoconstriction, presumably owing to a paucity of bronchial smooth muscle (Y. Alarie, personal communication).

Other common species of laboratory animals--including guinea pigs, cats, dogs, and monkeys--respond to sulfur dioxide inhalation principally with narrowing of airways. The narrowing is reflected in an increase in flow resistance. A reduction in dynamic compliance, which is probably secondary to the uneven distribution of ventilation associated with the changes in flow resistance, may also occur. The change in flow resistance may involve the upper airways (nasopharynx), the tracheobronchial system, or both. The cause may be mucosal swelling, excessive or retained mucous secretions, or smooth muscle constriction. The bronchoconstriction has been shown in cats and healthy people to be mediated by the vagal nerves, and it can be abolished by section of these nerves or by administration of atropine.[76] It has been hypothesized that the sensory or afferent arc of this reflex may be in the nasopharynx, at least in human subjects, and that a nasobronchial reflex is triggered that leads to bronchoconstriction. In cats[96] and rabbits,[8] irritation of the nasal mucosa is associated with bronchodilatation, rather than bronchoconstriction. An additional possible basis for bronchoconstriction is the direct action of humeral agents, released from injured tissues, on airway musculature. These include slow-reacting substances (SRS), histamine, serotonin, and prostaglandins.

The increase in flow resistance observed in guinea pigs may persist during an exposure to sulfur dioxide lasting several hours;[10] in other animal species, the response to similar concentrations of gas may reach a peak and begin to subside within a much shorter period.[31,40] The basis for variations in the course of response is unknown and may be related to the mechanism of response. Responses that are mediated reflexly are likely to appear and subside more rapidly than are those mediated through the release of hormones or enzymes. With respect to the timing of response, the results in healthy volunteers are equivocal. In one study, pulmonary flow resistance rose and then began to subside after about 10 min during continuous exposure to the gas;[38] in a more recent study,[16] both the volume of gas forcibly exhaled after 1.0 s ($FEV_{1.0}$) and the forced expiratory flow rate during the middle half of the expired volume ($FEF_{25\%-75\%}$) decreased progressively during 4-6 h of exposure (Figure 23). The functional measurements used in both studies of human subjects reflect airway caliber, although the flows generated during forced expiration are affected by additional factors as well.

Amdur[11] reported that a mean sulfur dioxide concentration of 0.26 ppm (range, 0.03-0.65 ppm) increased flow resistance in unanesthetized guinea pigs by 12.8% ($p < 0.001$); it is the lowest mean concentration reported to have this effect. Another

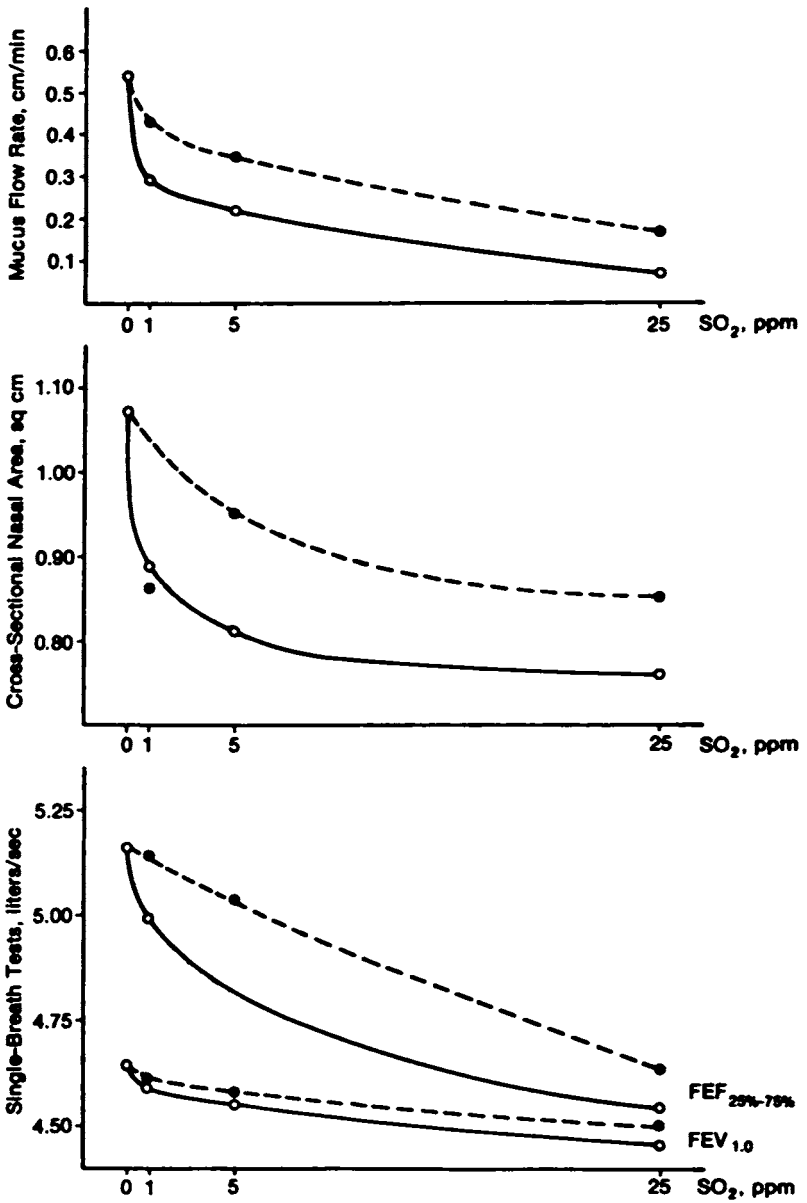

FIGURE 23 Dose-response relationship between SO_2 and mucus flow rate at slit 3 to 4, cross-sectional nasal area, and $FEF_{25\%-75\%}$ and $FEV_{1.0}$. Dotted lines represent 1-3 h exposures; full line, 4-6 h exposures. Reprinted with permission from Andersen *et al.*[16]

investigative team found no consistent change in the same measurement made in lightly anesthetized guinea pigs during 1 h of exposure to 1 ppm.[69] The animals used in the two studies were from different suppliers. In general, concentrations substantially higher than 1 ppm have been necessary to evoke increases in flow resistance in other species of anesthetized animals.[31,40] It is possible that even light anesthesia, as gauged by changes in respiratory frequency, may blunt the response to sulfur dioxide. Alternatively, untrained, restrained, and fully awake animals, may, depending on their surroundings, become apprehensive and struggle; when this happens, the variation in the measurement is likely to increase, and the response to the pollutant may be affected as well.

A subject of research that has received little attention concerns the question of whether realistic concentrations of sulfur oxides may induce changes in bronchial reactivity. Islam *et al.*[57] reported that anesthetized, intubated, spontaneously breathing dogs exposed to sulfur dioxide at 1, 2, 5, and 10 ppm for 1 h thereafter manifested increased reactivity to acetylcholine, a bronchoconstrictive agent. To assess bronchoconstriction, esophageal pressure was measured and expressed with respect to tidal volume. The maximal increase in pressure excursions occurred after sulfur dioxide at 2 ppm; 10 ppm caused less change than 1 and 5 ppm. In general, the maximal response to acetylcholine occurred 1-3 h after exposure to sulfur dioxide.

Changes in respiratory frequency and tidal volume were erratic; these changes would be expected to affect the dosage of acetylcholine independently of any underlying change in bronchial reactivity attributable to sulfur dioxide and to affect the measurement of esophageal pressure independently of any change in airway caliber. Moreover, from the description provided of the method of measuring esophageal pressure and tidal volume, it does not appear that a distinction could be made between changes in flow-resistive and elastic behavior of the lungs. Conclusions about the degree of bronchoconstriction that occurred appear unjustified.

In discussing the minimal changes in reactivity to acetylcholine seen after sulfur dioxide at 10 ppm, the authors postulated that this highest concentration may have induced a thick film of mucus over the surface epithelium that protected underlying sensory receptors. The question of whether sulfur oxides alter epithelial reactivity to bronchoconstrictive agents--whether they are drugs, allergens, or other pollutants--remains to be answered.

Chronic Exposures Reference was made earlier to the studies of Alarie *et al.*[3-5] in which cynomolgus monkeys and guinea pigs were

subjected to prolonged exposure to sulfur dioxide alone at 0.1-5 ppm, without evidence of functional impairment of or histologic damage to the lung. The latter concentration is over 160 times the annual primary standard. It might be argued that these studies did not use the most refined or appropriate techniques of analysis. Nonetheless, this absence of adverse findings fits the thesis that only a small fraction of sulfur dioxide penetrates beyond the upper airways and that the effects of the gas during acute exposures, particularly at this range of concentrations, are slight and evanescent, rather than cumulative.

Lewis *et al.*[67] did report finding a statistically significant change in the single-breath nitrogen-washout curve, indicative of a defect in distribution of ventilation, in a group of four beagles that had subsisted for 620 days in an environment containing sulfur dioxide at 13.4 mg/m^3 (~5 ppm). Respiratory mechanics, lung volumes, and diffusing capacity were unaffected. The same prolonged exposure appeared to have no harmful effect on another group of four beagles whose lungs had been "previously impaired" by exposure to nitrogen dioxide, NO_2, at 26 ppm for 191 days. The authors drew the conclusion "that lungs previously remodeled by a toxic agent are less likely to be altered physiologically by subsequent low-level airborne toxicants than those which have not been exposed." This hypothesis predicts, perhaps paradoxically, that some forms of permanent injury may protect the lung against later exposure to pollutants.

Pulmonary Clearance: Resistance to Infection There has been long-standing interest in the effect of sulfur dioxide on mucociliary clearance and resistance to infection. In general, short exposures have had little or no depressive effect on the frequency of ciliary beating, clearance of inanimate particles, or resistance to infection, unless the concentrations of sulfur dioxide were far higher than those found in community or occupational settings. The increased susceptibility to infection reported in rodents[34,65] may be a consequence of the injury to the nasopharyngeal tissues caused by the sulfur dioxide. Within 24 h, sulfur dioxide at 10 ppm may produce edema, necrosis, and desquamation of the respiratory epithelium, which is most severe in the region of the nasomaxillary turbinates.[45] In some instances, when a wide range of concentrations of sulfur dioxide has been studied, the lower concentrations have acted to accelerate bronchial clearance. An example is the study by Spiegelman *et al.*[95] in which donkeys were exposed to sulfur dioxide at 25-713 ppm through nasal catheters for 30 min. The lowest concentration was associated with accelerated bronchial clearance in one animal; there was no detectable change for the group between 53 and 300

ppm, and clearance was depressed at the highest concentrations. This biphasic pattern of response has also been noted in donkeys with low and high concentrations of cigarette smoke.[7]

Prolonging the exposure may lower the concentrations necessary for an effect on clearance. In the study by Ferin and Leach,[36] groups of rats were first exposed to sulfur dioxide at about 0.1, 1, or 20 ppm for 7 h/day, 5 days/week for a total of 10-25 days and thereafter exposed to an "inert" aerosol, titanium dioxide, TiO_2 (about 15 mg/m^3; mass median aerodynamic diameter, 1.5 μm; geometric standard deviation, 3.3). The amount of titanium dioxide retained in the lungs 10-25 days after the exposure, described as an index of "integrated alveolar clearance," was compared with that of control lungs. Sulfur dioxide at 0.1 ppm accelerated alveolar clearance measured after 10 and 23 days. Sulfur dioxide at 1 ppm also accelerated clearance after 10 days, but had no significant effect by the eighteenth and twentieth days and decreased the clearance measured on the twenty-fifth day. The results imply a complex response to sulfur dioxide that is delayed until weeks after exposure ends and may be biphasic: clearance is stimulated early, with a crossover on days 18 and 20, and depressed by day 25. The depression has a rather sharp threshold, being between 0.1 and 1 ppm.

The findings of Ferin and Leach are perhaps unexpected, especially inasmuch as many components of the clearance system have been shown to withstand massive concentrations of sulfur dioxide during a single exposure. The authors argued from their own results that, for the same total dose, repeated or extended exposure to a lower concentration of sulfur dioxide is more damaging to the process of clearance than is brief exposure to a higher concentration. The opposite may be said to typify changes in pulmonary structure and function in response to sulfur dioxide, which appear to be influenced more by concentration then by total dose.[4] It is reasonable to maintain that at present there is no basis for expecting "saturation" of the more proximal mucous lining of the airways at the doses of sulfur dioxide administered to these rats, that would culminate in increased exposure of alveolar tissues. The study of Ferin and Leach is provocative, but has elements of paradox. Attempts to confirm or illuminate the results are to be encouraged.

An earlier study by Fraser *et al.*[44] adduced no evidence of changes in ciliary-beat rate or relative number of alveolar cells laden with dust in rats after exposure to sulfur dioxide at 1 or 3 ppm plus graphite dust (median diameter, 1.5 μm) at 1 mg/m^3 for periods up to 119 consecutive days.

A study by Hirsch *et al.*[55] suggested that mucus clearance in the central airways may be particularly vulnerable to sulfur

dioxide. They exposed purebred beagles for 12 months to sulfur dioxide at 1 ppm (1.5 h twice a day, 5 days/week). At the end of the exposure, there was evidence (obtained with a bronchofiberscope) that tracheal mucus velocity was lower in these animals than in a small group of control animals. The two groups were not statistically different in respiratory mechanical function and gas exchange. The animals were studied only once, 24 h after the final exposure; apparently, it is not known when the change may have occurred, assuming that the two groups of animals were identical at the outset. How long the change might have persisted after the end of exposure was unreported. Such tentative findings warrant more rigorous study.

An indication that chronic exposure to sulfur dioxide may alter immunologic responses is found in the study of Zarkower.[104] Sulfur dioxide administered to mice at 2 ppm alone or in combination with carbon dust for periods up to 192 days produced complex and variable changes in antibody formation measured in lymphoid cells. The effect could be stimulative or suppressive, depending on the duration of exposure, the regional source of the lymph nodes, and whether carbon particles (mass median diameter, 1.8-2.2 μm; concentration, unspecified) were combined with the gas. The effects seen when sulfur dioxide and carbon were administered, separately were often similar, and their mechanisms were considered "puzzling." It remains unclear how these effects may be related to resistance to pulmonary infection or to the development of allergic sensitivity.

SULFUR-CONTAINING AEROSOLS

Among the factors likely to influence the biologic effect of an aerosol are its molecular composition, mass and molar concentrations, size, shape and density (factors incorporated in the term, aerodynamic size), solubility, and perhaps pH. The concentrations of droplet aerosols used in inhalation toxicology are usually expressed in units of mass, rather than moles. A less common practice has been to report the molar concentration of the solution from which the aerosol is generated. Paradoxically, the concentration of the parent solution influences the size of the particle, but not its molar concentration in air, once equilibrium is established at the ambient temperature and relative humidity. These relations among size, molar concentration, temperature, and relative humidity are modified somewhat by surface tension for very small particles.

Experimentally, particles as diverse as inert dusts, radionuclides, and pharmacologically active drugs have been administered

to test animals and human volunteers. In this section, the emphasis is on sulfur-containing particles, especially those containing sulfite, bisulfite, or sulfate in ionic or nonionic states. The sulfur-containing particles in ambient air are not necessarily pure compounds. They may include contaminants that either have an independent potential for toxicity, such as lead or cadmium, or are capable of oxidizing the sulfur that is present to sulfuric acid.

The three principal sulfate compounds formed in ambient air by the oxidation of sulfur dioxide are sulfuric acid; ammonium bisulfate, NH_4HSO_4; and ammonium sulfate, $(NH_4)_2SO_4$. The latter two are products of the reaction of ammonia, NH_3, with sulfuric acid. The physical processes by which particles form in the atmosphere and their size distribution are illustrated schematically in Figure 24. Sulfate-containing particles attributable to sulfur dioxide occur principally in the accumulation mode, in the size range of about 0.1 to 2-3 μm in mass median diameter (MMD). At a relative humidity of 50%, they have the following approximate pH values: sulfuric acid, <1; ammonium bisulfate, 1-2; and the ammonium sulfate, 5-6.

Animal Toxicology

Acute Exposures The biologic effects of acute exposures to sulfur-containing aerosols are as follows:

- *Sulfuric Acid*: One source of environmental sulfuric acid is the catalytic converter designed to reduce emission of carbon monoxide and hydrocarbons from cars. These catalysts oxidize the sulfur in gasoline to produce an ultrafine aerosol of sulfuric acid. Although such an aerosol might be expected to pose a particular hazard to the periphery of the lung for aerodynamic reasons,[79] a number of factors act to limit its concentration in ambient air. For example, ultrafine particles, like gas particles, disperse rapidly by diffusion; this dispersion is increased by the turbulence associated with moving traffic;[29] and the likelihood that the particles will grow in size by coagulation increases with their concentration. (The upper limit for toxicologic experimentation is about 100-200 $\mu g/m^3$, depending on size distribution and residence time in the ducts and chamber.) Original predictions of the amount of sulfuric acid that would be produced by the platinum and palladium catalysts in the converters have not been borne out. Apparently, less sulfur is oxidized to sulfuric acid than had been predicted.[20] In addition, for reasons just cited, the concentration of sulfuric acid that is produced decreases rapidly with distance and height.[26]

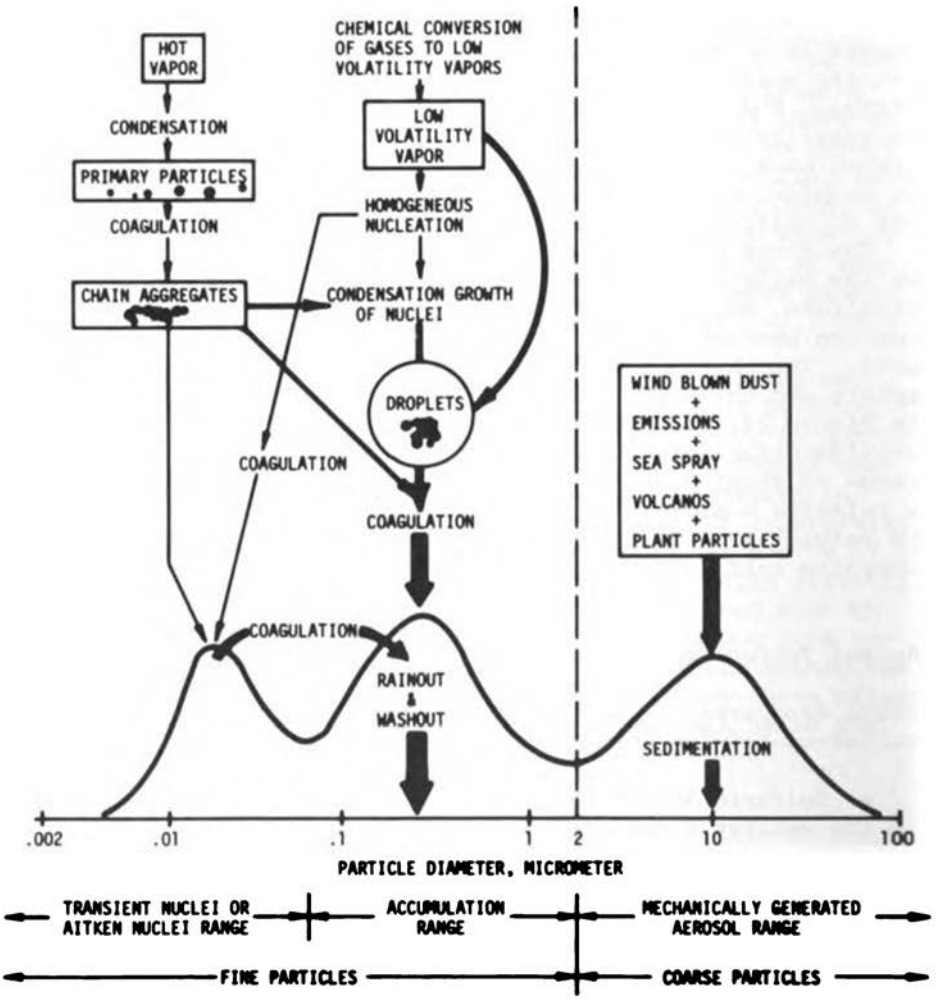

FIGURE 24 Schematic of a trimodal atmospheric aerosol size distribution, showing the principal modes, main sources of mass for each mode, and principal processes involved in inserting mass and removing mass from each mode. (The mode extending from approximately 0.005 to 0.1 μm is also referred to as the ultrafine or nuclei mode. The mode extending from approximately 0.1 to 2 μm is referred to as the accumulation mode.) Reprinted with permission from Whitby.[100]

For any specified concentration of sulfuric acid, the ultrafine particles might be expected to be highly irritating to the respiratory system, for several reasons: they are deposited at a higher rate than particles in the accumulation mode, particularly in small airways and air spaces, owing to their more vigorous Brownian motion; they are more numerous; and they have a greater surface area per unit volume. However, ultrafine particles of sulfuric acid may be more effectively neutralized by the gaseous ammonia in the upper airways than are larger particles of the acid, and this is likely to render them less irritating. The role of respiratory ammonia is considered later in this chapter. There is a scarcity of information on the comparative biologic effects of ultrafine and accumulation modes of sulfuric acid (Figure 24). In an unpublished study of lightly anesthetized guinea pigs, the changes in respiratory mechanics, compared with those seen during sham exposures, were small and did not differ between modes for a concentration of about 100 $\mu g/m^3$. The size distributions were as follows: MMD, ~0.04 μm, and σg, ~1.5; and MMD, ~0.6 μm, and σg, ~1.5. In any event, it appears reasonable to predict that whatever hazard posed by the ultrafine particles is likely to be confined to the interior of cars or to highways and adjacent areas where concentrations are likely to be maximal.

Amdur has ranked the relative irritancy of a number of sulfate-containing particles administered to guinea pigs at roughly comparable size and mass concentration.[11] She found that sulfuric acid and zinc ammonium sulfate, $Zn(NH_4)_2(SO_4)_2$, which is not ordinarily present in community air, provoked the greatest changes in pulmonary flow resistance, indicative of bronchoconstriction. Recently, Amdur *et al.* reported finding an almost rectilinear relation between the concentrations of sulfuric acid and the increase in pulmonary flow resistance.[13] The average increase for sulfuric acid at 50 and 150 $\mu g/m^3$ was slightly over 10%, and for 1,000 $\mu g/m^3$, over 70%. Aerosol size was reported as 1 μm; exposure lasted 1 h. It should be noted that ambient concentrations of sulfuric acid plus ammonium bisulfate (accumulation mode) of about 10-20 $\mu g/m^3$ have been observed in this country[28] and in Europe.[23]

In a study by Frank *et al.*[43] on lightly anesthetized guinea pigs, as yet unpublished, sulfuric acid concentrations of 100, 350, and 700 $\mu g/m^3$ were found to cause no significant increase in flow resistance. However, dynamic pulmonary compliance did tend to decrease during the exposure to 700 $\mu g/m^3$; this is consistent with an effect in the peripheral airways or parenchyma. The experimental preparation was similar to that of Amdur and co-workers (again, however, the animals were obtained from different sources);

exposure also lasted 1 h; the MMD was 0.7 μm (geometric standard deviation, or σg, 1.5) at a relative humidity of 70%. Additional work is clearly needed to resolve the question of dose-response relations in the guinea pig, a test animal that plays a prominent role in inhalation toxicology.

Sackner and co-workers[87] extended observations on the acute effects of sulfuric acid on ventilation, lung volume, and respiratory mechanics to dogs and sheep. Their intention was to test the effects of a particle diameter equivalent to that produced by the catalytic converter. However, the concentrations of 1,000 and 7,000 $\mu g/m^3$ that were generated were high enough to encourage significant coagulation and growth of the particles, so the size distribution of the inhaled particles may have been more typical of the accumulation mode. Exposure to sulfuric acid at 1,000 $\mu g/m^3$ for 10 min caused no changes in total respiratory flow resistance, static lung compliance, or functional residual capacity; 15 min after exposure to 7,000 $\mu g/m^3$, total respiratory conductance, the reciprocal of flow resistance, was reduced by 14% ($p < 0.05$) for a period of 15 min. Brief exposure to 1,000 $\mu g/m^3$ caused no change in tidal volume or respiratory frequency in conscious sheep. An earlier study[14] was cited in which healthy human subjects had shown rapid and shallow breathing during 15 min of exposure to sulfuric acid at 350-5,000 $\mu g/m^3$ (mean particle diameter, 1 μm).

Insofar as sulfuric acid (or any other irritant) alters respiratory frequency, tidal volume, mechanical function, or distribution of inhaled gas (all of which may affect either gas flow or the dimensions of airways and air spaces), secondary changes in the fraction of inhaled aerosol deposited in the respiratory system and in the site(s) of deposition may also be expected. Fairchild *et al.*[35] observed a change in the site of deposition of a radiolabeled streptococcal aerosol in mice after the administration of sulfuric acid at 30 $\mu g/m^3$ (count median diameter, or CMD, 0.25 μm), reflected in a slight shift from the parenchyma to the trachea. There were no changes in respiratory frequency, tidal volume, or minute ventilation during exposure to either aerosol. However, the same group found no change in the pattern of deposition produced by a tenfold increase in concentrations of sulfuric acid to 320 $\mu g/m^3$ (CMD, 0.6 μm). This apparent discrepancy was unexplained.

It should be noted that functional attributes other than ventilation and respiratory mechanics, including those which implicate biochemical systems, may be affected independently. Recently, Schlesinger and co-workers[88] observed a depression in bronchial clearance after exposure to sulfuric acid in the absence of any change in mechanical function. This dichotomy occurred in three

of four donkeys after administration of sulfuric acid at 194-1,364 $\mu g/m^3$ (aerometric median diameter, or AMD, 0.3-0.6 μm; σg, 1.5) for 1 h. The effect on bronchial clearance was progressive in one animal over the course of exposures. Dynamic compliance, pulmonary flow resistance, and the pattern of regional depositon of a radiolabeled insoluble aerosol were unchanged. (The results with ammonium sulfate in the same animals are described below.)

Theoretically, sulfuric acid might be expected to provoke a greater response in the respiratory system than either ammonium bisulfate or ammonium sulfate, owing to its lower pH. However, according to a recent hypothesis, the release of ammonia by the respiratory system may mitigate the effects of inhaled acid sulfates through partial or complete neutralization.[60] The highest concentrations of ammonia are in the oral passage, probably owing in great measure to both aerobic and anaerobic bacteria that are disposed around teeth and on the surfaces of the tongue and buccal mucosa. (To date, the principal site of ammonia production has been established only in human subjects.) The lower concentrations of ammonia encountered in the tracheobronchial system and parenchyma appear to be determined by blood ammonium ions. Concentrations ranging from 29 to about 2,200 $\mu g/m^3$ in the exhaled air of healthy adults have been found during mouth-breathing[56,60]--values several orders of magnitude greater than those in ambient air. Stoichiometrically, ammonia at 1 $\mu g/m^3$ can convert sulfuric acid at 5.8 $\mu g/m^3$ to ammonium bisulfate and at 2.9 $\mu g/m^3$ to ammonium sulfate.

To what extent inhaled sulfuric acid particles are neutralized before their deposition on the tissue surfaces is undetermined. The rate at which neutralization occurs should be influenced by several factors, including the relative concentrations of acid aerosol and ammonia, the relative humidity, and the time spent by the particle in the ammonia-rich atmosphere.

Figure 25 provides an estimate of the time required for neutralization of sulfuric acid at 20 $\mu g/m^3$ in an environment containing ammonia at 143 $\mu g/m^3$ (200 ppbv). Note that the rate of neutralization is inversely related to particle size. On this basis, one would predict that the larger the particle, the less likely it would be to undergo complete transformation before impacting on a mucosal surface, and, consequently, the greater would be its irritant effect.

Although this expectation is not borne out by the experimental observations of Amdur *et al.*[9,13] in which mechanical function was the measure of response, it is consistent with the study of Pattle and Cullumbine,[80] who found that 2.7-μm MMD particles of sulfuric acid were more lethal than 0.8-μm MMD particles for

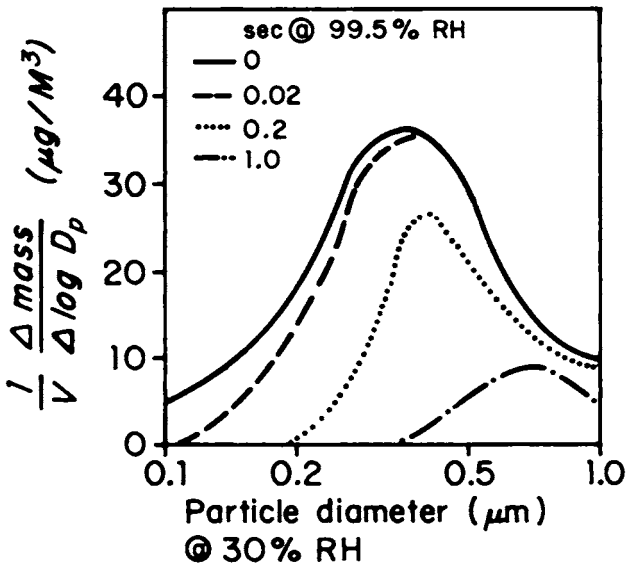

FIGURE 25 Theoretical sulfuric acid aerosol mass distribution at various times during the aerosol's neutralization by ammonia. The reaction was assumed to occur at 99.5% relative humidity. V = volume of air; D_p = diameter of particle. Reprinted with permission from Larson *et al.*[59]

guinea pigs. Of course, differences in aerodynamic size also affect the degree and loci of particle deposition--a complicating factor that may confound such a prediction. The following quotation from an article by Cullumbine *et al.*[32] may have pertinence:

> Quite early in this work it was noticed that fluctuations of the acid content of the mist occurred and these could be traced to the ammonia evolved from the faecal droppings and urine of the animals. These fluctuations could be prevented by keeping the animals on a wire mesh floor above a tray containing 10 percent sulphuric acid. The possibility of obtaining anomalous results without such precautions seems to have been overlooked by previous workers. We noticed, in fact, that enough ammonia could be generated from the excreta of the animals to neutralise an otherwise lethal concentration of acid mist. In

conformity with this we found that when ammonium carbonate was placed in the chamber, so that there was always an excess of ammonia present, and acid mist was supplied, which in the absence of ammonia would have caused 75 to 90 percent deaths, there were no fatalities and the guinea pigs after the experiment were macroscopically and microscopically normal. This would suggest that if sulphuric acid were the major toxic agent in a polluted fog, the latter could be rendered harmless by adding to it sufficient ammonia to neutralise the acid.

This suggestion that the ammonia in the droppings might have protective effect may partially explain why the pigs and sheep were unaffected at the Smithfield Show, London, whereas the cattle were all ill. It is admitted that the prize-cattle had been kept very much cleaner than had the pigs and sheep. (There is no doubt a species difference in sensitivity too.) [The Smithfield show took place during the 4-day lethal fog in London in December 1952.]

Inasmuch as respiratory ammonia, and particularly oral ammonia, may afford protection against inhaled acid sulfates, diminution or absence of the gas might help to define the animal species and individuals that are at increased risk. Insofar as ammonia-producing organisms reside in crevices and plaques around and between teeth, toothless subjects at both extremes of age may have low oral concentrations of ammonia and be especially vulnerable to sulfuric acid. The relation between concentration of respiratory ammonia and functional response to the aerosol has yet to be determined.

- *Ammonium Bisulfate and Ammonium Sulfate*: Charles and Menzel[27] reported that significant quantities of histamine were released from fragments of guinea pig lungs incubated with 10-200 μM ammonium sulfate; maximal release occurred at 100 μM. Of the other compounds tested, equal concentrations of ammonium nitrate and acetate were of intermediate effectiveness in releasing histamine, ammonium chloride caused minimal release, and sodium chloride had no effect. The concentration of an inhaled droplet of ammonium sulfate might fall within this range, depending on the relative humidity of the airways. Thus, at a relative humidity of 99.5%, assuming equilibration, its concentration would be about 275 mM. Once the particle struck the mucosal surface, it would be subject to considerable dilution. More recently, the same group reported that 1 μM ammonium sulfate in isotonic sucrose solution instilled into the trachea of isolated, perfused rat lungs was associated with the release of histamine

TABLE 12 Characteristics of Some Known Atmospheric Sulfates[a]

Formula	Name	Sources	Notable Chemical Properties	Probable Size Class by Mass Particle Diameter (D_p)
H_2SO_4	Sulfuric acid (oil of vitrol)	Atmospheric oxidation of sulfur dioxide; direct from manufacturing	Strong acid; very hygroscopic (drying agent at low RH)	0.1-1.0 μm
NH_4HSO_4	Ammonium bisulfate (acid ammonium sulfate)	Oxidation of sulfur dioxide with ammonia addition	Strong acid; hygroscopic	0.1-1.0 μm
$(NH_4)_3H(SO_4)_2$	Triammonium acid disulfate (letovicite)	Oxidation of sulfur dioxide plus ammonia	Acidic; deliquescent (?) at 65% RH	0.1-1.0 μm
$(NH_4)_2SO_4$	Ammonium sulfate (mascagnite)	Oxidation of sulfur dioxide plus ammonia	Weak acid; water-soluble; deliquescent at 80% RH	0.1-1.0 μm
Na_2SO_4	Sodium sulfate (Glauber's salt)	Paper pulping by kraft process	Water-soluble; deliquescent at 84% RH; relatively inert	<0.5 μm (uncontrolled pulp mill)
$CaSO_4$	Calcium sulfate (gypsum)	Wind-blown dust; manufacture of gypsum products	Low solubility in water; relatively inert	<1 μm
$MgSO_4$	Magnesium sulfate (epsom salts)	Sea spray; paper pulping	Very hygroscopic; relatively inert and nontoxic	<1 μm (sea spray); <0.5 μm

[a]Data from Wilson *et al.*[101]

and a reduction in tidal volume.[26] (The lungs were ventilated mechanically.) A similar response was produced by instillation of 14 μg of histamine. Lesser changes were seen with isotonic sucrose alone or combined with either 1 μM sodium sulfate or ammonium chloride.

To estimate the time that might be involved if the same dose of ammonium sulfate were administered as an aerosol, we assumed that the aerosol was monodispersed with a diameter of 1 μm and was crystalline with a density of 2 g/ml, and that the ventilatory rate was 100 ml/min. If the deposition rate of the particles were 100%, which is most unlikely, then approximately 2 days of continuous exposure would be required to achieve the same total dose.

The release of histamine, if it occurred *in vivo*, could provide a basis for the increase in flow resistance that Amdur and associates[13] reported for guinea pigs exposed to ammonium bisulfate and ammonium sulfate aerosols. The average percentage increases in sulfate expressed in thousands of micrograms per cubic meter were 13% and 38%, respectively. Note that ammonium sulfate evoked the greater response, which is unexpected, insofar as the acidity of an aerosol determines its irritant potential. If ammonium bisulfate were converted to ammonium sulfate by respiratory ammonia, there should be no difference in response to the two salts.

Other investigators have observed little if any functional change during or after exposure to submicrometric aerosols of one or both salts in several species of animals. These included dogs in which cardiovascular and pulmonary function were assessed,[83,86] sheep in which tracheal mucous velocity was measured,[86] and monkeys[21] and guinea pigs[74] in which respiratory mechanics was the principal focus. Mass concentrations ranging up to 4,560 $\mu g/m^3$ were administered. The investigators, using unanesthetized monkeys[21] or lightly anesthetized guinea pigs,[74] could elicit severe bronchoconstriction with a submicrometric aerosol of histamine, thereby demonstrating the responsiveness of the two preparations. As will be noted later, there appears to be a similar paucity of response to ammonium sulfate in human volunteers.

- *Other Sulfates*: Miscellaneous sulfate salts that may occur naturally (as in sea spray), may be generated industrially, or are present in trace amounts in community air have been studied in toxicologic experiments. These include zinc sulfate, $ZnSO_4$; zinc ammonium sulfate, $Zn(NH_4)_2(SO_4)$; copper sulfate, $CuSO_4$; ferric sulfate, $Fe_2(SO_4)_3$; sodium sulfate, Na_2SO_4; and manganese sulfate, $MnSO_4$. A list of known atmospheric sulfates is shown in Table 12.

The size of these airborne sulfates depends on how they are formed, the interval since formation, and the relative humidity.

When produced by mechanical phenomena, such as friction or wind, they are likely to exceed several micrometers in diameter (coarse mode). As coarse particles they may dominate the measurement of "total sulfate mass" obtained with a high-volume sampler. Their potential for irritating the respiratory system of unanesthetized guinea pigs reportedly spans a wide range; zinc sulfate can be highly irritating, whereas ferric sulfate and manganese sulfate are physiologically inert.[11] In contrast, anesthetized dogs have shown no changes in cardiopulmonary function as a result of many of the same aerosolized salts--namely, zinc sulfate, zinc ammonium sulfate, copper sulfate, sodium sulfate, and manganese sulfate--during exposures lasting 4 h and for an additional 2 h afterward.[85] In the latter studies, the aerosols were submicrometric (Dautrebande-30 aerosol generator) and administered in concentrations of 1,600-9,300 $\mu g/m^3$.

Chronic Exposures Alarie *et al.*[2,3] have recently reviewed their considerable experience in exposing monkeys and guinea pigs to sulfuric acid alone and in combination with sulfur dioxide and fly ash, for periods lasting 78 or 52 weeks, respectively. Periodically throughout the exposures, they measured respiratory mechanical function, distribution of ventilation, carbon monoxide uptake, blood-gas tensions, serum-enzyme concentrations, and blood counts. The experiments culminated with postmortem histologic examinations. Two concentrations of sulfuric acid were used, approximately 100 and 1,000 $\mu g/m^3$ (MMD, 0.75-1.17 μm; σg, 1.4-2.8); sulfur dioxide when administered ranged between 0.05 and 2 ppm; the concentration of fly ash was approximately 550 $\mu g/m^3$. The authors concluded that the sulfuric acid was responsible for whatever abnormalities of function were seen, that the other pollutants produced no supplementary effects, and that sulfuric acid caused abnormalities in monkeys only at ~1,000 $\mu g/m^3$, not at 100 $\mu g/m^3$. Two functional abnormalities were said to occur, a progressive increase in pulmonary flow resistance and an uneven distribution of ventilation. However, from the results presented in Figures 1 and 2 of their report, there appears to be no systematic difference between the two concentrations of sulfuric acid in the progressive changes in flow resistance. (In each instance, the sulfuric acid was administered as part of a mixture.) Furthermore, the changes in flow resistance with time were not always different in the treated and control monkeys. The monkeys were young at the outset and grew during the long period of study. One might therefore have expected an associated reduction in flow resistance as the airways grew in diameter, at least among control animals. This trend was apparent in only one of the two control groups; in the second, the slope

of the regression line was indistinguishable from those seen in most of the animals exposed to pollutants.

After exposure to sulfuric acid at ~1,000 $\mu g/m^3$, most lungs showed histologic evidence of epithelial damage in the bronchi and respiratory bronchioles; the findings were equivocal after exposure to 100 $\mu g/m^3$. Earlier, the same investigators had reported a higher degree of structural damage in lungs of monkeys in response to sulfuric acid at 2,430 $\mu g/m^3$ and 4,790 $\mu g/m^3$. Of special note was the conclusion that the guinea pigs, which are said to be particularly susceptible to inhaled irritants, showed no ill effects from approximately the same concentrations of sulfuric acid; however, the exposures lasted only 52 weeks.

Series of studies by other groups of investigators, which involved the exposure of beagles to sulfuric acid alone or in combination with sulfur dioxide[67] and irradiated or nonirradiated auto exhaust,[98] are too deficient in information to allow any judgment. The authors did conclude that exposure to sulfuric acid at 100 $\mu g/m$ (size not specified) for 18 months was unassociated with functional damage, whether the sulfuric acid was administered alone or in combination with other pollutants, whereas the administration of sulfuric acid at approximately 900 $\mu g/m^3$ (90% of the particles smaller than 0.5 μm in diameter) for 620 days affected expiratory flow resistance, diffusing capacity, and lung volume. Pathologic changes were found at the latter concentration.

Aerosol-Gas Mixtures

Amdur and Underhill[15] have postulated that, if soluble metallic salts are present in aerosols that are mixed with sulfur dioxide, they catalyze the conversion of the gas to sulfuric acid, which causes a synergistic or exaggerated response. Individually, manganese chloride, $MnCl_2$; ferrous sulfate, $FeSO_4$; and sodium orthovanadate, Na_3VO_4, had virtually no effect on mechanical function in guinea pigs. When they were mixed with sulfur dioxide, the effects exceeded that of the gas alone. It was suggested that the gas-aerosol reaction occurred once the salt became a droplet in the high relative humidity of the respiratory tract. A corollary of this hypothesis is that the effect of mixing an aerosol salt with sulfur dioxide is determined by the solubility of sulfur dioxide in the salt.[12] In support of this hypothesis, Amdur and Underhill[15] found that the percentage increase in pulmonary flow resistance produced by the combination of sulfur dioxide with aerosols of ammonium thiocyanate, NH_4SCN, potassium chloride, KCl, or sodium chloride, NaCl, correlated with the

solubility of sulfur dioxide in these salts. Again, the absorption of sulfur dioxide was thought to have occurred in the airways once the particles had become droplets. (In these experiments, the salts were probably in crystalline form before inhalation.)

Considerable interest has been generated by these two sets of experiments, for they lend support to the widely held belief that the effect of air pollution on health is probably attributable to combinations of, rather than individual, pollutants. Nonetheless, it is difficult to justify the assumption underlying these reported examples of synergism--namely, that the requisite gas-aerosol interaction took place in the airways; the problem has been discussed in a recent review.[79] It will be recalled that the mucosal surface of the upper airways is a highly efficient scrubber of sulfur dioxide; by comparison, the absorptive surface of the droplet aerosol (at the concentrations used in these experiments or under realistic circumstances) is quite small. If the aerosol is to provide a competitive surface, high concentrations are necessary. Moreover, the average time allowed for oxidation of the sulfur dioxide in the airways before the gas itself is absorbed by the mucosal surfaces is a few seconds at most and is likely to be considerably shorter; the potential for conversion of the sulfur dioxide to sulfuric acid once the particle is deposited on the mucosal surface is unknown, but is probably slight. An alternative basis for synergism is for the aerosol to be a droplet in ambient air and for the interaction to occur before inhalation. The latter circumstance has been tested by administering sulfur dioxide with either a droplet sodium chloride aerosol (high relative humidity) or a dry sodium chloride aerosol (low relative humidity).[70] The mixture was found to impair mechanical function in guinea pigs only when the ambient aerosol was in droplet form. The pH of this droplet was under 4; there was no evidence that sulfate ion was present; whether the effect was due to hydrogen ion, sulfite ion, or bisulfite ion is speculative.

Two groups have examined the consequences of administering sulfuric acid and ozone together. The methods of analysis differed radically, and the conclusions drawn may be said to conflict. In the first study, Cavender *et al.*[25] exposed rats and guinea pigs to sulfuric acid, ozone, or the combination for 2 or 7 days, killed the animals, and measured the ratio of lung weight to body weight and examined the lungs histologically. No effects were seen in either species with concentrations of sulfuric acid below 10 mg/m^3 (MMD, 1 μm). Ozone alone at 2 ppm produced lesions primarily in terminal bronchioles and proximal alveoli. The lesions were similar in type and magnitude when sulfuric acid was added in concentrations up to 10 mg/m^3. The

authors concluded that the two agents were not interactive in producing effects.

More recently, Last and Cross[62] found evidence that sulfuric acid and ozone act synergistically. They exposed rats *in vivo* and thereafter carried out biochemical assays *in vitro* on explants of tracheal tissue and lung homogenates. Three days after the animals' exposure (lasting 3 days) to the gas-aerosol mixture (ozone at 0.4-0.5 ppm plus sulfuric acid at 1 mg/m^3), the tracheal explants showed excessive glycoprotein secretions. Ozone alone caused a decrease in secretory state at this time. Massive doses of sulfuric acid alone (in excess of 100 mg/m^3) were required to change secretory rate. Three days after exposure to the same gas-aerosol mixture, the lung homogenates showed exaggerated increases in deoxyribonucleic acid, ribonucleic acid, and protein content, compared with the smaller increases caused by ozone alone. Sulfuric acid alone had no effect. The changes noted were presumed to reflect inflammation.

Because sulfur oxides and photochemical oxidants coexist in a number of communities, there is interest in toxicologic studies of their potential interaction (see the section on human experimentation). However, such studies are complex and require exceeding care in design and execution if their results are to be unambiguous and useful.

Mutagenesis and Carcinogenesis

It has been suggested that the sulfur dioxide-sulfite-bisulfite complex may act as an environmental mutagen, owing to its ability to deaminate cytosine, a component of deoxyribonucleic acid. Whatever mutagenic action is exhibited *in vitro*, however, is weak, especially at physiologic pH.[82,89,93]

To test the potential of sulfur dioxide to cause neoplasms, Peacock and Spence[81] exposed mice chronically, 5 days/week, to the gas at 500 ppm. (Duration of exposure was unspecified.) The mice were heterozygous and highly susceptible to chemical induction of pulmonary adenoma. Exposed mice over 300 days old showed an average incidence of lung tumors (adenomas and malignancies combined) that exceeded the incidence of spontaneous tumors in control animals. The authors stated that a colleague's independent statistical analysis indicated that the difference could be "a matter of chance." While relating this uncertain increase in incidence of lung tumors to chronic inflammation and hyperplasia associated with the high concentration of sulfur dioxide, they concluded that classification of the gas as a chemical carcinogen was not justified.

Laskin *et al.*,[61] in reviewing their own attempts to induce pulmonary carcinoma experimentally, described an exploratory study that suggested that sulfur dioxide may act as a cocarcinogen. They exposed groups of rats and hamsters to sulfur dioxide alone (10 ppm), to benzo[a]pyrene (a carcinogen) and sulfur dioxide in combination (10 mg/m^3 and 3.5 ppm), and to both regimens administered in sequence. The effect of benzo[a]pyrene alone was undetermined. The experiment spanned 794 days. None of the animals breathing filtered air or sulfur dioxide alone developed either metaplasia or carcinoma of the lung. Two of 21 rats that received benzo[a]pyrene in combination with sulfur dioxide and five of 21 rats receiving benzo[a]pyrene plus both concentrations of sulfur dioxide developed squamous cell carcinomas. The hamsters were impervious to exposure. The findings should be considered provocative, but inconclusive. Whether sulfur dioxide is a cocarcinogen remains moot.

HUMAN EXPERIMENTATION

In spite of growing ethical and legal constraints, human experimentation continues to provide information critical to the setting of air-quality standards. Such experimentation is confined to relatively short exposures to pollutants. To study possible effects of frequent or long exposures and to obtain guidance in establishing acceptable experimental procedures for human volunteers, the use of animals is required. Among the important questions addressed by clinical research are:

- What are the dose-response relations for sulfur dioxide and specific molecular forms of sulfur-containing particles in human subjects during acute exposures? Do the responses have implications for health or well-being?
- Are persons with underlying cardiopulmonary disease more sensitive than healthy persons to these pollutants?
- Can otherwise apparently healthy persons who are unusually sensitive to the pollutants be identified? If so, what is the basis for this increased sensitivity, or "hypersensitivity"?
- Can combinations of sulfur oxides and other airborne pollutants or of sulfur oxides and other forms of environmental or biologic stress produce an exaggerated or synergistic response?

In this respect, the increasing attention that is being given to the role of exercise in the physiologic response to pollutants is encouraging. (Greater exploitation of exercise, or perhaps of hyperventilation, its analogue, is to be encouraged in animal

toxicology as well.) To our knowledge, the possibility that pollutants may interact with different forms of psychologic stress has not been tested.

Sulfur Dioxide

The effect that acute exposure to low concentrations of sulfur dioxide may have on pulmonary function in healthy subjects was cited earlier in this chapter. In one study,[39] sulfur dioxide at 1 ppm elicited a significant increase in pulmonary flow resistance in one of 11 subjects during exposures lasting 15 min. In a second study,[16] sulfur dioxide at 1 ppm administered to 15 resting young men for 6 h was associated with progressive decreases in nasal mucus flow rate, $FEF_{25\%-75\%}$, and $FEV_{1.0}$ and an increase in nasal flow resistance.

In a study by Bates and Hazucha,[18] four healthy subjects showed an average reduction in maximal expiratory flow rates during exposure to sulfur dioxide at 0.75 ppm; the individual responses were not reported. The changes were evident after 0.5 h and either persisted or increased in magnitude during the remainder of the 2-h exposure, depending on the type of measurement. Recovery was still incomplete 0.5 h after exposure was ended. Sulfur dioxide at 0.37 ppm evoked no functional changes in the same subjects. Insofar as these results can be compared with those of other studies, they appear to represent the most reactive healthy population yet exposed to the gas. (See section on sulfur dioxide plus aerosols and/or ozone for additional discussion of this report.)

In a study,[17] comprising a series of experiments over a period of 4 yr, a small increase in specific airway flow resistance (flow resistance corrected for lung volume) was seen in response to sulfur dioxide at 1 ppm, but only if the subjects took 25 maximal breaths of the gas starting from residual volume. The procedure was designed to increase dosage to the laryngotracheobronchial airways. In one subject, there was a threefold increase in specific airway flow resistance with this procedure. As expected, sulfur dioxide at 3 ppm elicited greater changes in function than did 1 ppm. The magnitudes of these changes were proportional to the numbers of deep breaths taken.

Two recent studies have involved persons with underlying lung disease, as well as healthy persons. Weir and Bromberg[99] exposed nonsmoking healthy subjects and smokers who demonstrated functional defects associated with early obstructive pulmonary disease to sulfur dioxide at 0, 0.3, 1.0, and 3.0 ppm. The subjects resided in an environmental chamber maintained at 22 ± 1°C

and 50 ± 5% relative humidity. The exposures were administered in random sequence for 120 h continuously to the healthy subjects, and for 96 h to the smokers. Testing was done at 24-h intervals. Sulfur dioxide at 0.3 ppm elicited no functional changes. Sulfur dioxide at 1.0 ppm caused a significant reduction in dynamic compliance measured at 120 breaths/min after 24 and 48 h of exposure; results of other tests of ventilation and respiratory mechanics were unaffected. The reduction in dynamic compliance was greater and more prolonged with sulfur dioxide at 3.0 ppm. A notable finding was the absence of clear-cut evidence of functional changes among the subjects with underlying lung disease. Their intersubject and intrasubject variability far exceeded the variation associated with exposure to all concentrations of sulfur dioxide. A variety of symptoms were noted in both groups: headache, nasal congestion, throat soreness, cough, nosebleed, gastrointestinal discomfort, and rash.

In a second study, M. J. Jaeger, D. Tribble, and H. Wittig (unpublished data) exposed 40 healthy nonsmokers and 40 subjects with mild asthma to air and to sulfur dioxide at 0.5 ppm for periods of 3 h. Forced expiratory performance, closing volume, airway flow resistance, and lung volumes were measured. As a group, the healthy subjects showed no functional changes that could be judged adverse; indeed, vital capacity (VC), maximal volume of gas that can be forcefully exhaled in 1 s after full inspiration (FEV_1), and MMFR tended to rise with time, whether clean air or sulfur dioxide was administered. The response of the group with asthma to sulfur dioxide was interpreted as showing slight functional impairment; i.e., MMFR was said to increase less during exposure to sulfur dioxide than during the sham exposure. The other functional tests were unaffected. Among the healthy subjects, a 13-yr-old boy experienced shortness of breath and had functional evidence of bronchoconstriction. On the evening after exposure to sulfur dioxide, two of the asthmatic subjects experienced shortness of breath, which required medication.

Sulfate Aerosols

A number of studies involving the exposure of volunteers to submicrometric sulfate aerosols are under way or just completed. The generalization may be made that, thus far, the results suggest that concentrations of the different sulfate aerosols under 1,000 $\mu g/m^3$ appear to produce only infrequent changes in results of conventional tests of pulmonary function and that the changes may be characterized as slight or transient.

Sackner *et al.*[87] found no changes in total respiratory flow resistance, VC, or $FEV_{1.0}$, nor any symptoms of discomfort in healthy volunteers exposed to sulfuric acid at 10, 100, or 1,000 $\mu g/m^3$ for 10-min intervals during three successive hours. Particle size was not specified, but was reported to be "equivalent to those produced by catalytic convertors" on cars. The subjects were at rest.

Sackner *et al.*[84] also exposed six healthy subjects for 10 min to the following salts at 1,000 $\mu g/m^3$ (MMAD, < 0.1 μm): zinc sulfate, zinc ammonium sulfate, ammonium sulfate, and sodium sulfate. Once again, the subjects were at rest. A wide variety of respiratory and cardiovascular tests were performed during the following 3 h, including those designed to detect impairment in small-airway function and the distribution of ventilation. There were no significant changes in function as a consequence of exposure.

Hackney *et al.*[50] recently studied the effects of ammonium sulfate, ammonium bisulfate, and sulfuric acid aerosols on three groups of adult male volunteers: healthy subjects, "sensitive" subjects with a history of high reactivity to inhaled irritants, and patients with asthma. The respective concentrations were 100, 85, and 75 $\mu g/m^3$. The aerosols were polydispersed with an MMAD of about 0.3 μm. For the studies with ammonium sulfate, each of the three groups of subjects was exposed to the aerosol at a relative humidity of 40%; the healthy subjects were also exposed to the aerosol at a relative humidity of 85%. (Ammonium sulfate is a dry crystal at 40% relative humidity and a droplet at 85% relative humidity. Hydration of the crystal can be expected to occur in the high relative humidity of the upper airways. The physical state of the aerosol in the ambient atmosphere might have important consequences for health if soluble gases, such as sulfur dioxide, were also present.) Exposure to the other two sulfate aerosols was at only 40% relative humidity. A sequence of 1 or 2 days of sham exposures in the chamber was followed by exposure to ammonium sulfate for three consecutive days among the healthy and "sensitive" subjects and for 2 days among the asthmatics. The subjects were at rest throughout the studies. The functional measurements included lung volume, forced expiratory maneuvers, closing volume (an index of the patency of peripheral airways), and total respiratory flow resistance at different frequencies.

There was no evidence of cumulative effects of exposure over the 3 days. The change from low to high relative humidity did not appear to influence the response to ammonium sulfate, but was associated with manifestations of heat stress. (The chamber temperature was 31°C in all experiments to stimulate an episode

of pollution during a summer day.) In general, there was "little or no evidence of adverse health effects from these exposures."

Koenig *et al.*[58] found little or no functional change in healthy subjects exposed for 2 h to sodium sulfate at approximately 1 mg/m^3 (MMD, 0.45 μm; σg, 1.7; relative humidity, >82%). Nine subjects were studied, two-thirds during intermittent, moderate exercise sufficient to increase minute ventilation by a factor of about 6. (See Figure 26 for functional change attributable to exercise alone.)

Sulfur Dioxide Plus an Aerosol or Ozone

Morgan *et al.*[73] tested the functional effects of sulfur dioxide mixed with a droplet aerosol of sodium chloride in healthy subjects at rest and after moderate exercise. The respective concentrations were 1.0 ± 0.1 ppm and 1.0 ± 0.1 mg/m^3 (MMD, 0.9 μm; σg, 2.0; relative humidity, >75%); exposure lasted 2 h. Essentially the same mixture has been found to alter respiratory mechanical function in guinea pigs. (No response had been

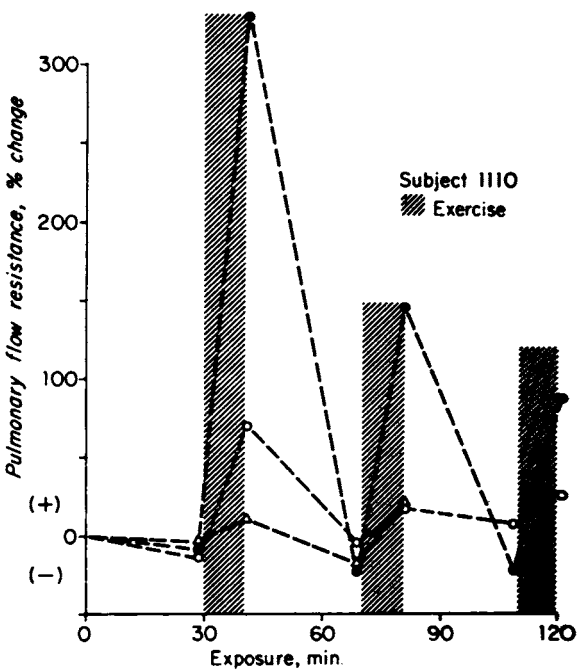

FIGURE 26 Effect of exercise on pulmonary flow resistance. Data from Koenig *et al.*[58]

elicited in the animals by the same concentrations of either sulfur dioxide or aerosol alone or by the combination administered at a relative humidity below 40%, at which the particles were dry.[71] At rest, only one of the 10 subjects showed consistent changes in mechanical function, apparently involving both central and peripheral airways. Flow resistance rose in five of the seven exercising subjects. In each instance, the value returned to baseline during the following period of rest, despite continued exposure. There were three periods of exercise during exposure, with the greatest functional change occurring in response to the first period. The diminished responses seen with later exercise suggested a form of adaptation. Figure 26 shows the relation of the changes in flow resistance to exercise in one subject and compares his responses to the sulfur dioxide-sodium chloride droplet system and to sodium sulfate. Figure 27 shows the average response of six subjects breathing clean air and seven subjects exposed to the gas-aerosol mixture.

Several years ago, Bates and Hazucha[18,53] published two reports on a study that has stirred considerable interest in inhalation toxicology. It involved the administration of sulfur dioxide and ozone separately and in combination to a small group of healthy subjects. The subjects were at rest, the concentration of each gas was about 0.37 ppm, and the exposure lasted 2 h. Sulfur dioxide alone evoked no functional response, whereas ozone caused a relatively slight reduction in $FEV_{1.0}$; these observations were consistent with the earlier experience of other investigators. However, when the two gases were combined, a significant and exaggerated impairment of ventilatory performance resulted.

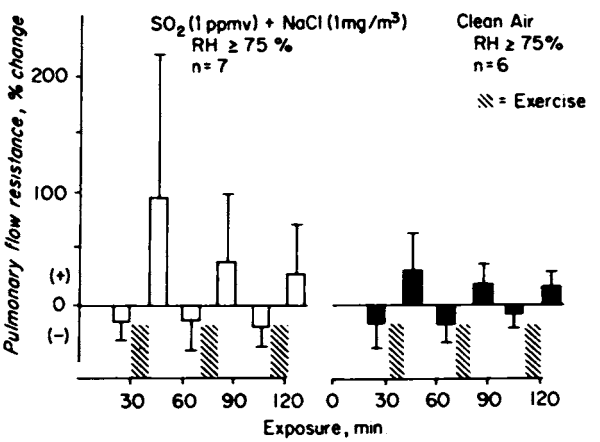

FIGURE 27 Effect of sulfur dioxide and sodium chloride on pulmonary flow resistance. Data from Morgan *et al.*[73]

The finding was considered as possibly the first convincing demonstration of synergism in human subjects arising from relatively low concentrations of two common urban pollutants.

To determine the physical-chemical basis for the observation, a collaborative study was undertaken, spearheaded by Bell and associates at Rancho Los Amigos Hospital in Los Angeles and including the original team of Bates and Hazucha.[22] This time, it was shown that prechamber mixing of the two gases, particularly in high concentrations before dilution, as in the original experiments in Montreal, led to the formation of an ultrafine aerosol. Presumably, the ultrafine aerosol comprised sulfuric acid or its products of neutralization with ammonia (Table 13). The presence of human subjects in the chambers catalyzed this phenomenon, chiefly during exercise. The subjects may have been responsible for emitting (exhaling?) nonmethane hydrocarbons, which with ozone and sulfur dioxide formed a reactive system culminating in particle formation. Exercise may have acted to increase this input of hydrocarbons and to improve the mixing of reactive elements in the chamber. The chamber used for the original study

TABLE 13 Particle Characterization in Rancho Los Amigos Chamber[a]

Condition[b]	Number of Condensation Nuclei/cc	Number of Particles/cc (diameter, 0.5-10 μm)	Sulfate Concentration, $\mu g/m^3$
Los Angeles air	30,000	≥30	5-15
Chamber, no subjects:			
Clean air	≤50	~0.01	--
SO_2 at 0.37 ppm	≤50	~0.01	--
O_3 at 0.37 ppm	5,000	~0.01	--
O_3 at 0.37 ppm + SO_2 at 0.37 ppm	90,000	~0.01	--
Chamber, 3 subjects, rest (exercise):			
Clean air	≤50	0.3 (2)	~0
O_3 at 0.37 ppm	8,000 (22,000)	0.3 (2)	~0
O_3 at 0.37 ppm + SO_2 at 0.37 ppm	100,000 (250,000)	0.3 (2)	0.5-1.5

[a]Data from Bell *et al.*[22]

[b]Temperature, 31°C; relative humidity, 35%.

in Montreal had lacked the elaborate air-purification system of the one in Los Angeles. The authors suggested that the subjects in Montreal may therefore have been exposed to "respirable sulfur aerosol" at 100-200 $\mu g/m^3$, reflecting the sum of background contamination and newly formed particles (Table 14). By comparison, the 24-h average sulfate concentration in the Los Angeles

TABLE 14 Filter Data from the Montreal Chamber during a $SO_2 + O_3$ Study, February-March 1976[a]

Sampling Date (1976)	Condition[b]	Concentration of Sulfur Aerosol as Sulfate, $\mu g/m^3$	Total Sample or Respirable Sample[c]
Feb. 23	Lab. air outside chamber	21 ± 7	*T*
Feb. 24		15 ± 7	*R*
Feb. 16	Chamber air, 1 subject	33 ± 7	*T*
Feb. 9		29 ± 7	*R*
Mar. 2	Chamber air, no subjects	--	*T*
Feb. 3		5 ± 5	*R*
Feb. 19	O_3 at 0.37 ppm, 1 subject	31 ± 6	*T*
Feb. 5		-11 ± 33	*R*
Feb. 26	SO_2 at 0.37 ppm, 1 subject	83 ± 140	*T*
Feb. 12		-48 ± 130	*R*
Feb. 27	SO_2 at 0.37 ppm + O_3 at 0.37 ppm, 1 subject	230 ± 140	*T*
Mar. 1		222 ± 250	*R*

[a]Data from Bell *et al.*[22]

[b]Chamber temperature ranged from 22 to 24°C, and relative humidity from 30 to 47%.

[c]Respirable (*R*) refers to the mass fraction of the total aerosol sample that can deposit on the nonciliated airways, determined from filters after a Dorr-Oliver Nylon Cyclone operated at 1.7 L/min. Total samples (*T*) were collected on the filter without the preceding Cyclone.

basin has been found to range from 4 to 20 $\mu g/m^3$, and the 2-h maximal concentration during smog episodes may be as high as 71 $\mu g/m^3$.[54]

The physiologic portion of the study was as follows: four healthy and four "sensitive" subjects, defined as having a history of hyperreactivity to inhaled irritants, were exposed on days 1 and 2 to purified air, on day 3 to ozone at 0.37 ppm, and on day 4 to ozone at 0.37 ppm plus sulfur dioxide at 0.37 ppm. Additional regimens involved exposure of the four sensitive subjects to purified air on day 1, and to either ozone at 0.37 ppm on days 2 and 3 or sulfur dioxide at 0.37 ppm on day 2. (In an earlier study, a difference in response between the first and second days of exposure to ozone at 0.5 ppm alone had been observed in the same laboratory, with the response being more marked on the second occasion.[51] However, no interaction between days was noted at this time.)

The results seen among the Los Angeles residents under the stringent control of the local environmental chamber were less conclusive than reported originally. For example, when the results from the healthy and the sensitive groups were combined, FVC after exposure to the mixture of gases was lower by only 3% than on the 2 days preceding the sham exposure ($p < 0.05$), whereas FEV_1 was 4% lower than on all other days ($p < 0.05$). Changes in the single-breath nitrogen washout curve indicative of maldistribution of ventilation were significant for the sensitive subjects alone, but not for the combined groups. For these analyses, the results of tests performed after exposure to ozone or to ozone plus sulfur dioxide were compared with those obtained during the first 2 days of sham exposure. The authors acknowledged that the variation in FVC and FEV_1 "occurring in the normal course of life over periods of weeks or months" was greater than the changes attributed to the irritant gases. They justified their analytic procedure by noting that such measurements showed little change over short periods involving repeated sham exposures.

Another procedure carried out in this detailed retrospective study was to bring the four original subjects from Montreal to Los Angeles to be tested. The comparative functional changes found in the two cities in response to the mixture of gases, circumstances in which there were significant differences in chamber concentrations of submicrometric sulfate aerosols, are shown in Table 15. The synergism described in the original reports[22,53] was wholly accounted for by two subjects, 32 and 34. In Los Angeles, these two subjects manifested no changes in ventilatory performance.

In the final discussion, the authors suggested that whatever exaggeration of the effect of ozone was produced among the

TABLE 15 Canadian Subjects' Responses to Ozone at 0.37 ppm + Sulfur Dioxide at 0.37 ppm--Present Los Angeles Study versus Previous (Montreal) Study[a]

Subject	Percent Change from Control Values			
	FVC		FEV_1	
	Montreal	L.A.	Montreal	L.A.
31	-2	-6	-9	-13
32	-51	0	-58	-2
33	-5	-2	-1	-6
34	-29	-3	-30	-2
Mean	-22	-2.7	-24	-5.2

[a]Data from Bell *et al.*[22]

subjects from Los Angeles by the addition of sulfur dioxide may have been due to a reaction of the two gases in the airways or on the mucous layer. That is, sulfuric acid or some other irritating by-product could have been produced *in vivo*. The inference was made that the chamber in Montreal, by inadvertence, may have been more appropriate than the one at Rancho Los Amigos Hospital for assessing biologic effects of high oxidant and sulfur pollution.

Another study, similar in objective, has just been completed by Bedi *et al.*[19] They exposed nine healthy young adults, one of whom had asthma in childhood, to sulfur dioxide and ozone, separately, and in combination and to clean air. The order of exposures was randomized. Exposure lasted 2 h and involved intermittent exercise. The temperature and relative humidity of the chamber were maintained at 25°C and 45%; inlet air was passed through activated charcoal and particulate filters at a rate of 500 L/min, providing a turnover time for the chamber of about 22 min. Functional tests included forced expiratory volumes, single-breath nitrogen washout curves to assess the patency of peripheral airways and distribution of ventilation, and airway flow resistance. Symptoms were also assessed. There was no significant difference between the responses to ozone alone and responses to the mixture of gases. The unequivocal synergism that had been elicited in two residents in Montreal[18,53] and the equivocal synergism in the four residents of Los Angeles[22] were not evident.

CONCLUSION

Sulfur Dioxide

To what extent the irritative action of sulfur dioxide is attributable to hydrogen, sulfite, or bisulfite ions formed when the gas enters solution in body fluids is speculative. Sulfite oxidase, an enzyme found in the lung and elsewhere in the body, oxidizes sulfite to sulfate, which appears to be innocuous. A probable effect of this reaction is to confine the toxicity of the inhaled gas to the lungs.

It is difficult to postulate a sharp threshold for the functional response of healthy persons exposed to sulfur dioxide for periods lasting up to several hours. In one recently completed but unpublished study on 40 subjects, no effects of 0.5 ppm were observed after 3 h. In an earlier study on four subjects, there was a progressive average reduction in forced expiratory flow rate during 2 h of exposure to 0.75 ppm. Another study in which the subjects were exposed for 6 h to sulfur dioxide at 1 ppm adduced evidence of slowed nasal mucus flow rate, narrowing of the nasal passages, and a progressive but limited reduction in forced expiratory flow rate. It should be noted, however, that there have been a number of studies involving concentrations of the gas ranging from 1 to 3 ppm, in which the functional effects were either infrequent or absent, short-lived despite continued exposure, evoked only by repeated deep breathing, or seen only after continuous exposure for 24 h or longer.

In the unpublished study cited in the previous paragraph, two of 40 persons with a diagnosis of asthma showed no functional changes during or just after exposure to sulfur dioxide at 0.5 ppm for 3 h, but reported symptoms consistent with bronchoconstriction that evening. Medication was taken to relieve the symptoms.

It is reasonable to conclude that there is no toxicologic evidence that the current 24-h standard of 0.14 ppm (365 $\mu g/m^3$) for sulfur dioxide is inadequate to protect public health.

In studies involving chronic exposure of several species of animals, including monkeys, to sulfur dioxide, there has been no evidence of structural damage by light microscopy or impairment of conventional functional indexes below 5 ppm. There have been reports that prolonged exposure to sulfur dioxide at 1 ppm may slow either alveolar clearance of insoluble particles or tracheal mucous velocity. The significance of immunologic changes produced by prolonged exposure to sulfur dioxide at 2 ppm, described in a single study, is unclear.

The sulfite-bisulfite complex is weakly mutagenic at physiologic pH. There is no evidence that sulfur dioxide or the

sulfur-containing aerosols found in ambient air are carcinogens. It has been hypothesized on the basis of an exploratory study that sulfur dioxide may be a cocarcinogen, but this hypothesis has yet to be tested rigorously.

Table 16 summarizes human pulmonary responses to sulfur dioxide at concentrations under 5 ppm.

Sulfur-Containing Aerosols

There is virtually no toxicologic evidence to show that specific sulfate-containing aerosols, when administered alone in concentrations similar to those reported in community or regional studies, induce adverse structural or functional effects in the respiratory system. If one accepts a single observation presented at a workshop several years ago, but not yet published or confirmed by other investigators who have used a variety of animal species, it may be stated that short-term exposure to sulfuric acid at around 100 $\mu g/m^3$ can induce changes in respiratory mechanical function in guinea pigs. Concentrations nearly twice as high have decreased tracheobronchial clearance in donkeys that showed no change in mechanical function. Another completed but unpublished study revealed no difference in the response of lightly anesthetized guinea pigs to sulfuric acid administered in two size ranges; the mass median diameters were 0.04 and 0.7 μm; the mass concentration of acid was 100 $\mu g/m^3$. The smaller size (nuclei mode) might occur in proximity to cars equipped with catalytic converters and fueled with sulfur-containing gasoline. The larger size (accumulation mode) would be associated with regional air pollution as a consequence of the oxidation of sulfur dioxide.

It should be emphasized that the number of studies of this type that have been completed is small and that the acid sulfate aerosols have not been administered in conjunction with exercise or hyperpnea, which should reduce the time allowed for ammonia to neutralize the particles in the upper airways. Certainly, there is a need to study the possible amplification of effects that may arise when sulfur dioxide, ozone, and acid sulfate particles are combined, as apparently happened in a study conducted in Montreal.

Ammonium bisulfate and ammonium sulfate are the salts formed by the neutralization of sulfuric acid by ammonia. In an earlier study on guinea pigs, flow resistance was found to be acutely increased by these salts at concentrations of about 1 mg/m^3. In more recent studies on a variety of animals, on healthy persons, and on patients with asthma, there has been no convincing evidence of functional alterations with exposure to concentrations up to

TABLE 16 Pulmonary Functional Responses (Ventilatory and Mechanical) to Sulfur Dioxide Concentrations Under 5 ppm in Human Volunteers

Procedure	Results	Reference
15 healthy men, 20-28 yr old, exposed at rest to 1 ppm for 6 h	Nasal mucus flow rate not significantly changed; nasal airway caliber reduced (p <0.05); decreased $FEF_{25\%-75\%}$; generally, changes progressively greater with time; no subjective complaints	16
4 normal subjects exposed at rest to 0.37 or 0.75 ppm for 2 h	No functional changes at 0.37 ppm; progressive reduction in ventilatory function at 0.75 ppm; recovery incomplete 30 min after end of exposure	18
9 healthy men, 18-27 yr old, exposed to 0.40 ppm during intermittent exercise for 2 h	No changes in pulmonary mechanics, maximal voluntary ventilation, or closing volumes; subjects could not distinguish subjectively between clean air and SO_2	19
10 healthy men, 25-34 yr old, exposed at rest and during hyperventilation to 2.1 ± 0.2 ppm for 30 min; mouth-breathing	One "possible" reactor; otherwise no changes in pulmonary mechanics or thoracic gas volume	24
11 healthy men, 22-56 yr old, exposed at rest to 1 ppm for 10 min; mouth-breathing	One subject with history of occasional wheezing had increased flow resistance (+7%, p <0.01); one subject had decreased flow resistance (-23%, p <0.01)	39

TABLE 16 Continued

Procedure	Results	Reference
40 healthy nonsmokers, 25 ± 5.7 yr old, and 40 subjects with mild asthma, 27 ± 9.2 yr old, exposed at rest to 0.5 ppm for 3 h; mouth-breathing	Equivocal changes in healthy subjects, i.e., average ventilatory performance increased less during exposure to SO_2 than during sham exposure; this pattern more pronounced in asthmatics; airway resistance did not change; one healthy 13-yr-old boy experienced shortness of breath and increased airway resistance after exposure; two asthmatics required treatment for dyspnea the next night	M. J. Jaeger, D. Tribble, and H. Wittig, unpublished data
Healthy volunteers 18-47 yr old:	Effects were short-lived	63
a. 13 subjects exposed at rest to 1 ppm for 1 h	a. No changes in airway resistance or ventilatory function	
b. 12 subjects took 25 maximal breaths of 1 ppm	b. Specific airway resistance increased 12% ($p < 0.001$) above changes produced with clean air; no change in ventilatory function	
c. 14 subjects took 8 deep breaths of 1 ppm	c. Results inconclusive	
d. 17 subjects took 2-32 deep breaths of 3 ppm	d. Increase in airway resistance related to number of deep breaths of SO_2 taken	

TABLE 16 Continued

Procedure	Results	Reference
15 healthy volunteers exposed at rest to 2.5 ppm either by nose or by mouth for 10 min	Decrease in specific airway conductance maximal after 5 min; averaged 18% for nose-breathing, 26% for mouth-breathing	72
Healthy men, 18-45 yr old, exposed at rest by mask to 1.34-80 ppm for 10 min or in chamber to 1-23 ppm for 60 min	Little change in flow resistance or clinical findings below 30 ppm by mask or 5 ppm in chamber	90
9 healthy volunteers, 20-40 yr old, exposed at rest to 0.5 and 1 ppm for 15 min; mouth-breathing	$MEF_{50\%VC}$ reduced at 1 ppm (averaged about 6%; $p < 0.02$); 1-ppm SO_2 mixed with saline aerosol produced no functional change	92
3 healthy men exposed at rest to 2.0-2.5 ppm for 5 min; mouth-breathing	Flow resistance (interrupter method) increased 15-21%	97
a. 4 groups of 3 healthy men, 21-28 yr old, exposed at rest in random sequence continuously for 120 h to 0, 0.3, 1, and 3 ppm	a. Minimal reversible decrease in airway conductance and in dynamic compliance at 3 ppm only; no dose-related symptoms	99
b. 7 male smokers, 25-49 yr old, with early evidence of chronic obstructive pulmonary disease, exposed at rest continuously for 96 h in random sequence to 0, 0.3, 1, and 3 ppm	b. Intersubject and intrasubject variability in functional tests and subjective responses exceeded variance due to exposure to SO_2; no evidence of greater susceptibility than in healthy subjects	

several milligrams per cubic meter, for periods lasting up to several hours.

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8 EPIDEMIOLOGIC STUDIES OF HEALTH EFFECTS OF SULFUR OXIDES

There have been extensive and repeated reviews of the literature on the health effects of sulfur oxides on man.[15,26,44,45(pp.243-288),47,56] Rather than rework this well-tilled area, we believe it more appropriate to comment briefly on selected epidemiologic studies and to consider the more recent information.

It should be pointed out first that sulfur oxides as air pollutants exist not in isolation, but rather as components of complex mixtures. There is interaction between the components, both gaseous and particulate, and this makes the identification of single components difficult. Another complicating factor is that ambient concentrations of air pollutants are measured in limited numbers of sites, which are often selected for regulatory purposes, rather than for measurement of actual exposures of people. The estimation of pollution dose is further complicated by the fact that, except for outdoor workers, most people spend most of the day indoors, where the extent of exposure to pollutants can be quite different from that outside. Thus, the question should be asked: "How representative are pollutant concentrations measured at a single site of the exposures sustained by those living near the site?" Most studies have not tried to answer this question, but have assumed the representativeness of reported data.

Sulfur oxides exist in both gaseous and particulate forms, such as sulfur dioxide and sulfates, respectively. The particulate form in general is derived from the gaseous at a molecular level, so the particles are very small. Particle sizes beyond the molecular occur as a result of agglomeration, condensation, and other mechanisms, but in virtually all cases the particles are still small, usually less than 1 μm in diameter. [See National Academy of Sciences[45(pp. 3-153)] for a more extensive discussion of this aspect.] These particles are within the respirable size range. The proportion of respirable particles deposited in the lungs depends on their physical and chemical characteristics. The

sulfate-containing fraction of respirable size makes up a relatively small percentage of the total suspended particles (TSP), which constitute the sample collected by high-volume sampling methods. In fact, with some types of filters used, some small particles may pass through the filter system and not be collected at all. Conversely, some filters react with sulfur dioxide to form sulfate, thus giving falsely high values for suspended sulfates. Collection systems that concentrate on the mass respirable particles (MRP) in addition to the TSP should be used, in order eventually to establish standards for MRP, as well as TSP.

Laboratory studies have demonstrated that the sulfates vary greatly in their toxicity to animals,[1] and presumably they vary in their toxicity to man. Identification of the precise type of sulfate collected has proved to be extraordinarily difficult, and the identification of the total amount of sulfates does not provide all the information needed to determine risk of exposure. Furthermore, if sulfuric acid mist is collected, the acid can react with ammonia in the atmosphere to form ammonium sulfate, a less toxic substance than sulfuric acid mist. Such a change would result in an underestimation of the potential hazard or the later attribution of a greater effect on an exposed population to a less toxic substance. In some places, such as London, the acid deposited on the filter is measured and assumed to represent sulfuric acid; it is recognized that an unknown amount will be neutralized by ammonia in the atmosphere and that there are other acids in the air.

Any of these factors can lead to erroneous conclusions or account for different results being obtained by different observers. These factors must be considered in the evaluation of the various studies reported. In most studies, the precise pollutant concentrations are of little value, because the variations around the estimates and the generalizability of these measurements cannot be determined. However, for establishing exposure gradients, it is very likely that values that are significantly different from each other do represent points along an exposure curve that can be referred to as "higher" or "lower" than each other. Other factors that affect populations also have to be evaluated as to their effects on health. Such factors include tobacco use, occupational exposure, socioeconomic status, extent of education, and ethnic origins. Similarly, with respect to the degree of exposure, the type of measurement and various kinds of interference with it must be considered. For example, in sulfur dioxide measurement, the bubbler effect may vary. If the reagent fluid is too cold, the reaction does not occur with sufficient rapidity; if it is too hot, the reaction products decay or evaporate. In both instances, the sulfur dioxide concentration

is underestimated, and effects on health will be attributed to a lower concentration than was actually present.

Annual average values by themselves do not give complete information with respect to exposure. We do not have sufficient information to state whether a mean value derived from a number of observations with only slight variation is safer, or has less effect, than one derived from observations with marked variations, e.g., very low and moderately high values that could exceed a concentration above which effects occur. Intuitively, one would presume that the value with the highest variations had more effect.

Data from occupational exposures have limited applicability for estimating health effects in general populations, although estimation of exposure may be more accurate in the occupational setting. The working population is not representative of the general population, because it is formed by industry selection or by self-selection. Thus, the unhealthy are excluded, as well as the very young and the elderly. The working population does age and can develop disease, but the aged and the diseased are likely to be selected out of an exposed occupational group. If an effect is seen in a working population, the only conclusion one can draw is that there will probably be a larger and more widespread effect in the general population exposed to these same pollutant concentrations. But, if no effect is seen, one cannot conclude that no effect will occur in the general population at the measured or even lower exposures.

In spite of the various difficulties in identifying both exposure and outcome, there are data that can be summarized. And, although little of the work that has been done has considered all the above issues, we believe that the available data provide some insight into the health effects of sulfur oxides as assessed by epidemiologic techniques. There have been several recent reviews of the detailed data base for what are believed to be the health effects of sulfur oxides, including five that have been published within the last 5 years.[15,26,44,45(pp.243-288),47] Generally, the work of Firket on the Meuse Valley, the Belgian air pollution disaster of 1930, is described first, followed by the episodes at Donora in 1948 and at London in 1952 and 1962. Succeeding paragraphs or chapters bring the data up to about 1973. Each of these reviews can be referred to by any reader unfamiliar with the field. The present assessment does not review that material again. However, one recent series of investigations requires specific discussion.

In 1974, the first Community Health and Environmental Surveillance System (CHESS) report, *Health Consequences of Sulfur Oxides*, was published.[57] It covered the work done in 1970-1971 by the Environmental Protection Agency (EPA) in the CHESS program, which

at that time included several cities of various degrees of pollution exposure, both children and adults, and both ill and healthy subjects. A variety of epidemiologic studies were carried out, including descriptive studies of the prevalence rates of acute and chronic respiratory symptoms and of morbidity patterns, panel studies for "attack rates," and visits to hospital emergency rooms. The plan was that each of these studies be associated with either actual measures or at least reasonable estimates of ambient concentrations of oxides of sulfur, including sulfur dioxide, TSP, and suspended sulfates (SS). These CHESS studies have come under sharp criticism, which for the most part has been justified. However, some of the criticism might have been avoided had the CHESS results been published in the peer-reviewed scientific literature, rather than in monograph form. The recent "Brown Committee" report[58] details some of the criticisms of CHESS.

CHESS was an ambitious and worthwhile undertaking in 1968. It utilized a national program of standardized epidemiologic studies to determine the health effects of exposure to various concentrations of the common air pollutants (primarily sulfur dioxide, TSP, and SS). Although the difficulties involved in doing coordinated field research in several parts of the country simultaneously seem to have been fully appreciated by the research program team, the studies initially lacked sufficient quality control to make them useful for identifying specific concentrations of pollutants that could be associated with adverse health effects. The environmental monitoring techniques initially used lacked adequate sensitivity or lacked personnel of sufficient technical skill and experience to perform them. These problems frequently led to missing data points for which doubtful estimates had to be made. The health indexes focused on selected acute and chronic diseases, usually based on retrospective hypotheses that had been summarized in the initial air-quality criteria documents in 1969.[55,56] These indexes included: for the study of acute effects, worsening of existing disease, as monitored by the use of panels of well-defined groups of patients; and for the study of chronic effects, population studies of respiratory symptoms and pulmonary function in adults and children and measures of pollution. Although the CHESS findings reported so far are provocative and challenging, they cannot be used alone to alter or to confirm standards for sulfur dioxide and total suspended particles or for making judgments for a new standard for suspended sulfates. The report did reawaken concern for the role of sulfates in health.

Since the initial criteria documents appeared in 1969, additional data, aside from CHESS, have become available. The

applicability of these data in judging a concentration for a standard has been considered. Such a judgment requires information of many kinds, including scientific assessment of the data, as well as the entire process of standard-setting, which has social, economic, and political components that we believe are beyond the scope of this review. Thus, we must caution that, although we mention specific concentrations of sulfur oxides, we do so only for the purposes of scientific discussion. Conceivably, when such concentrations are considered with respect to standard-setting, political, economic, or other necessary social components of the standard-setting process must be evaluated.

For discussing who is at risk as a result of exposure to sulfur oxides, we have decided to consider the most "sensitive" persons and to include any measured effect. It must be emphasized that some of these effects may not represent disease. An observed effect may be temporary and have no permanent health implication. For example, an increase in the prevalence of nonproductive cough may not necessarily be an indicator of future productive cough. More information on dose-response associations is needed, to improve the quality of decisions as to what constitutes an acceptable risk. An excess of 1 day's morbidity from any particular pollutant concentration may be an adverse effect, but the judgment of the importance of such a finding is based on social, cultural, and economic determinations of acceptable risk.

Because there is no way to control all potentially confounding variables in epidemiologic research--particularly in the kinds of studies required to identify specific concentrations of pollutants to which potentially susceptible people in large groups might be reacting--we have accepted some data with the knowledge that alternative explanations might be offered by others. We believe that the studies that we have selected, although not perfect, all provide reliable data that are useful for drawing conclusions that, if not correct absolutely, are relatively consistent. We have relied heavily on what MacMahon and Pugh[39] have considered as causal associations. We have paraphrased their criteria as follows:

- *Time sequence*: In spite of inability to identify precisely the exposure that preceded the outcome, the probability of such a sequence must exist.
- *Strength of association*: The importance of a dose-response relationship is critical in estimating the effect of an air pollutant on health. Because of complexities of both exposure and outcome, we cannot accept as possible an all-or-none effect.
- *Consonance with existing knowledge*: Plausible biologic mechanisms must be consistent, disease distributions must be

consistent with hypothesized causal factors, and efforts to remove noncausal or alternative explanations must have little effect on the hypothesized causal factors associated with the disease in question.

We have worked from the premise that there is no doubt that short-term or acutely high concentrations of SO_x and particles that occurred throughout the industrialized world before the 1960s were associated with excess mortality. This is a moot point currently, because such concentrations are not likely to recur anywhere, even if current standards were relaxed modestly. We have sought to report information applicable to the identification of an acute effect, with "acute" being defined as measured by a 24-h average sample. Although there is reason to speculate from laboratory studies in animals and human beings as to the potential effect of short-time peak exposures, there are no data with which to make such a judgment for effects on general populations or groups of patients. Chronic exposures are judged on the basis of annual averages of 24-h values. Again, because of the lack of data, we cannot comment on the effects of peak exposures within the annual averages, except to point out that on occasion we have used winter averages as indicators of chronic exposures. This is not an unreasonable assumption for sulfur dioxide, in that most exposures in the studies reported were related to the use of fossil fuel to generate power for winter heating and industrial use.

In each case, because we cannot separate effects of particles from effects of sulfur dioxide, we refer to measured concentrations of both. The nature of interaction effects has not been properly evaluated in any case, so that we have no way of judging the importance of the interactions. Where necessary, we convert particulate measurements in terms of British smoke units to TSP (see Figure 28). Much of the currently produced particulate matter is not black or has various gradations of blackness; with the British smoke technique, these particles are not adequately measured. This method does sample the smaller particles that are in the respirable range. TSP measurements use a gravimetric method that measures weight of all particles collected. The particles collected can vary in size over a considerable range and frequently include those not of respirable size (>7 μm). Thus, high values of TSP can be influenced disproportionately by particles that are less likely to reach the lower airways. As a corollary, it would be possible to reduce the concentrations of TSP and have no effect on lower airways, because only the larger nonrespirable particles would have been eliminated. However, the larger particles may have effects on the upper airway and

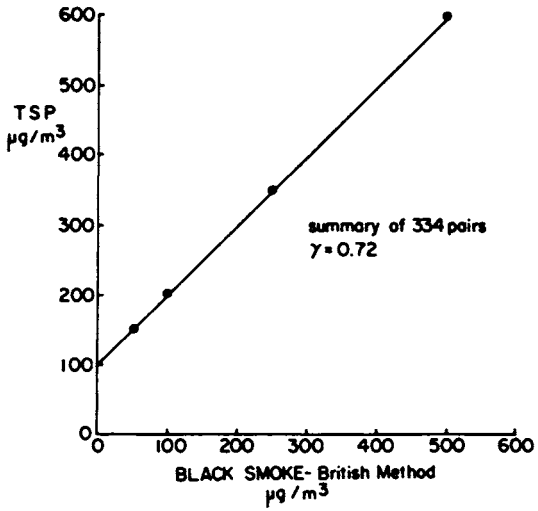

FIGURE 28 Relationship of black-smoke (British method) values and total suspended particles values. Plotted from data in Commins and Waller.[10]

gastrointestinal tract after being swallowed. There is a great need to obtain data on the effect of respirable particles (mass median diameter, 3.5 μm) and on the effects on man of particles in the accumulation mode (0.1-1.0 μm), which contains most of the sulfate. Similarly, British data for sulfur dioxide have generally been measured by back-titration of a hydrogen peroxide solution, whereas studies in the United States formerly used sulfation rates by lead candle techniques that measure total sulfur and more recently have used techniques that measure sulfur dioxide directly.

ACUTE EFFECTS MEASURED IN PATIENTS

Between 1958 and 1975, Lawther *et al.* studied a group of patients with chronic bronchitis. Using a diary technique, they collected daily assessments of symptoms for various periods. The earlier work, in 1958-1960, indicated that black smoke at 300 $\mu g/m^3$ (TSP equivalent, 380 $\mu g/m^3$) and sulfur dioxide at similar concentrations were associated with increased symptoms. With the general reduction in smoke pollution in London, more recent studies by Lawther's group[33,34] in populations of patients showed lower

correlations with pollution. There also appeared to be an adaptive effect, in that patients seemed more sensitive in early winter. The minimal daily concentrations associated with symptoms in these patients were approximately 250-300 $\mu g/m^3$ for sulfur dioxide and 250 $\mu g/m^3$ for smoke (TSP equivalent, 350 $\mu g/m^3$).

Emerson[14] made pulmonary-function measurements weekly on 18 patients with chronic obstructive lung disease over a period of 12-82 weeks during 1969 and 1970 in London. At that time, the maximal 24-h average smoke concentration was 241 $\mu g/m^3$ (TSP equivalent, 350 $\mu g/m^3$) and the sulfur dioxide concentration was 722 $\mu g/m^3$. Although the results of pulmonary-function tests varied with daily pollutant concentration and with those of the previous 4 days, the correlations were weak and as often in the negative as in the positive direction. The author concluded that pollution in London at the time of his study was not great enough to affect lung function in the patients studied.

Cohen *et al.*[8] in West Virginia followed a small group of asthmatic patients living in the vicinity of a coal-fired power plant. Exposure to the discharge from the plant depended heavily on wind direction, which was variable. Over a 7-month period, each of the 20 subjects completed a weekly diary on the status of his or her asthma or asthmatic bronchitis. Daily pollution measurements from two sites were available. Increased frequency of asthmatic attacks was associated with low temperature, which appeared to be more important than the pollution indexes. However, increased frequency of episodes was also associated with sulfur dioxide above 200 $\mu g/m^3$ and TSP over 150 $\mu g/m^3$ after temperature adjustment; this suggested that, at low temperature, these relatively high pollutant concentrations were associated with slightly increased morbidity among asthmatics. All concentrations of pollutants were considerably lower than those reported by Lawther *et al.* and Emerson.

Goldstein and Block,[19] studying asthmatic admission rates in several districts in New York City, found significant correlations with sulfur dioxide concentrations in one community, but not in another. They concluded that such correlations were unlikely to have arisen by chance and that unknown factors must have been operative in some communities, which presumably interacted with pollution to produce the results seen.

Chiaramonte *et al.*[7] reviewed the pediatric emergency-room visits to the Long Island College Hospital for the week of November 23-29, 1966. They compared these visits with those in the week before and the week after. Only sulfur dioxide concentrations were reported. Peak 24-h values of about 2,000 $\mu g/m^3$ (0.76 ppm) were reported for 2 days, and then they subsided. Usual values in this area ranged from 180 to 500 $\mu g/m^3$ (0.07 to

0.19 ppm). There was a delay of about 2 days before a peak in emergency-room visits of children with respiratory obstruction. The reported sulfur dioxide concentrations seem to be rather high, particularly for the days not associated with pollution. Data on particles were not reported, but the concentrations presumably ran parallel to those of sulfur dioxide. These data on pollution presumably came from the New York metropolitan area monitoring network and should be valid. Because the usual background sulfur dioxide concentrations measured at this site were so high, it makes one question the validity of the measurements. The exact concentrations at which effects occurred cannot be identified.

ACUTE EFFECTS MEASURED IN POPULATIONS

Although an earlier report by Buechley *et al.*[3] indicated that excess total mortality in New York City was associated with sulfur dioxide concentrations over 300 $\mu g/m^3$ (0.115 ppm), later data of Buechley from a period during which sulfur dioxide pollution had been reduced by a factor of 10 indicated the same correlation with the pollution index.[2] Thus, their measure of pollution may be an indicator of some other environmental factor that is correlated with sulfur dioxide, and this active agent may not have been reduced in the 5 years between reports. An alternative explanation is that only a small fraction of the population is at risk and that the fraction that was at risk at 300 $\mu g/m^3$ (0.115 ppm) was the same as that at risk at 30 $\mu g/m^3$ (0.012 ppm). A third explanation, suggested by Goldstein and Landovitz,[20,21] is that the measurement of pollution was based on a single monitoring station and data from that station may have been far from representative of the actual exposures. More acceptable would be the possibility that some local phenomena may have been operative during the second study to reduce the measured sulfur dioxide substantially. However, sulfur dioxide had been and has continued to act as an indicator variable, and that is why the effect has seemed consistent over the years. Schimmel and coworkers,[49,50] using the same data base, including a single air monitoring station to represent the metropolitan area, have pointed out the difficulties (including autocorrelation of season, temperature, and air pollution) of using time-trend data of this type. They are now convinced that they cannot demonstrate an effect on daily mortality of sulfur dioxide at concentrations below 300 $\mu g/m^3$ (0.115 ppm).

Martin[40] made observations on the relation of excess mortality and morbidity to sulfur dioxide and smoke concentrations in

metropolitan London from 1958 to 1962 and stated that the excesses appeared to follow a dose-response pattern. The data are plotted in Figure 29. From his tabulated data, we have calculated the intercepts for zero excess mortality or morbidity for sulfur dioxide and smoke (Table 17). The value for zero excess mortality for sulfur dioxide is 277 $\mu g/m^3$ (0.104 ppm), and for morbidity, 340 $\mu g/m^3$ (0.128 ppm). These are remarkably consistent with the values suggested by Schimmel *et al.*,[49,50] below which they could not identify an effect of sulfur dioxide.

Van der Lende *et al.*[59] reported on a series of studies conducted in two communities in Holland in 1969 and 1972. They demonstrated an improvement in pulmonary function between the two studies, whereas one would have expected a reduction due to aging. There was approximately a 10% improvement in function. They attributed this unanticipated finding to an acute reduction in air pollution. In 1969, the mean daily smoke concentrations were 100-140 $\mu g/m^3$ (TSP equivalent, 230 $\mu g/m^3$) and 24-h average sulfur dioxide concentrations were 200-300 $\mu g/m^3$ (0.076-0.115 ppm) during the 5 days in which the survey was conducted. During

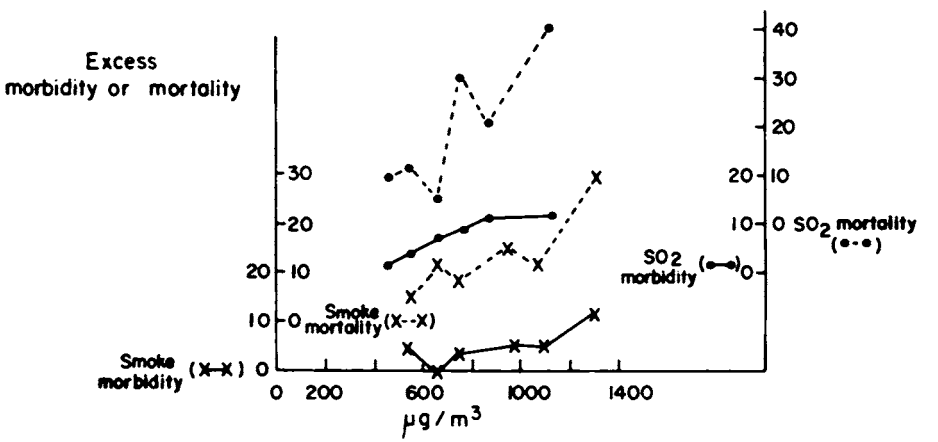

FIGURE 29 Association of black smoke (British method) and sulfur dioxide to excess mortality and morbidity (deviations from a 15-day moving average). Plotted from data in Martin.[40] (Note change in zero level for each curve.) Data not converted from British smoke units to TSP, because it is not clear that the previously mentioned relationship can be extended linearly to values as high as these.

TABLE 17 Intercepts for Zero Excess Mortality and Morbidity for Sulfur Dioxide and Black Smoke[a]

Pollutant	Excess	Intercept, $\mu g/m^3$	r
Sulfur dioxide	Mortality	277	0.44
	Morbidity	340	0.45
Smoke	Mortality	417[b]	0.52
	Morbidity	516[b]	0.42

[a]Calculated from Martin.[40]

[b]British smoke units not converted to TSP.

the later survey, the black smoke and sulfur dioxide concentrations were 30 $\mu g/m^3$ [TSP equivalent, 130 $\mu g/m^3$ and 75 $\mu g/m^3$ (0.029 ppm)], respectively. Thus, their conclusion, although somewhat tentative, was that they had demonstrated that pollutants at the higher concentrations observed were associated with an acute decrease in pulmonary function that was reversible.

Stebbings *et al.*[54] assessed the impact on pulmonary function in elementary-school children in Pittsburgh of an inversion with increased pollutants. They were not able to measure pulmonary function until a day or so after the pollution peak. They reasoned that, if pollution had had an effect, they would see an improvement in pulmonary function over a week or so when they made daily measurements of pulmonary function. The 24-h peak values were 500-700 $\mu g/m^3$ for TSP and 250-300 $\mu g/m^3$ (0.095-0.115 ppm) for sulfur dioxide. Their initial analysis did not show any consistent trend. For controls, they used two schools where the concentrations were relatively low, but they questioned whether these were appropriate controls. They may have missed the effect, inasmuch as their measurements started after pollution had subsided from its peak.

Although the studies cited represent small numbers of patients or selected population groups, there appears to be a convergence of the data: excess acute morbidity and mortality seem to become apparent at sulfur dioxide concentrations above 300 $\mu g/m^3$ (0.115 ppm) in association with comparable concentrations of particles measured in 24-h samples. These data must be considered cautiously, because the variations around exposure estimates have generally not been reported. Furthermore, inasmuch as the exposures to sulfur dioxide and particles result from a common source and generally are highly correlated with each other, it

is impossible in these studies to separate these associations to attribute the components of risk to individual pollutants.

CHRONIC EFFECTS

Two types of chronic effects need to be discussed: in one, we must be concerned with the direct production of disease; in the other, we must consider the production of increased susceptibility to the development of disease on exposure to another environmental agent (e.g., cigarette smoke) by prior exposure to excessive concentrations of sulfur oxides and particles.

Chronic Effects Measured in Adults

During the 1960s, there was a reduction of particles (black smoke) in the air in London, on the basis of annual average 24-h samples, from over 450 to 140 $\mu g/m^3$ (TSP equivalent reduction, from 550 to 230 $\mu g/m^3$). In the same period, the sulfur dioxide concentrations stayed at approximately 250 $\mu g/m^3$ (0.095 ppm). Fletcher *et al.*[18] found a decrease in phlegm production in working men who had not changed their smoking habits during the same period. The particles at high concentrations alone or in association with sulfur dioxide appeared to be acting as a pulmonary tract irritant, which was reduced by a reduction in particles, in spite of maintenance of the sulfur dioxide concentrations.

The series of studies in Berlin, N.H.,[16,17] can be used to separate the effects of sulfur oxides and particles. An improvement in respiratory symptoms and pulmonary function was noted between 1961 and 1967. During this time, the concentrations of TSP measured by high-volume samplers decreased from 180 to 131 $\mu g/m^3$. Sulfur dioxide "equivalents" were measured by lead peroxide candles, which measured a variety of sulfur compounds.* Over the same period, sulfur dioxide equivalents decreased from 0.021 to 0.014 ppm (56 to 37 $\mu g/m^3$). A followup that compared the results in 1967 with those in 1973 showed that no change was demonstrable in either respiratory symptoms or pulmonary function. This second period had a further decrease in particles from 131 to 80 $\mu g/m^3$; sulfur dioxide equivalents, however, increased, from 0.014 to 0.025 ppm (37 to 66 $\mu g/m^3$). Thus, sulfur dioxide equivalents were higher than in 1961. These findings suggest

*Equivalents found according to: mg SO_3 per 100 cm^2 per day × 35.5 × 2.660 = $\mu g/m^3$.

that the sulfur compounds were not having any effect at the concentrations measured in all these studies and that the earlier decrease in the TSP was associated with a reduction in respiratory symptoms and with improved pulmonary function, whereas the further decline in TSP resulted in no further improvement in respiratory symptoms or function. An alternative explanation would be that the sulfur dioxide concentrations in the 1973 study were causing more symptoms, which were not apparent because of the continued reduction in TSP. This interpretation seems unlikely, given the concentrations of sulfur dioxide measured.

These results should be generalized cautiously to other areas, inasmuch as Berlin, N.H., is exposed to the effluent from a pulp mill, which may differ from the usual urban pollution. To the extent that similar observations can be made in other communities, the results may be useful in defining a lower limit at which no effects can be seen.

Sawicki and Lawrence[48] studied a random sample of adults in Cracow, Poland. The measured extent of pollution permitted them to classify the subjects into two groups: high-pollution and low-pollution. The concentrations in the high-pollution area were for British standard smoke an annual mean of 169 $\mu g/m^3$ (TSP equivalent, 240 $\mu g/m^3$) and for sulfur dioxide an annual mean of 130 $\mu g/m^3$ (0.05 ppm). Concentrations in the low-pollution area were for British standard smoke an annual mean of 78 $\mu g/m^3$ (TSP equivalent, 180 $\mu g/m^3$) and for sulfur dioxide an annual mean of 42 $\mu g/m^3$ (0.016 ppm). Persons residing in the more polluted area had more respiratory symptoms and poorer pulmonary function than those residing in the area with less pollution. Crude rates for chronic bronchitis in males were 12% in the low-pollution area and 19% in the high-pollution area, and for asthmatic disease, 5% and 9%, respectively. Standardizing these rates to the total male sample population of Cracow produced the following results: chronic bronchitis, 15% in the low-pollution area and 14% in the high-pollution area; and asthma, 6% and 8%, respectively. These differences are not statistically significant. Sawicki and Lawrence pointed out that many of the inhabitants worked outside their areas of residence and that the exposures at their places of residence therefore might not represent their true exposures.

Chronic Effects Measured in Children

Lunn *et al.*[37,38] studied children living in several districts in Sheffield, England. They found excess respiratory illnesses and reduced $FEV_{0.75}$ associated with annual concentrations of sulfur dioxide and particles equal to 120 $\mu g/m^3$ (0.046 ppm) for sulfur dioxide and 180 $\mu g/m^3$ for TSP equivalents. Similarly, Douglas

and Waller[13] followed the 1946 birth cohort in Great Britain and found an effect up to 15 years of age in association with annual average sulfur dioxide concentrations estimated to be 120 $\mu g/m^3$ (0.046 ppm) and particle concentrations of 230 $\mu g/m^3$ (TSP equivalents). These differences did not persist to the age of 20 at these concentrations,[9] but the full effect of taking up cigarette-smoking has not yet been assessed in the cohort, because one would have to wait another 20 years for the cohort to be at maximal risk.

Mostardi and Leonard[42] studied 42 high-school students from an urban setting and 50 from a rural area. The method of selecting the subjects was not specified. Air pollution was measured by lead peroxide candle and TSP. Concentrations of sulfur dioxide equivalents were 96-100 $\mu g/m^3$ (0.037-0.038 ppm) for the urban area and 34-72 $\mu g/m^3$ (0.013-0.027 ppm) for the rural area. Concentrations of TSP were 77-109 $\mu g/m^3$ (24-h annual average) for the urban area and 71-83 $\mu g/m^3$ for the rural area. Values were obtained over 4-5 years. They observed lower maximal oxygen consumption, FVC, and $FEV_{0.75}$ in the urban group than in the rural group. These differences persisted even when the three black students in the urban group were excluded. The authors cautioned that the small numbers may not be representative and that the study needs replication. They did obtain data on smoking histories, but apparently did not use the information. They did not indicate whether the smoking habits were the same in the two groups. More smokers or heavier smokers in the urban group could account for the differences found.

Mostardi and Martell[43] had studied larger groups from the same urban and rural areas in 1970 (173 urban, 161 rural). They used simple tests of pulmonary function (FVC and $FEV_{0.75}$) and included only subjects who had been residing in the area for 4 yr or more. The two groups had similar anthropometric characteristics. The data were analyzed separately by sex. They also repeated their analyses of males after excluding those who admitted that they were smokers. They reported that the smokers from the less polluted area had higher values for pulmonary function than the smokers from the more polluted area. This constituted a similarity to their observations for all males and for the females. They concluded that the different proportions of smokers in the two groups (14 of 115, or 12%, of urban males and six of 96, or 6%, of rural males) did not influence their results. Of much greater importance, however, is the question of racial mix. In the first report,[42] the authors indicated that blacks were only in the urban population. In this study, there was no mention of race. If there were blacks in the urban population, this could account for the lower values for pulmonary function in that group,

because blacks tend to have lower values of pulmonary function, corrected for age and height, than whites. Because of this weakness, the study has limited applicability.

Chapman *et al.*,[6] from the EPA, reported a study of children in two communities during the 1971-1972 school year. Testing was done in the fall, winter, and spring. Average concentrations based on 24-h samples were: for sulfur dioxide, 11 and 23 $\mu g/m^3$ (0.004 and 0.009 ppm); for suspended sulfates, 10 and 13 $\mu g/m^3$; for TSP, 78 and 110 $\mu g/m^3$; and for respirable particles, 36 and 44 $\mu g/m^3$. This study was done primarily to evaluate exposure to particles. Effects were assessed by means of tests of pulmonary function ($FEV_{0.75}$). Results were adjusted for age and height. The authors analyzed blacks and whites by sex separately. During the first two survey periods, they used a hot-wire anemometer to measure pulmonary function. This device has been reported to give aberrant results, owing to collection of mucus on the wire and protective screen.[4] Therefore, the investigators substituted a dry-seal bellows spirometer in the third survey. No data were given in either of these two reports[4,6] to demonstrate the comparability of the two instruments, and the change in instrumentation could have affected the results. For the older children (9-13 years old), there were no data on cigarette-smoking. The authors did point out that the educational status of parents was higher in the less polluted community; this could be confounding, in that higher educational attainment and therefore higher social class have been associated with better pulmonary function. They concluded that the particulate exposure had had a strong deleterious effect on the $FEV_{0.75}$ in the children in the more polluted community. They did not believe that the concentrations of sulfur dioxide or suspended sulfates were significant contributors to the effects noted. In view of the lack of data on cigarette-smoking and the change of equipment to measure respiratory function, this conclusion seems unwarranted.

Hammer *et al.*[24] surveyed elementary-school children (grades 1-6) in two communities. The children took home questionnaires that asked about previous respiratory illnesses of all children in the household aged 12 yr or younger, living conditions, and parental smoking. Children with a history of asthma and residence of less than 3 yr in their current homes were excluded. Black and white children were analyzed separately. Reported pollutant concentrations are summarized in Table 18. Suspended nitrates were reported to be very low and thought to be insignificant. Response rates were about 80% in each community, but no information was given concerning the group that failed to respond. In one community, it was apparent that two physicians were "biasing" the data by their choice of diagnosis. This had

TABLE 18 Pollution in Two New York Metropolitan Areas[a]

Pollutant	Area	Pollutant Concentrations (24-Hour Annual Averages), $\mu g/m^3$ 1960-1970	1971-1972
Sulfur dioxide	1	Est. low	22-23
	2	175-425	40-50
Total suspended particles	1	No data	34-36
	2	85-195	60-90
Respirable suspended particles	1	No data	28
	2	No data	34-43
Suspended sulfates	1	No data	10
	2	~20	14

[a]Summarized from Hammer *et al.*[24] Area 1, Riverhead; Area 2, Queens, Bronx, and Sheepshead Bay.

to be taken into account in the analyses. Exposure to cigarette smoke in the home, type of fuel used for cooking and heating, educational status of the household, number of persons per room, and family size and composition were some of the items considered in the analysis. In accordance with their best estimates, the authors concluded that there was an excess of lower respiratory disease morbidity in children when average annual sulfur dioxide concentrations were 175-250 $\mu g/m^3$ (0.068-0.095 ppm), TSP concentrations were 85-110 $\mu g/m^3$, and suspended sulfate concentrations were 13-14 $\mu g/m^3$. As with all studies, the actual exposures of the children were estimated. The suggested concentrations of sulfur dioxide and TSP are consistent with those reported by others. No analyses were reported that tried to separate the effects of the three pollutants. Thus, these data would not be sufficient as a basis for setting a standard for sulfates.

There are more studies on the effects of chronic exposure to sulfur oxides and particles than on the effects of acute exposure. As with the acute exposures, stated chronic exposures are summary estimates, often from a single measuring site. Indoor exposures are not taken into account, and those stated are usually annual averages without estimates of variation. In other instances, ranges are given. Different methods have been used to measure the exposures, and our attempts to convert to a standard scale are not precise. Analyses of these studies in general have not tried to separate the effects of particles and sulfur dioxide.

Two studies have apparently been more concerned with the particulate component.[6,16] There is a need for studies of areas with relatively high sulfur dioxide and low particulate pollution and areas with high particulate pollution and low sulfur dioxide. Consideration must also be given to the effect on persons spending most of their time indoors, where the pollution mix may be quite different from the outdoor mix.

SULFATES

Conversion to sulfate, including sulfuric acid, is a major pathway by which sulfur dioxide and probably other sulfur compounds are removed from the atmosphere. A number of studies have tried to evaluate the effects of exposure to sulfates. These have been reviewed in an American Petroleum Institute monograph on microparticulate sulfates.[15] Only selected studies in that review and some more recent studies are commented on here.

In two studies, by Dohan[11] and Dohan and Taylor,[12] sickness absences in working populations were related to concentrations of suspended sulfates. The crude data indicated an association that was augmented by an epidemic of influenza. This study was replicated by Ipsen and co-workers,[28,29] who did more extensive analyses and studied three different groups. They also showed the crude association of sulfate to sickness absences, but pointed out that there was a seasonal pattern that produced considerable autocorrelation. When they took this autocorrelation into account, they were no longer able to demonstrate the association between sickness absences and suspended sulfates. They concluded that the sulfate concentrations measured (up to 35 $\mu g/m^3$) were not having a significant effect on sickness absences.

Another frequently quoted series of studies are the analyses of mortality data conducted by Lave and Seskin. Their initial studies used published mortality data by county boroughs for England and Wales; measures of air pollution represented by deposit index (total dustfall per month), smoke, or sulfur dioxide; and socioeconomic variables measured as population density (persons/acre × 10) and social class (I-V).[30] Because the pollution variables are so highly correlated with each other, any one tended to give similar results when regressed against bronchitis mortality. Each significantly correlated with bronchitis mortality when social class was taken into account. However, we are not able from the data presented to identify specifically which component of the air pollution was the more important. Similar findings were apparent for lung cancer and for pneumonia. However, in at least one set of analyses, there was a significant negative association between lung-cancer death rates and the pollution

measures; this suggests that pollution is good for people, that people who develop lung cancer move to cleaner environments (not likely at that time in England), or that there are other factors that are not being taken into account in the model being used. Cigarette-smoking, which was not considered in the analyses, could alter all the findings reported.

Lave and Seskin extended their analyses in a later paper[31] in which they attempted to assess the relative effects of air pollution, climate, and home heating on mortality rates in the United States. These data were for 117 standard metropolitan statistical areas (SMSAs) for 1960. In those analyses, they used mean TSP and minimal sulfate values as the pollution variables of interest. In general, the inclusion of the climatic and home-heating variables reduced the magnitude of the coefficients associated with the pollution variables and reduced the significance of the association while increasing the total r^2. In no case did the inclusion of these variables eliminate the significant associations previously described; but in each case in which the kind of fuel used in the home was included, the pollution variables were no longer significant. The authors pointed out that, as would be expected, the proportion of people over 65 was the largest contributor to the total mortality rate. Again, no data were given on smoking.

A more extensive discussion and analyses that included varying numbers of SMSAs for 1960, 1961, and 1969 were published in a book by the same authors.[32] The findings were essentially the same as previously described.

Despite the large volume of work and effort put forth by these authors, there are enough inconsistencies both within their own analyses and between their analyses and those of others to make it difficult to accept their various models as valid. Total mortality in SMSAs appeared to be most affected by the proportion of people over 65. However, when age groups lower than 65 are considered, this same variable, with the proportions of nonwhite and poor, became an indicator for the socioeconomic status of the SMSA. Thus, it appears that these variables were acting as surrogates; therefore, the pollution variables could similarly have been acting as surrogates in this model. The authors reported that lower death rates were associated with damp SMSAs (as measured by relative humidity). But they also reported that SMSAs with greater precipitation have higher death rates and that death rates decreased as the number of hot days (above 32°C, or 90°F) increased. The latter is in contrast with most of the reports in the literature, which indicate an increase in death rates during heat waves.

Lave and Seskin's approach used detailed analyses of a large number of factors. The authors pointed out some of the limitations

of their data, but those did not restrict their conclusions. Some of the associations could have occurred by chance alone, in view of the large number of comparisons made. The authors also had to rely heavily on the representativeness of the monitoring data for each SMSA. As previously discussed, a given monitoring station is significantly affected by the micrometeorology around it and may not be representative of its region at all.[21] Major shifts in the pollution variables could significantly alter the outcome of the regression analyses performed. Such studies should be repeated with more and better air-pollutant measurements and population data and with data on smoking and occupation. Lave and Seskin have stated that large numbers are needed to show any effect. This is undoubtedly true, but it would be worthwhile to examine more carefully and specifically identified exposed populations, so that such factors as cigarette-smoking and occupation could be examined.

If we ignore all the difficulties just mentioned in interpreting the Lave and Seskin data and attempt to use their derived prediction equations for total mortality to estimate effects of TSP or minimal sulfates, we are immediately faced with the additional problem of the multicollinearity of the independent variables. Thus, we believe that any estimate made from their equations cannot consider more than one component at a time and that the practice of summing the estimated components of the pollution variables to obtain estimated total change in death rates is inappropriate. Furthermore, many of the estimates that have been made from these data do not adequately consider the variability of the estimates. In fact, for most of them the 10% confidence interval includes zero change in the death rate.

Data from Winkelstein *et al.* also have been used to estimate excess mortality.[61] Winkelstein *et al.* noted a positive correlation between mortality from chronic respiratory diseases and sulfation rate, as measured by the lead candle, in the lowest two economic strata of a five-stratum classification. They noted no association between sulfation rate and total mortality or mortality from cancer of the bronchus, trachea, and lung in white men 50 yr old or older. Again, it is difficult to assess the significance of their findings. The lead candle was used, and what portion of the measurement was due to sulfate or to sulfur dioxide is not known. They also had no data on smoking or on occupational exposures, which could have severely affected their results.

In attempting to use these data to assess the risk of cancer, Winkelstein and Kantor[60] noted a positive association with particulate air pollution and stomach cancer in men and women 50-68 yr old. No such correlation was demonstrated with cancer of the bronchus, trachea, or lung or in persons over 70 yr old.

The finding by Ipsen and co-workers[28,29] of little effect of suspended sulfate up to 35 $\mu g/m^3$ and the limitations associated with the analyses of Lave and Seskin and of Winkelstein and co-workers indicate that there are not adequate data to establish a sulfate standard, and other more recent studies from CHESS designed to show the relative contribution of TSP, sulfur dioxide, and suspended sulfates have not yet been analyzed. A further problem with the sulfates is that they do not all have the same toxicity, so the standard would have to be limited to selected sulfates; and it has proved extremely difficult to identify the specific sulfates.

SULFUR TRIOXIDE GAS, SULFUROUS ACID, AND SULFATE AND BISULFITE IONS

There are very limited data concerning the effect of sulfur trioxide gas, SO_3, on man. It is presumed that the sulfur dioxide in the atmosphere is converted to sulfur trioxide or sulfurous acid, H_2SO_3, and eventually to sulfuric acid or a sulfate.

Studies by McJilton *et al.*[41] did identify sulfite ion in their mixture of sulfur dioxide and high-humidity air that had been allowed to age. An increase in bisulfite ion has been measured in men exposed to sulfur dioxide in chambers.[22]

Bisulfite ion has been shown to have biologic activity, but its role and the relevance of these observations to man is not clear.

CANCER

The role that sulfur oxides may play in the genesis of human cancer--particularly lung cancer--is still unclear. (See Chapter 7 for discussion of studies in animals.)

Lee and Fraumeni,[35] in a study of smelter workers, reported that exposure to arsenicals was strongly correlated with lung cancer in the workers. Sulfur oxides appeared to be acting as a possible promoter, rather than as a causative agent. The concentrations of sulfur dioxide were considerably above 1 ppm (2,600 $\mu g/m^3$).

Pike *et al.*[46] have reviewed the increased urban incidence of lung cancer, compared with that in rural communities, and concluded that there is a small urban-rural gradient that is overwhelmed by cigarette-smoking. This small gradient has been attributed to benzopyrene by Carnow and Meier;[5] their study, however, had only very gross estimates of exposure, and there was

considerable uncertainty about the extent of exposure. After standardizing for smoking history, Hammond,[25] in his prospective study, was unable to find any urban effect. Shy[52] also reviewed the role of air pollution in lung cancer and concluded that the concentrations of benzopyrene in general ambient air are so low that the probability of its having a role in the production of the urban-rural gradient in lung cancer is unlikely. Thus, an interaction between sulfur oxides and benzopyrene seems even more unlikely.

Because air pollution is such a complex mixture of compounds, it will probably be extremely difficult to identify the cancer-causing factors in it. In addition, the positive interaction of sulfur oxides or other air pollutants with known carcinogens (e.g., by cigarette-smoking and occupational exposure) should not be overlooked as a possibility. Holland[27] emphasized the complexity of the urban exposure and the difficulty in resolving the "urban" effect. Despite this caveat, current evidence does not suggest a significant role for the sulfur oxides in urban atmospheres in the United States in the production of lung cancer.

ANNOYANCE

The social awareness of air pollution has been studied in a few areas on the basis of annoyance reactions among the populace. This awareness has been related more to total suspended particles than to sulfur oxides. The results from different studies have been presented in a document on particulate matter.[55] The data include those from a study carried out in St. Louis, where suspended particles at around 100 $\mu g/m^3$ produced annoyance reactions in a considerable number of persons.[51]

A similar study was done in Birmingham, Alabama,[53] in which air pollution and annoyance were correlated. In that study, dustfall and total suspended particles were evaluated. The association between suspended particles and adverse public opinion was weaker than that between dustfall and adverse public opinion. Sulfur dioxide showed no relationship. However, the concentrations of sulfur dioxide in the communities tested were low. Because annoyance reactions are highly influenced by cultural and social factors, acceptable pollution may vary from area to area and may need to be determined for each area. Although surveys on annoyance may have many problems, it is possible to quantify such reactions when proper survey techniques are expertly applied.[36]

ESTIMATE OF PERSONS AT RISK

Several investigators have attempted to estimate the impact of air pollution on the general public health. To do this, they have used a variety of estimates of risk. Each of these analyses suffered from the extreme crudeness of the data base for assessing the risk. Our interpretation of these data does not encourage us to choose one analysis over another as being more reliable. Thus, when we consider the potential error in each measure, we are left with ranges of effects that are extreme. For example, Hamilton and Manne[23] used data of Lave and Seskin[31] and Winkelstein *et al.*[61] to obtain a range of excess mortality of 0.2-1.9% of total U.S. mortality for persons 1-74 yr old. For total mortality at all ages, the range becomes 0.1-1.0%. Great caution must be used in applying these results, because of the criticisms of the data on which they are based. As pointed out by Hamilton and Manne, these attributed deaths can be compared with those attributed to cigarette-smoking (approximately 17%) and those attributed to automobile accidents (approximately 5%).

DOSE-RESPONSE RELATIONSHIPS

A goal in the evaluation of the various epidemiologic studies is to develop a dose-response association for sulfur oxides and particles. We are concerned about the effects of short-term (24-h) and long-term (years) exposures, so we need to construct separate dose-response relationships for acute and chronic exposures. We have also selected studies that had reasonably adequate exposure data and, where appropriate, had controlled for cigarette-smoking. It must be emphasized that such an association does not necessarily imply causality. Furthermore, because sulfur oxides and particles have a common source, they are highly correlated and may also be surrogates for some other, more active pollutant.

Figure 30 shows the relationship for the acute effects. Only one study plotted reported no effects. We have not included the data from Stebbings *et al.*,[54] because of their own caveats and because the data were not obtained during the peak period of exposure. Obviously, the data in Figure 30 are limited and indicate the need for more such studies, preferably under conditions of high particulate and low sulfur dioxide concentrations and vice versa. To the extent that these are reliable data, it appears that a TSP concentration of 180 $\mu g/m^3$ and a sulfur dioxide concentration of 180 $\mu g/m^3$ (0.069 ppm) as 24-h concentrations probably should not be exceeded, if the most sensitive asthmatic subjects are to be protected. Cohen *et al.*[8] (3 in Figure 30)

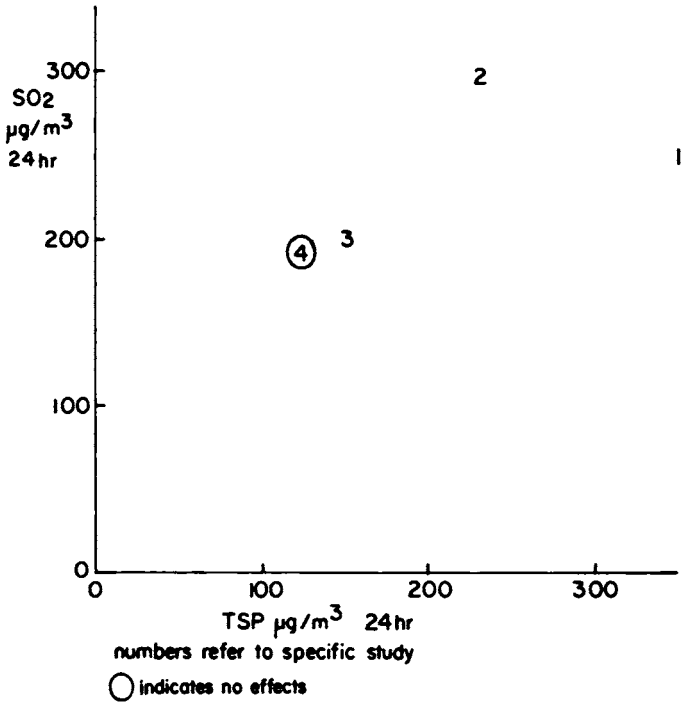

FIGURE 30 Acute dose-response relationships from selected studies: 1, diary data on bronchitis patients (Lawther *et al.*[34]); 2, decreased pulmonary function (van der Lende *et al.*[59]); 3, asthmatic attacks (Cohen *et al.*[8]); 4, lack of change in pulmonary function (Emerson[14]).

indicated that temperature had a much stronger effect than the extent of pollution. Other studies of asthmatics have shown them to be quite a heterogeneous group. Therefore, generalization from these studies must be done cautiously. If one considers these reversible symptoms in asthmatic patients acceptable, then a 24-h value somewhat above a TSP of 180 $\mu g/m^3$ and a sulfur dioxide concentration of 180 $\mu g/m^3$ (0.069 ppm) may be considered acceptable.

More data are available to construct the chronic-effects relationships based on annual averages of 24-h values. These are portrayed in Figure 31. It should be noted that one of the studies indicated no effect (11 in Figure 31), whereas another (14 in

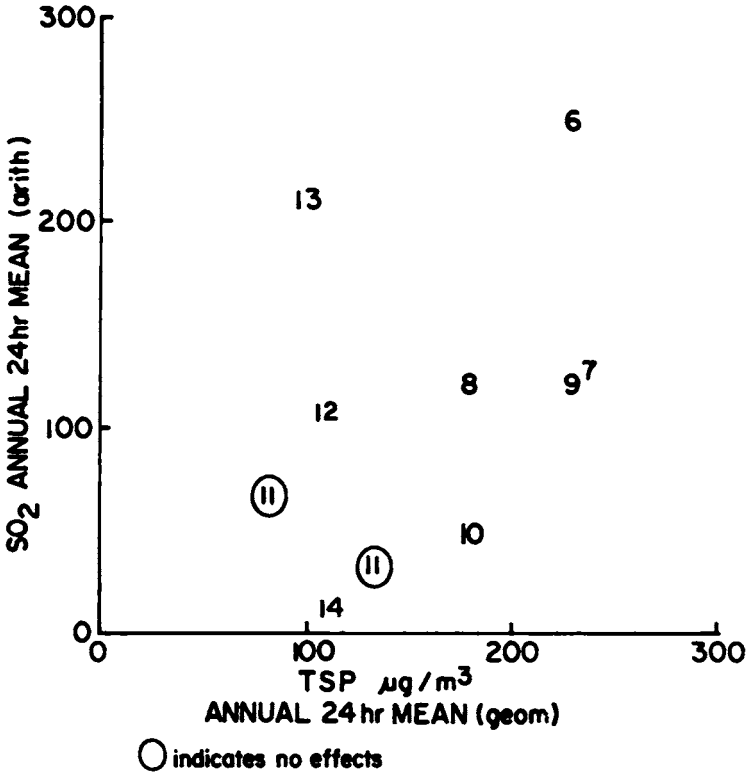

FIGURE 31 Chronic dose-response relationships from selected studies: 6, decreased phlegm production (Fletcher *et al.*[18]); 7, prevalence of chronic nonspecific respiratory disease (Sawicki and Lawrence[48]); 8, respiratory symptoms and pulmonary function in children (Lunn *et al.*[38]); 9, lower respiratory symptoms (Douglas and Waller[13]); 10, effect of particles--respiratory symptoms and decreased pulmonary function in adults--SO_x apparently without effect (Ferris *et al.*[17]); 11, no effects of particles or sulfur oxides (Ferris *et al.*[16]); 12, slightly decreased pulmonary function (Mostardi and Martell[43]); 13, increased lower respiratory tract involvement in children (Hammer *et al.*[24]); 14, possible slight decrease in pulmonary function (Chapman *et al.*[6]).

Figure 31) seemed to show an effect at about the same concentrations. This may be due to the use of different methods to assess health effects, to the use of different techniques in the measurements of air pollution, to actual differences in the composition of the air-pollution mix, or to the inherent variabilities in the measurement of pollutant concentrations and the assessment of health effects. As noted earlier, we cannot comment on the relative effect of a mean value that has relatively little variation about it, compared with one that has considerable fluctuations. It should be emphasized that more data are needed in the range around the primary standards, to obtain more complete documentation as to their adequacy.

In summary, sulfur dioxide does not occur as a single pollutant, and in all the aforementioned investigations it has been difficult to separate the effects of sulfur dioxide from those of particles or other pollutants. For acute or short-term exposure (24 h), concentrations of sulfur oxides somewhat below the present 24-h standard act as weak precipitators of asthmatic attacks and produce small reversible changes in pulmonary function. For chronic exposures, annual mean 24-h exposures somewhat above the current primary standard are associated with some increase in morbidity. With increasing concentrations of sulfur dioxide and particles, there appears to be a dose-response relationship between exposure and morbidity and, at high concentrations, mortality. Further investigations at or near the current primary standards are needed before changes in the current standard should be made.

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