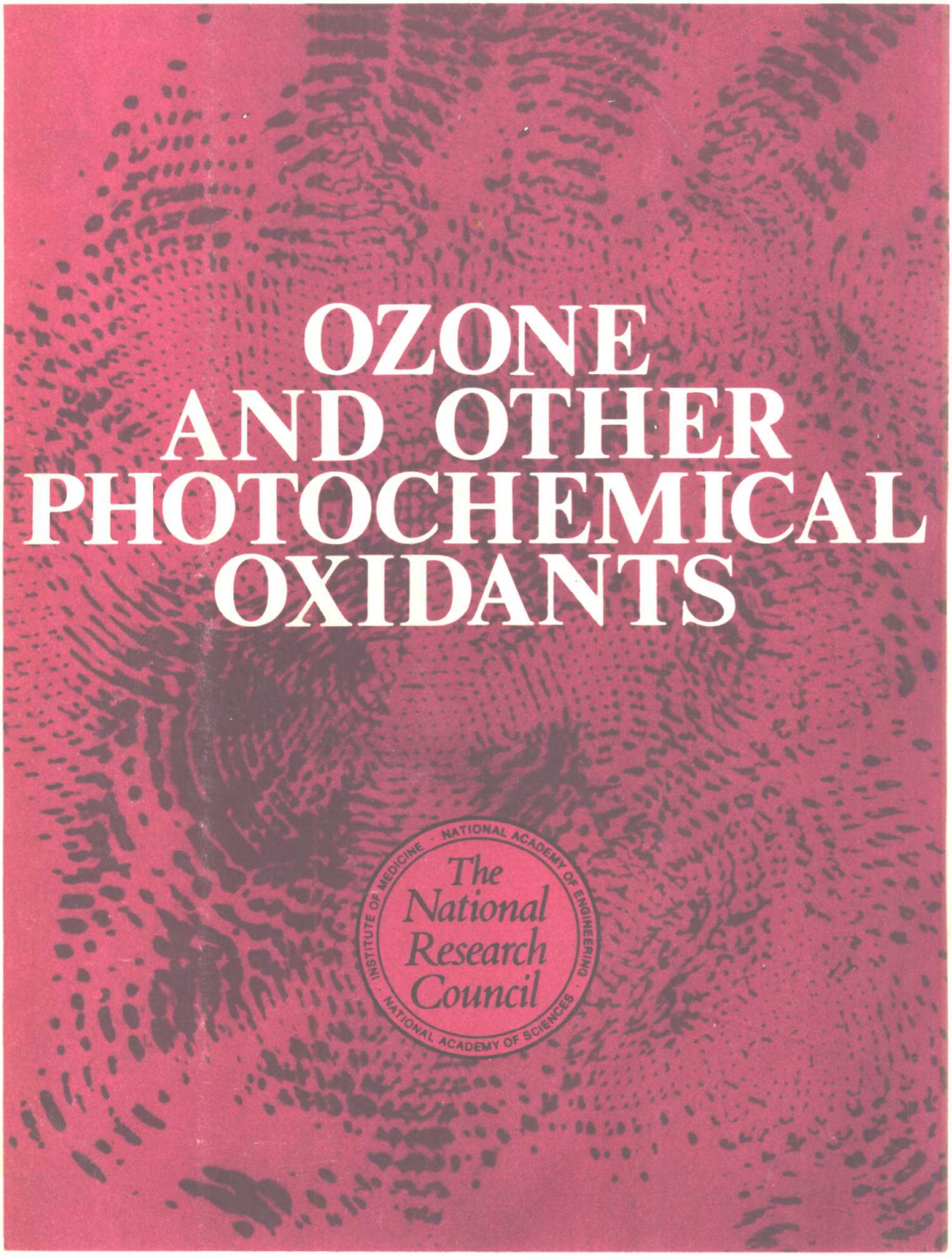
Medical and Biologic Effects of Environmental Pollutants



Medical and Biologic Effects of Environmental Pollutants

OZONE AND OTHER PHOTOCHEMICAL OXIDANTS

Committee on
Medical and Biologic Effects of
Environmental Pollutants

DIVISION OF MEDICAL SCIENCES
ASSEMBLY OF LIFE SCIENCES
NATIONAL RESEARCH COUNCIL

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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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This document was written by the Subcommittee on Ozone and Other Photochemical Oxidants under the chairmanship of Dr. Sheldon K. Friedlander. The members of the subcommittee and its consultants were chosen for their competence to prepare sections of the report. The entire document was critically reviewed by the subcommittee, and it represents the combined effort and cooperation of all its members and consultants.

The authors of the individual sections were as follows: Dr. Kyle D. Bayes, chemical origin; Dr. Daniel Grosjean, aerosols; Dr. Alan Q. Eschenroeder, atmospheric concentrations of photochemical oxidants and models for predicting air quality; Dr. Peter K. Mueller, measurement and methods; Drs. Karl A. Bell and Bernard Altshuler, respiratory transport and absorption; Dr. Sheldon D. Murphy in collaboration with Drs. Bernard D. Goldstein and Margaret Hitchcock, toxicology; Dr. Jack D. Hackney, controlled studies on humans; Dr. James R. McCarroll, epidemiologic studies; Dr. Walter W. Heck in collaboration with Drs. John B. Mudd and Paul R. Miller, plants and microorganisms; Dr. Miller in collaboration with Dr. Marshall White, ecosystems; and Dr. James R. McNesby, effects of photochemical oxidants on materials. Dr. Friedlander prepared the executive summary.

The document was reviewed by the Report Review Committee of the National Academy of Sciences; by the parent Committee on Medical and

Biologic Effects of Environmental Pollutants (MBEEP); by the Associate Editor, Dr. Ronald F. Coburn, and several anonymous reviewers; by the Advisory Center on Toxicology of the Assembly of Life Sciences (ALS); by the Committee on Atmospheric Sciences of the Commission on Natural Resources' Environmental Studies Board; and by the Committee on National Statistics of the Assembly of Mathematical and Physical Sciences.

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Executive Summary

In the early 1950's, it was reported by Haagen-Smit[1] that many of the characteristics of photochemical smog could be explained by the presence of ozone and other photochemical oxidants. These substances, he believed, were formed in the atmosphere as a result of chemical reactions involving nitrogen oxides and hydrocarbons present in automobile exhaust. Significant quantities of nitrogen oxides were also emitted by power plants.

Considerable time elapsed before there was general acceptance of Haagen-Smit's important discovery, in part because of its subtle nature. For the first time, a major air pollution problem was demonstrated to be caused by a pollutant generated in the atmosphere. Its effect often did not become apparent until many miles downwind from the source. (The same suspicion has been attached to sulfate-containing aerosols for many years, but the proof that the sulfate is damaging is not as well established.) In addition, a new pollution source, automobile exhaust, had been shown to be of prime importance.

After the pioneering studies of Haagen-Smit, an extensive scientific literature developed on the properties, measurement, and effects of photochemical smog. The attempt to control engine emission has had a profound effect on the automobile and petroleum industries. Estimated costs and associated benefits of automobile emission control each run into the billions per year.[2]

By the Clean Air Act Amendments of 1970, Congress set automobile

emission standards and instructed the Environmental Protection Agency (EPA) to set ambient air quality standards. Included in the Act was a requirement to review the standards periodically. It is hoped that this report will be of value to both Congress and the EPA in discharging their responsibilities for the review of these standards.

However, the Subcommittee on Ozone and Other Photochemical Oxidants did not discuss—and does not necessarily endorse—the adoption of fixed federal standards as the prime approach to pollution control. The subcommittee also did not attempt to determine the concentration at which the standard should be set, except to recognize the difficulty of arriving at such a number. There was, however, general skepticism concerning the applicability of the concept of threshold concentration (the concentration below which there are no biologic effects).

This report deals primarily with the origins and effects of ozone and other photochemical oxidants. It is limited, more or less, to the problem of urban pollution and to such closely related topics as natural background in the earth's boundary layer. No consideration is given to the stratospheric ozone layer and the effects produced by supersonic transport (SST) emission or halocarbons.

The reference method recommended by the federal government for the determination of oxidant measures ozone, which serves as an *indicator* of photochemical smog. Other agents formed in the photochemical system include a variety of free radicals in the gas phase and sulfates, nitrates, and oxygenated organic compounds in the particulate phase. A measurement of ozone alone provides only limited information on the concentrations of the other agents because of the complex chemical and mixing processes involved. How these other agents form and what their effects are remain poorly understood. Recommendations on studies involving such agents are found throughout this report.

We still lack an adequate dose-response relationship for humans exposed to ozone, particularly at concentrations less than about 0.2 ppm. The data base for the development of such a relationship for both short- and long-term exposures is inadequate. Although some data from controlled studies are available for concentrations above 0.3 ppm, methods for extrapolating to lower concentrations are needed. Moreover, it is not clear how to weight the results of pulmonary function tests on humans, animal studies, and epidemiologic studies in a general dose-response relationship.

Despite uncertainties concerning the causative agents and their effects, we must proceed with the regulation of emissions that lead to the formation of photochemical smog. At the same time, research should continue on identifying the individual harmful agents in photochemical smog and

determining their effects. Otherwise, there is danger of focusing on an indicator (ozone) while the formation and behavior of associated pollutants, which create a major part of the problem, are not adequately understood.

Approximately the first third of this report is concerned with the origins and measurement of ozone and other photochemical oxidants and the relationship of atmospheric concentrations to emissions. The middle third deals with toxicologic studies and effects on humans, and the last with effects on plants, ecosystems, and materials.

Each chapter is accompanied by a summary and/or a set of recommendations. Some of the most important points are identified in this Executive Summary, particularly those which cut across several fields. In some cases, the recommendations have been abstracted directly from the other chapters. For detailed recommendations, however, the reader is referred to the chapters themselves.

ORIGINS AND MEASUREMENT

The extensive scientific literature covering the chemistry of smog reactions is reviewed in Chapter 2. Even in the case of a single hydrocarbon with typical concentrations of the oxides of nitrogen, carbon monoxide, water vapor, and other trace components, several hundred chemical reactions take place. The urban atmosphere contains not just one but hundreds of different hydrocarbons, each with its own reactivity and oxidation products. Only a few of the reaction mechanisms and rate constants needed to construct realistic models of polluted atmospheres have been determined in laboratory studies under carefully controlled conditions. *Serious gaps remain in the present models, and further fundamental research on kinetics and mechanisms is necessary.* For example, rate constants are needed for almost all the reactions of hydroperoxy and alkylperoxy radicals. The homogeneous and heterogeneous reactions of the oxides of nitrogen with water also need study.

Smog-chamber studies are needed for validating both detailed chemical models and lumped models. Measurements of more products and the reactive intermediates, including such free radicals as hydroxyl and hydroperoxy, will provide more stringent tests for models. *There are useful interactions among modeling studies, smog-chamber experiments, atmospheric measurements, and fundamental chemical kinetics; it is not possible to ignore one without hindering progress in the others.*

The possibility that free radicals, particularly hydroperoxy, have significant effects on biologic surfaces should be investigated.

The available information on aerosol formation in photochemical smog

is reviewed in Chapter 3. The story told there is still not complete, but there is evidence that reactions involving ozone contribute significantly to the formation of both the organic and sulfate-containing components of the aerosol. Laboratory studies show that both cyclic olefins and C_{6+} diolefins are efficient aerosol precursors that lead to the formation of difunctional oxygenated organic compounds (such as dicarboxylic acids) of low vapor pressure. These compounds have also been found in the smog aerosol. Cyclic olefins have been identified in both gasoline and auto exhaust and might be an important source of secondary aerosol organics; sources of diolefins are unknown. The role of aromatics as aerosol precursors is not understood.

Aerosol organics in the atmosphere could be reduced by control of emission of nitrogen oxides and *total* hydrocarbons. However, the identification and control of a few *specific* aerosol precursors in gasoline and other sources might prove a more efficient approach.

Our knowledge of the chemical and physical processes that govern aerosol formation in the atmosphere is limited, and further research in the field is badly needed. Attention should be focused on laboratory studies of aerosol formation from aromatic hydrocarbons. The concentrations of aerosol precursors in the atmosphere should be determined; more data on organic compounds in ambient aerosols are needed to estimate the relative importance of olefinic and aromatic hydrocarbons as aerosol precursors.

The health effects of difunctional oxygenated organic compounds should be investigated in both animal and human studies.

A critical question concerning atmospheric concentrations of ozone and other photochemical oxidants is: "What fraction of the observed values in each locale can be controlled by reduction of emissions?" Some contend that natural background concentrations exceed the federal ambient air quality standard (0.08 ppm). Another point of view is that background ozone concentrations rarely exceed about 0.05–0.06 ppm at the surface and that higher concentrations are caused by man-made sources.

The data reviewed in Chapter 4 support the second point of view. Measurements in remote areas of the Northern Hemisphere, when compared with those in the lower 48 states of the United States, support the contention that man-made sources are involved in cases where the standard is exceeded. Further measurements are needed to establish this contention with more certainty. Some of the difficulties involved in such studies become apparent when it is noted that the effect of pollution—particularly nitric oxide emission—is to *reduce* ozone concentrations locally.

Theoretical interpretation of the experimental observations will help in determining the relative roles played by stratospheric injection, plant emission, background methane, and transport to surfaces in the natural portion of the tropospheric ozone cycle.

The most complete data on ozone and other oxidant concentrations have been obtained for the Los Angeles air basin, because of the severity of the problem there. Further measurements are needed in the central and eastern areas of the United States, to broaden the foundations of a national control strategy. Such studies should be designed with specific goals in mind, and not carried out as routine monitoring exercises.

Rational air pollution control strategies require the establishment of reliable relationships between air quality and emission (Chapter 5). Diffusion models for inert (nonreacting) agents have long been used in air pollution control and in the study of air pollution effects. Major advances have been made in incorporating the complex chemical reaction schemes of photochemical smog in diffusion models for air basins. In addition to these deterministic models, statistical relationships that are based on aerometric data and that relate oxidant concentrations to emission measurements have been determined.

Improvements in deterministic (photochemical/diffusion) methods are based largely on accounting for more physicochemical effects in the structure of the model. *Specific research subjects for improved models include photochemical aerosol formation and the effects of turbulence on chemical reaction rates.* The challenge to the researcher is to incorporate the study of these subjects without needlessly complicating already complex models. How accurate a mathematical simulation is required? What, roughly, will be the effect of omitting some particular chemical or physical component? What is the sensitivity of model outputs to inaccuracies in the inputs?

One of the most important contributions of research in this field will be the development of criteria to define the limits of applicability of existing models, rather than creating a single supermodel that will incorporate all effects.

Specific goals are essential in model development and in data collection for model-testing. Examples of goals are determining oxidant isopleths and relating visibility degradation to emission sources. *Monitoring programs should be designed with specific goals of data analysis or modeling. It should not be expected that, from the data alone, useful information will emerge directly, or that someone else will spontaneously dig out the important results.* Two important steps that can be undertaken by those who produce models to encourage application and aid the user are the compilation of a catalog of air quality models that describes their

capabilities in terms of a common set of performance standards and the improvement of model output to permit easy access by the user.

Methods of measuring the components of photochemical smog are reviewed in Chapter 6. There have been significant advances in the calibration of instruments for monitoring ozone in ambient air. A method based on the absorption of ultraviolet radiation at 254 nm has been adopted by California for the calibration of air monitoring instruments. The method is based on the use of a commercially available instrument that measures ultraviolet absorption as a *transfer standard* in the calibration process.

It is important to separate (conceptually and in practice) the calibration process from the monitoring process. Photochemical oxidants consisting primarily of ozone were continuously monitored first in southern California by measuring the color change of potassium iodide solutions brought into contact with ambient air. This measurement continues to yield valid photochemical oxidant data in California. However, it has yielded questionable data at ambient air monitoring sites elsewhere in the United States. For this reason, at the end of 1971, the EPA adopted a continuous monitoring process that involves the measurement of the chemiluminescence produced when ozone in air is brought into contact with ethylene. When it is *calibrated* with the ultraviolet-absorption method, this reference procedure for monitoring ozone in ambient air is widely accepted. *The evaluation of nationally applicable primary calibration procedures for ozone measurement should continue.*

Instruments based on differential ultraviolet absorption still need to be evaluated, and possibly modified, before their acceptance for *monitoring* ozone in polluted atmospheres on a nationwide scale. The California Air Resources Board and other air pollution control agencies are evaluating ultraviolet absorption with both chemiluminescence and potassium iodide instruments.

There is no commercially available instrument for the continuous monitoring of any of the chemical species present in the particulate component of photochemical smog. Methods should be developed for the direct and continuous measurement of such species. Species of interest include sulfates, nitrates, some oxygenated organic compounds, and lead.

HEALTH EFFECTS

A great deal is known about the deposition of aerosol particles in the lung and their later clearance. Less is known about the uptake of gases such as ozone and other oxidants that can react with biopolymers in the

mucous and tissue layers. Such information is important in understanding the site and mechanism of pollutant gas action in humans and the effects of copollutants like nitrogen dioxide and ozone, and in the extrapolation of dose-response data from animals to humans. What has been done in this field is reviewed in Chapter 7, which also discusses the information necessary for improved understanding of the transport process.

The solubility of the gas is important. For example, experimental data from studies carried out with dogs show that nearly 100% of highly soluble sulfur dioxide inhaled through the nose is removed before reaching the first bifurcation in the lung, whereas 27–70% (depending on initial concentration) of ozone, which is less soluble in water, is removed in the same region. In addition to solubility, chemical reactions in the surface layers are of great importance.

A concerted effort is needed to increase our understanding of the transfer and uptake of reactive gases in the lung. A program in this field should involve *in vitro* model studies, animal experiments, and clinical studies. More information is required on the chemical, physical, and morphologic properties of the mucous layer and the kinetics of the reactions of ozone in the mucous and tissue layers. Experimental data on uptake and dosage for ozone and other oxidants are difficult to obtain for the tracheobronchial and pulmonary regions. Such data for animals and humans will be needed to test the present simple transport models, before further refinements are made.

Toxicologic research (Chapter 8) on the effects of ozone in laboratory animals has demonstrated that exposure to airborne ozone at less than 1 ppm for a few hours produces numerous changes in cell and organ structure and function. The lowest concentrations that produce these changes differ somewhat among different species of laboratory animals and with the effect under observation. However, several functional and morphologic indexes of response to ozone are altered with exposures to concentrations of about 0.2–0.5 ppm over periods ranging from a few minutes to several weeks.

Recent studies involving repeated or prolonged exposures of laboratory animals to ozone have suggested that changes indicative of chronic lung disease (such as decreased elasticity of the lungs) also require concentrations of 0.2–0.5 ppm.

Exposures to ozone for a few hours result in a marked increase in the susceptibility of animals to controlled doses of infectious organisms introduced into the lung. This is the most sensitive test of any yet reported; significantly increased susceptibility of mice to one microorganism occurred after exposure to ozone at a concentration as low as 0.08 ppm.

Other reports with different microorganisms or different species have suggested that somewhat higher concentrations are required. *These findings suggest the need for carefully planned epidemiologic studies on the incidence of lung infection in human populations exposed to oxidant air pollution.* How do such studies relate to reported cases of human adaptation to long-term oxidant exposure?

Extrapulmonary effects have also been observed in laboratory animals at concentrations of about 0.2 ppm. These include reduced voluntary activity, chromosomal aberrations in circulating lymphocytes of hamsters, increased neonatal mortality, and greater incidence of jaw abnormalities in offspring of mice exposed to ozone. The mechanisms of these effects are largely unknown. *Reports of chromosomal aberrations in hamsters and of mutagenic activity of ozone in microorganisms and tissue cultures raise the question of a possible genetic or carcinogenic hazard. This should be tested experimentally and epidemiologically.*

There is evidence that nutrition affects animal response to ozone. Increased susceptibility has been reported in animals deficient in vitamin E—or the converse (protection conferred by administration of vitamin E).

Convincing new information on the health effects of oxidant exposure has emerged from controlled studies on humans, from which tentative dose-response curves have been constructed. These data are reviewed in Chapter 9, with the types of experimental facilities now available for such measurements. *The new data show reduced pulmonary function in healthy smokers and nonsmokers after exposure to ozone at 0.37 ppm and higher for 2 h. (The federal standard is 0.08 ppm for a 1-h exposure.)* Other gases and aerosols found in an urban atmosphere were not present in these experiments.

With various tests of ventilatory function, it has been shown that healthy male college students experienced no effect of sulfur dioxide at 0.37 ppm, a 10% decline in function with ozone at 0.37 ppm, and a 20–40% decline in function with a combination of sulfur dioxide at 0.37 ppm and ozone at 0.37 ppm. Other experiments have suggested an adaptation of southern Californians to chronic exposure to ambient ozone.

Further studies are needed to give better dose-response information and to provide a frequency distribution of the population response to oxidants alone and in combination with other pollutants at various concentrations. Such studies should include the effects of mixed pollutants over ranges corresponding to the ambient atmosphere. The mixtures should be carefully characterized to be sure of the effects of trace pollutants on sulfate aerosol formation. The design of such studies should

permit extrapolation from animals to humans and from small groups of humans to populations. Further research on the possibility of human adaptation to chronic exposure to oxidants is desirable.

Safety, ethical, and legal considerations require that the utmost care be exercised in human experimentation. The risk inherent in this work can be minimized by the proper design of facilities for human exposure to reactive gases, such as ozone and sulfur dioxide, and reactive gas mixtures. *Standards for the exposure of humans to such controlled atmospheres should be discussed by national groups and agencies, such as the American Medical Association and the National Institutes of Health.*

Studies of the reactions of population groups to photochemical smog are reviewed in Chapter 10. Such studies played a major role in the establishment of the current federal standards. Included were eye irritation studies, effects on asthmatics, and the responses of groups of high-school athletes. Uncertainties in the design of these experiments and interpretation of the data make further epidemiologic studies essential.

Two major studies are being conducted by the EPA in Los Angeles on the effects of photochemical oxidants on health. The first is a survey of schoolchildren in seven communities representing different degrees of oxidant exposure. Rather detailed environmental monitoring data are being taken, and specific health characteristics are being followed, including chronic respiratory disease in adults, lower respiratory disease in children, acute respiratory disease in both children and adults, pulmonary function in children, aggravation of asthma, irritation of mucous membranes, and tissue residues of trace metals. Complete data from this study will not be available until about 1980.

The second study is only beginning and will attempt to correlate the effects of photochemical oxidants and cigarette-smoking in promoting chronic respiratory signs and symptoms in cohorts of adolescents and their families. Pulmonary function tests will be included.

These studies are being carried out by EPA as part of the CHESS (Community Health Effects Surveillance Studies) program. *The results of these studies should be released as soon as possible for evaluation by the general scientific community.* This will permit the design and initiation of additional studies with modifications where necessary to supplement what has been done. *The continuation of epidemiologic studies, including those of the CHESS program, is vital to our understanding of the effects of air pollution on health.*

Other epidemiologic studies should be designed to seek analogues in human populations of effects observed in toxicologic and clinical studies,