Meetings

Air Pollution Medical Research

Scientists involved in air pollution medical research were provided the opportunity, at the Ninth Air Pollution Medical Research Conference, to review their history, take a look at their present status, and examine some future directions for research. Previous meetings were reported in *Science* [**141**, 832 (1963); **145**, 184 (1964); **154**, 1588 (1966)].

The Past

This series of Air Pollution Medical Research Conferences was "born" at the School of Medicine at the University of California in Los Angeles, in December 1956, when 21 investigators considered a number of research problems. Simulation of air pollution for experimental purposes was considered, as was the relationship of experimental and epidemiological data. The simple matter of how to do an experiment on air pollution was discussed.

The next several meetings were devoted to possible effects, as delineated by experimental and epidemiological studies. The group considered whether the information was adequate for public policies for control. People still say, "Do you know enough about air pollution to do something about it?" Scientists have, since 1959 when California first set air quality standards.

Some meetings emphasized statistics and epidemiology; one or two stressed community understanding.

Investigations are now in a phase where behind each conference is the thought, "How well can we use the information we have and keep getting—how to apply what we are learning?"

In 1957, pollution control was primarily a matter of smoke control from industrial chimneys. It was almost as local as things could be. The automobile and the power plant as major sources were suggested, but the role of medical research, in evaluating their possible consequences, was virtually unknown.

In 1959, the automobile industry indicated that California's requirements could be met in a year. But it took 5 years—in 1965, controls on exhaust from motor vehicles were required on the 1966 models to be sold in California. As soon as the practicality of this control program was demonstrated, it was adopted nationally.

There has been a change in values—acceptance of good air quality as a goal has been so rapid that public expectation is often ahead of the control program.

A few years ago, the relative importance of the health effects of air pollution, water pollution, and occupational exposures, found air pollution easily the most insignificant. But now air pollution programs are prominent, if not ahead of their companion programs, in governmental attention and research.

Part of the scientific uncertainty at the 1968 meeting, and in the future of air pollution research, lies in the rapidity of change in air pollution policy and air pollution control practices during the past decade.

The Present

Air pollution medical research is now in its "adolescence." Like many adolescents, scientists are in the process of losing some of their innocence about air pollution. They now know that specific effects of a single pollutant at commonly observed concentrations are not very likely. They know that most of the effects of pollutant exposure on health are the result of several pollutants reacting together, and often these pollutants and other factors reacting together.

Furthermore, they know also that the reaction to pollutants among even susceptible populations is not universal and identical. There is a wide variation of population sensitivity. In ten experimental subjects, one may be found whose effects are deviant from the group average. This does not mean that a process which is reflected by only one or two of these individuals may not be of great importance for a similar fraction of the general population.

There are three principal types of relevance for what was said at the 1968 meeting. First is relevance to air quality criteria. The second is relevance to medical science—the bank of knowledge, techniques, and concepts on which the scientific group depends to meet the unexpected problems, and which is essential in sustaining growth in scientific competence. The third major axis is that relevant to medical practice, to health care, to planning for health facilities, and ultimately to the responsibilities as doctors to individual fellow citizens. All three of these have relevance to public policy and to international cooperation.

Air Quality Criteria

Air quality criteria refer to evidence relating dose of pollution to associated effects.

With respect to specific air quality criteria, a series of papers concerned themselves with oxidant exposures. The group learned from reports of H. K. Ury (California State Department of Health, Berkeley) and B. W. Armstrong (University of Southern California, Los Angeles) that persons with chronic respiratory conditions have increased airway resistance when breathing air containing oxidant, and that this relationship is significant on exposure to oxidant in the neighborhood of 0.1 part per million. They learned from T. D. Sterling (Washington University) that there is suggestive evidence of a 3-day lag for the association of oxidants with admissions to hospitals for allergic, cardiac, and respiratory conditions. They learned from R. S. McMillan (University of Southern California) that despite careful tests to see whether lung function changes occurred in school children, we do not yet have evidence that such lung functions are altered by oxidant. Armstrong also discussed the problem of altered exercise tolerance associated with oxidant exposures, and some powerful ideas derived from animal studies were presented by L. O. Emik (University of California, Riverside), R. Rylander (National Institute of Public Health, Stockholm), K. H. Kilburn (Duke University Medical Center), and by R. H. Suhs (Presbyterian–St. Luke's Hospital, Chicago), J. L. Lumeng (University of Chicago), and M. H. Lepper (Presbyterian–St. Luke's Hospital). These studies will help in the design of future studies of the effects on human populations.

Concerning carbon monoxide, one of

the extraordinary things about meetings of this sort should be emphasized. Three papers by S. M. Ayres (St. Vincent's Hospital, New York City), S. I. Cohen (California State Department of Health), and M. Stupfel (Research Center for Atmospheric Pollution, Paris) were of substantial relevance to this problem. Each had rather modest conclusions of its own, but when all three are taken together, the findings buttress each other to the point that, following this meeting, it will be virtually impossible for responsible medical scientists to ignore the relevance of carbon monoxide to heart function and, possibly, heart diseases, Stupfel showed that 50 parts per million of carbon monoxide in unanesthetized rats had, as its only consequence, some reversible alterations in the electrocardiogram. Cohen reported a suggestive association of high community exposures to carbon monoxide with the case-fatality rate in hospital patients admitted with myocardial infarctions (heart attacks). Ayres reported an increase in coronary blood flow, and an increase in oxygen extraction, in human subjects experimentally exposed to brief, high levels of carbon monoxide (which lead to a realistic equilibrium level of carboxyhemoglobin). The same subjects had an increase in oxygen consumption and a decrease in mixed venous partial pressures of oxygen. Questions, as to whether children and adults behave differently to carbon monoxide exposure, were raised by a correlation study by E. J. Cassell (Mount Sinai School of Medicine, New York City). The possible association of headache with carbon monoxide levels was suggested.

As previously mentioned, it is no longer realistic to consider only individual pollutants in talking about pollutant effects. Accordingly, it is quite appropriate to note that sulfur dioxide and particulate (matter) exposures were considered together, not only in the epidemiologic studies in which their association was first noted, but also in experimental studies by G. G. Burton (Loma Linda University Medical Center). We heard data reported by R. E. Snell (Children's Convalescent Hospital Center, Washington, D.C.) on the effects of as little as 0.5 part per million of sulfur dioxide on pulmonary function in healthy persons. We need continued effort to find an experiment with human subjects which will reflect the expected synergism (total reaction which is more than the sum of the reactions to individual substances) that has been predicted from epidemiologic study.

Although, in general, this appears not to have been shown, it is important to note that in Burton's study one individual out of ten appeared to show this class of abnormality. This type of response may be more relevant to general population effects than those of the nine so-called "normal." J. Ipsen (University of Pennsylvania School of Medicine), M. Deane (California State Department of Public Health), and M. P. Verma (The Continental Research Institute, New York City) documented an association of combined exposures to sulfur dioxide and particulate matter with absenteeism of workmen. R. H. Hagstrom (Vanderbilt University) reported further on the possible association of particulate pollution with lung cancer, when socioeconomic factors were controlled for. There was evidence that chronic pulmonary disease is associated, not only with poverty and mobility and massively with tobacco smoking but also possibly with pollution according to reports of J. H. Stebbins (The Johns Hopkins University), P. E. Enterline (University of Pittsburgh), K. Biersteker (Municipal Health Department, Rotterdam), and M. Hashimoto (Ministry of Health and Welfare, Tokyo). Indeed, the finding of a significant association of pollutant levels with school absences was found by B. Paccagnella (Universita Degli Studi, Ferrara) in his study of school children in Ferrara, Italy (not in the portion of Ferrara with the highest pollution level, but in the portion of Ferrara with the lowest socioeconomic status).

We are thus beginning to narrow the gap which previously tended to separate the interpretation of experimental from epidemiologic findings in this gas-particulate complex.

For nitrogen oxides there were a number of extremely important studies. Longitudinal study by K. L. Gregory (National Center for Air Pollution Control, Cincinnati) of the survivors of the brief, presumably high-level exposures generated by the Cleveland Clinic fire appeared to show no difference between the longevity of exposed persons and that of controls. The role of nitrogen oxides in increased sensitivity to infection was suggested by T. L. Lewis (National Center for Air Pollution Control) and M. C. Henry (Illinois Institute of Technology Research Institute, Chicago; and structural changes in the lining cells of the terminal airway were again documented by G. Freeman (Stanford Research Institute). The possibility that persons with emphysema might show lung-function reactions to nitrogen dioxide exposure was considered in a preliminary paper by S. Rokaw (Rancho Los Amigos Hospital, Downey, Calif.), the main results of which will be awaited with great interest. With respect to the pollutant nitrogen dioxide, this meeting would seem to have been particularly constructive in adding to the knowledge and to the approaches which are relevant.

The possibility that asbestosis could be produced in urban populations from exposure to widespread, but low, levels of asbestos was discussed by I. J. Selikoff (Mount Sinai School of Medicine). Such exposures may take two or three decades to manifest themselves. It is reassuring that pathological changes previously reported to be associated with asbestos exposure, in nonoccupationally exposed persons in Finland and in South Africa, could have been derived from soil asbestos rather than from general neighborhood air pollution. This problem will require more attention in the future.

Medical Models

The models by which we study the health effects of air pollution are increasingly more effective. Lag periods between exposure to pollutants and effects on absences and symptoms were demonstrated. It is important to stress that models encourage a universal view of the fund of knowledge about air pollution. A model which is useful for studying changes in pulmonary function on exposure to oxidant could, for instance, also be useful for studying the effects of specific pollutants in an occupational setting.

The models have also been of increasing importance on a microscale. G. G. Green (Channing Laboratory, Boston City Hospital) discussed the importance of bacterial clearance by the alveolar macrophage in the lungs. A. Bouhuys (John B. Pierce Foundation, New Haven, Conn.) demonstrated the significance of histamine-release-producing pulmonary reactions from inhaled materials. B. Goldstein (University of Southern California) introduced the idea that lipid peroxidation (oxidation of fatty substances), which is thought to be associated with aging, may also be a specific reaction to ozone exposure. The importance of oxygen consumption

in the heart and the general circulation as an index of carbon monoxide exposure was presented. It is not necessary, perhaps, to stress the scientific importance of these papers, for they speak for themselves.

It is worth mentioning that certain things were not reported at this meeting, but are nevertheless of substantial research importance. First, there were no reports of the experimental exposure of human subjects to photochemical pollutants. This type of exposure would be of great importance in efforts to evaluate lung-function changes and to separate the effects of pollutant mixtures from the effects of ozone. There were no reports of exposure to lead as a community air pollutant, and none that was specifically oriented to point sources, such as sulfuric acid mist, fluoride, and others. The group who reported negative results, on the basis of careful experimentation on important questions made a real contribution. The entire group is grateful to them for defining their efforts, because it is only in this way that the progress of research can be evaluated and the soundness of policy be tested. Indeed, these scientists did an exceptionally good job in pointing out the limitations of their work and the implications of their findings.

Relevance to Medical Practice

Acute effects of air pollution have now been studied with sufficient care so that one can begin to predict, from air pollutant and other factors, how many additional people will be admitted to hospitals for respiratory and other conditions during high-pollution periods. It is also possible to get a feel for the relationship of acute pollution exposures to symptoms, to work, and school absences for respiratory conditions. And we are beginning to have a feel for the relevance of acute exposures to particle clearance mechanisms and possibly this is applicable to clearance of bacteria and to bacterial infection.

The chronic effects of air pollution were discussed mostly with respect to the respiratory system. Autoimmune mechanisms were suggested by Suhs, Lumeng, and Lepper as a factor in the evolution of chronic bronchitis. Aided by the splendid methodological work of W. M. Thurlbeck (McGill University), S. Ishikawa (University of Manitoba) and others were able to show that frequency of emphysema was much greater in autopsied persons in St. Louis than in Winnipeg. We now realize that smoking, age, and location are major factors in the occurrence of the condition, and the element which contributes to location is most likely to be community air pollution. R. S. Mitchell (University of Colorado) showed convincing data that the prevalence of the disease is underestimated by 50 percent.

The findings linking carbon monoxide to heart disease may have some significance for treatment of this condition by indicating that the use of oxygen early in the treatment may reduce the risks posed by carbon monoxide.

At the meeting in 1966, attention was directed to the importance of air pollution effects on children. At this meeting, there were four reports concerning the effects of air pollution on children. Paccagnella reported on the relationship of sulfur dioxide and particulate pollution to absenteeism of school children in Ferrara, Italy; there were reports of the relationship of pulmonary function to absenteeism in school children in Los Angeles, and of the relationship of symptoms (in children in contrast to adults) in New York City, by Cassell. A number of studies on the effects of air pollution on pulmonary function and school absenteeism in children in Japan were reported by Hashimoto. Clearly, this is a group of findings which will be relevant to practicing pediatricians. Again, the variability of populations, both in sensitivity and in mobility, will be extremely important. One could hope to have some studies of the effects of air pollution on children with asthma. Indeed, one could hope for more studies of asthma in children. The epidemiology of asthma is virtually unstudied, not only in this country, but elsewhere.

The clinical findings reported at this meeting only serve to emphasize the fact that one can no longer afford to consider air pollution as an exclusive interest. If illness experience of husbands is likely to be shared by wives—(as Enterline suggested) if one can reasonably infer that the illness of parents is likely to be shared by their children—if poverty (in addition to the devastating effects of poverty itself) is associated with increased effects of air pollution, scientists and physicians cannot in good conscience ignore these factors. It seems particularly urgent that if poverty is one of the important factors in chronic respiratory disease, it is time we set the explicit goal of finding out why this is so, and seeing what can be done to rectify it. If smoking cigarettes and air pollution have additive effects, as some of the papers strongly suggest for emphysema, this should not be ignored. Some of these findings can be incorporated into the clinical practice of medicine. The goal, of course, is that no environmental exposure should have any deleterious effects on the health of patients.

Future Indications

The ninth conference was an important meeting. It occurred at the same time strenuous efforts are being made to apply what is known within the framework of governmental policy. Indeed, 2 years hence, at the next meeting, the investigators will probably know how their data have been incorporated into air quality criteria, and applied to air quality standards. The impatient voice, calling for numerical air quality goals based on health considerations, was not a solitary one. Someone must answer it.

The importance of international cooperation in air pollution was emphasized by those who came from overseas, speaking often in languages which were not familiar to them. They contributed a rich store of scientific information. They also contributed a perspective on the relationship of research to policies and problems in their own countries. Their participation underlined something which is easily forgotten—that is, that knowledge of air pollution health effects is universal. Accordingly, it should be expected that documents on air quality criteria will reflect the world's experience with the relevant exposure problems.

In summary, this is a period in which this invisible college of air pollution medical scientists at adolescence is being "tested."

In orientation to the tasks ahead, needs must be examined in relation to goals. In general, better models are needed, both mathematical and biological. Specifically, additional studies are needed on the following:

Tolerance to ozone and oxidant exposures in humans; experimental exposure to photochemical mixtures to determine whether the effects of such exposures on pulmonary function are different than the effects from ozone exposure; the interaction of exposure to different pollutants—are effects additive, synergistic (more than additive), or less than additive; the effects of carbon monoxide on the cardio-

vascular system and on blood clotting; effects of carbon monoxide on the central nervous system and on complex sensory-motor performance; effects of nitrogen oxides and ozone on the structural protein of the lungs; significance of shifts in oxyhemoglobin dissociation consequent to air pollution exposure; effects of lead exposure on porphyrin synthesis; effects of community exposure to beryllium and asbestos; occurrence and mechanisms of sensitivity of children to air pollution exposures; role of air pollution in the epidemiology of asthma; role of air pollution in the epidemiology of emphysema; methods of treating air pollution reactions and of protecting unusually sensitive individuals; interaction of air pollution exposures with other respiratory exposures; magnitude and significance of domestic air pollution (within homes, schools, offices in public buildings, and other places).

We investigators are asked to be both good scientists and good scientific citizens during the next few years. We must continue devoting zeal to the kinds of things which scientific peers will respect, and which will advance the several disciplines.

Whether it be to our taste or not, in order to provide a basis for action, what is reasonably well known must be separated carefully from what we need to know. What is reasonably well known must serve as a basis for policy if it is relevant, and what knowledge is needed in order to act must become a priority, a priority for uncommitted public resources, so that the policies can become as constructive as the public interest demands.

But at the same time scientists are asked how these findings can be used for relief of a public which is growing tired of air pollution, and anxious about its effects on health. We can surely pass this test. If what the next few years demand is done, we shall be given more to do with other environmental problems—such as the effect of poverty on illness, the influence of migration, the impact of noise, and extremes of temperature. If we fail to pass these tests, there will be more confusion, more contention, more strife, and more uncertainty. If so, unfortunately, there is also likely to be more smog and more health effects resulting from it.

For the scientists attending this meeting, it was only an episode in the intellectual history which we are writing. As scientists, we must continue to write articles for the scientific literature, correspond with one another, visit each others' laboratories, challenge hypotheses, raise questions about the interpretation of data, speculate, and measure.

Above all, we should seek to understand the nature of the changes which man and his technology are making in our habitat. Once this understanding is at hand, there is an obligation to make it known, not only through meetings like this, but also in medical practice, through local medical societies, in various committees on which we serve, and as citizens relating to respective governments.

Proceedings will be published in the AMA Archives of Environmental Health.

JOHN R. GOLDSMITH
RUTH HARTMAN
State of California Department of Public Health, Berkeley

Calendar of Events

Courses

The **Marine Biological Laboratory** will conduct summer courses in (i) Experimental Marine Botany, (ii) Marine Ecology, (iii) Embryology, (iv) Physiology, and (v) Experimental Invertebrate Zoology. Each course is divided into two sessions. The first session, 16 June–26 July, is the formal course program and starts each day with a lecture. The postcourse research session, 27 July–30 August, divides the students into research projects with members of the instruction staff. Applications should be requested from the Laboratory and must be returned *before 1 March*. Limited financial aid for students is available. Two special research training programs on "Fertilization and Gamete Physiology" and "Excitable Membrane Biophysics and Physiology" will also be presented. (Homer P. Smith, General Manager, Marine Biological Laboratory, Woods Hole, Mass. 02543)

Laser Applications, St. Louis, Mo., 28 Apr.–2 May. The subject areas covered will include principles of gas, liquid, and solid-state lasers, parameter measurements, and beam control; applications in guidance, computers, communications and tracking, meteorology, diagnostics, medical, holography, and welding and machining. Fee: $275. (Dr. G. L. Esterson, Box 1048, Washington University, St. Louis, Mo. 63130)

Pathagenesis and Pathology of Infectious Diseases, Burlington, Vt., 21–25 July. This course is designed for the microbiologist with an advanced degree and for medical technologists with a broad background in diagnostic microbiology. An effort will be made to acquaint the participant with the lesions and clinical syndromes caused by common human pathogens. Current concepts of the pathogenesis of bacterial, fungal, and viral diseases will be emphasized. Registration fee: $30. (Dr. J. E. Craighead, Department of Pathology, College of Medicine, University of Vermont, Burlington 05401)

Mössbauer Spectroscopy, Washington, D.C., 16–20 June. This is an introductory course on the theory and interpretation of Mössbauer spectroscopy. Topics to be covered include the theory, instrumentation, and application to chemistry, metallurgy, and nuclear and solid-state physics and biology. Fee: $130. (Dr. Leopold May, Department of Chemistry, Catholic University of America, Washington, D.C. 20017)

Developmental Biology, La Jolla, Calif., 30 June–25 July. Is designed for those engaged in developmental research who wish to become proficient in the use of various molecular and cellular techniques. Participants are limited to 20. Is sponsored by the National Science Foundation which will defray the cost of travel and subsistence for each participant. Deadline for receipt of applications is *15 March*. (Dr. Herbert Stern, Department of Biology, University of California, San Diego, La Jolla 92037)

Physical Measurement and Analysis, Cambridge, Mass., 18–29 August. Is intended for professional people who make and analyze measurements or who design or supervise the design of experimental equipment incorporating measuring apparatus. The course will provide the background needed to make and interpret from dynamical and statistical points of view, measurements in the general mechanical engineering field. Measurements discussed will include displacement, strain, force, torque, velocity, acceleration, flow, temperature, vacuum, wear and surface characteristics. Methods for making measurements will include optical (lasers), mechanical, pneumatic, electric (resistive, inductive, capacitive), electromagnetic, photographic, acoustical, and radioisotope techniques. Fee: $450. (Director of the Summer Session, Room E19-356, Massachusetts Institute of Technology, Cambridge 02139)

Physics of Quantum Elctronics, Tucson, Ariz., 16–27 June. The topics covered will include stimulated light scattering and self-trapping phenomena, photon statistics, physics of ultra-short pulses, nonlinear optical amplification processes, Rayleigh scattering and light beat spectroscopy, self-induced transparency, laser physics, quantum theory of coherence in radiation and superfluid systems. (S. F. Jacobs, Optical Science Center, University of Arizona, Tucson 85721, or M. O. Scully, Department of Physics, Massachusetts Institute of Technology, Cambridge 02139)

Solid State Chemistry—The Nature and Properties of Materials, Montreal, Canada, 29–30 May. Is designed for teachers, industrial chemists, and others who are not specialists in solids, who would like to update their knowledge of materials. Lectures will cover the nature of crystalline and noncrystalline solids, the preparation of materials, and the electronic, optical, mechanical, and chemical properties of solids. Emphasis will be placed on the fundamentals of solid-state chemistry. (Professor Marcel Bourgon, Department of Chemistry, University of Montreal, Montreal, P.Q., Canada)