The methods and plan of a pilot study to obtain definitive data on the effects of air pollution on the health of selected cardiac and respiratory patients in their homes.

Measuring Reactions to Air Pollution

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THE nature and extent of the effect of airborne contaminants upon man's health are still matters for speculation. Most of the available and very scanty data have been gathered from three sources—the broad field of industrial toxicology, the several studies of catastrophes involving large groups subjected to extraordinary exposures (epidemic situations), and in the analyses of morbidity and mortality records.

Clinical and toxicological studies have their principal application in the protection of the industrial worker. The studies usually are supplemented by experimental investigations with animals and men to permit controlled observations of changes resulting from contacts with noxious materials. However, toxic and irritant materials rarely give trouble in an industrial environment until they are present in concentrations far greater than ever recorded in the usual urban situation. Consequently, values observed in the plant or obtained in the laboratory are not easily applicable to community problems.

An epidemic is defined as an unusual and widespread occurrence of disease. The catastrophic smog incidents and various accidents fall into this category. Since they represent the extremes, the amount of usable information contributed is therefore necessarily limited.

Analyses of excess morbidity and mortality rates in areas of low and high pollution unfortunately have definite deficiencies. If such data are used, we must assume that uncontrolled factors, such as age, race, and socioeconomic status, have no significance. This assumption obviously is not warranted in the face of considerable evidence to the contrary.

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Epidemiological Approach

Although the three sources of data have certain applications, they do not give enough information to permit the formulation of acceptable solutions for the low-level air pollution problems of cities (endemic situations). Since these situations concern the whole community, population studies using epidemiological techniques immediately come to mind. Today, we expect that a rounded investigation will make use of all approaches—clinical, experimental, statistical, and epidemiological studies of epidemic and endemic exposures.

The starting point for the classical studies of infectious disease usually has been an identifiable clinical reaction. At first we search for the agent or, if it is known, the demonstration of its characteristics and mode of transmission. Later, we try to determine host, parasite, and environmental factors governing the incidence and prevalence of the disease.

However, man is resistant and resilient. He can withstand and adapt to stresses and insults. This ability differs with age, sex, race, nutritional state, and other variables, but man's reactions are frequently subclinical, nebulous, or transitory. This is particularly true of exposures to toxic materials in the low levels found in community air contamination.

Accordingly, some workers believe air contaminants in low concentrations will never be demonstrated as the primary cause of disease but can be evaluated only as possible contributing factors. The epidemiologist learns early to accept the concept of disease as a summation of a complex of host, agent, and environmental factors. However, the community and industry insist upon exact quantification of single variables, particularly in pollution problems.

Past and present attempts to apply epidemiological techniques to air pollution studies have been elementary and limited in scope. These attempts have dealt with persons in respiratory contact with a complex of materials in widely varying degrees of duration and concentration. The objective usually has been to relate all illnesses having any possible relationship to these exposures, however slight. This goal has been forced upon the investigators because they must work without a definite clinical reaction, specific or nonspecific, associated with such exposures. Accordingly, their findings are received and interpreted with enthusiasm or with doubt, depending upon the desires and motives of their audience.

Today, communities require the extension and refinement of epidemiological observations by carefully comparing selected components of a population exposed to accurately described environmental conditions. The proper selection of indexes, therefore, is all-important. The difficulties encountered in the use of morbidity and mortality rates for the common respiratory and cardiac diseases are well known.

Still, the average duration of upper respiratory diseases or asthmatic attacks, the mortality rate of individuals with cardiac or pulmonary lesions, and similar measurements may deserve investigation. Whether they will serve or not will require many careful trials. At the moment, no entirely satisfactory study has ever been designed, and it is generally accepted that the search for methods to measure objectively human reactions to air contaminants must continue.

Such studies are not entered into lightly. The goal, essentially, is to relate the incidence, severity, and outcome of a group of clinical reactions, which may have a variety of etiological agents, to the presence or absence of a combination of air pollutants which may vary, absolutely or relatively, from time to time. Since precise morbidity surveys are costly and difficult, and the objectives are so illusory, few have been attempted. None thus far have succeeded in relating human disease unequivocally to differences in air pollution.

Preliminary Planning and Observations

Recognizing the limitations of analytical observations, a project to determine the feasibility of morbidity surveys was planned. The primary objective was to determine if practical investigations could be designed to permit reasonably accurate descriptions of the incidence, prevalence, and prognosis of disease in a population exposed to varying concentrations of air contaminants under urban conditions.

A field team, working under the close supervision of a competent advisory committee, was formed to conduct appropriate trials and test procedures and to appraise possible indexes. It seemed desirable and requisite to explore carefully all the various approaches before planning or embarking on a large-scale investigation.

One reason for this attitude was the considerable doubt of the validity of characterizing atmospheric pollution as high or low. The extreme variability of measurements and the significant overlapping of the observations have long been recognized. It seemed essential,

therefore, to obtain more specific estimates of the environment for correlation with the patients' reactions. Another reason was the resistance demonstrated daily by smokers and workers exposed to relatively high concentrations of a great variety of irritants. This implied that the observation of apparently healthy or even somewhat incapacitated individuals would not give significant results unless sizable samples were followed for many years.

However, some persons are unusually susceptible—the newly born and those with chronic cardiac or respiratory diseases. Their marked sensitivity due to a low respiratory reserve was notable in the epidemic incidents of London, Donora, and the Meuse Valley. A further advantage can be gained by restricting the choice of subjects to such persons. Since they may be confined or at least significantly disabled, they tend to remain in one locale instead of spending one-third of the day at work, one-third at home, and the remaining third elsewhere. Because exposure in each locale usually differs widely both in degree and kind of pollution, the use of patients with limited mobility diminishes the error of extrapolating environmental measurements made at 2, 3, or more external sampling stations.

As the planning progressed, various considerations led the investigative team to an even more circumscribed approach for the initial effort—use of exact measurements of a small group of selected individuals and their environment. We now believe that until such observations are available, large field surveys cannot be properly planned or conducted with any hope of success.

The Pilot Study

In our pilot study in Cincinnati, the pollution to which the test subjects were exposed was measured specifically. Persons with obviously diminished respiratory reserve, as indicated by breathlessness, were chosen and followed during January through April 1955, in order to include several periods of high concentrations of air pollutants. These carefully selected individuals were believed most likely to react clinically to variations in degree and amount of contamination.

The selected goal was to prove or disprove the hypothesis: "Fluctuations in air pollution, as measured by soiling of filter paper, are negatively correlated with variations in the patients' well-being as assessed subjectively by diaries and questionnaires and objectively by instrumental methods." Other useful observations were to be made at the same time, for example, the effect of temperature and humidity on cardiorespiratory patients.

We also hoped to find a more precise relationship between air pollution and well-being than is possible by designating pollution as high and low. Carefully observed clinical responses to many different degrees of air contamination might supply a curve demonstrating a more precise relationship. If a specific association could be demonstrated by such an

Nature of disability of 28 patients studied simultaneously, January–April 1955

Age	Sex		Nature of disability					
	Male	Female	Cardiac		Chest		Cardiac and chest	
			Male	Female	Male	Female	Male	Female
50–54	1	3	0	2	1	0	0	1
55–59	5	4	3	1	1	2	1	1
60–64	1	2	0	2	0	0	1	0
65–69	2	2	2	2	0	0	0	0
70–74	2	1	1	0	1	1	0	0
75–79	1	1	0	0	0	0	1	1
80–84	2	0	1	0	1	0	0	0
85–89	1	0	0	0	1	0	0	0
Totals	15	13	7	7	5	3	3	3

approach, the methodology for further studies could be arranged readily. A failure to show an association with these precise measurements would have a greater significance.

Patient Selection and Followup

Twenty-eight persons were recruited through out-patient departments, private physicians, and institutions for the aged (table). This was the smallest sample expected to supply definitive results. Twice as many would have been better. However, in addition to limitations imposed by the cost of instruments, serious difficulties were encountered in recruiting the proper type of cooperative patient who lived in a significantly polluted area.

Practical considerations required modification of the original criteria. One patient was hospitalized almost immediately, and it was necessary for various reasons to drop four more patients and to select others. Changes of this nature were required throughout the trial. Forty patients were followed for varying periods. Immobilization of the patient in the home became more important, not only because the measurement of atmospheric pollution was most specific there, but also because failure to contact the patient at the proper time upset the statistical plan and increased the work of the staff of visiting nurses.

The lung function tests employed were better adapted to following the progress of chest than of cardiac patients. However, this series contains few chest patients, although they were chosen whenever possible, because:

1. Such individuals appear to remain at work or at least spend more time outside their homes, until the disease becomes advanced and they are hospitalized.
2. They tend to reside in the less smoky areas of the town.
3. Epidemic smog incidents have indicated that cardiac patients are almost equally susceptible to atmospheric pollution.

Furthermore, tuberculous patients were deliberately avoided because the disease is frequently focal. Allergic asthmatics were likewise excluded because, ordinarily, allergens could be expected to vary independently of atmospheric pollution.

In the plan, the group was to be under observation by December 1, 1954. Unavoidable delays in assembling the equipment and the need for soundproof cabinets forced postponement until early January 1955. We hoped for the occurrence of a sufficient number of inversions to permit an appraisal of the value of this approach.

In this experimental effort, we were primarily concerned with variations in the individual patient's condition. The results do not depend upon changes in the sensitive individuals as a group from the beginning to the end of the trial period or on terminal differences between groups of patients exposed to different levels of air contamination. Thus, the weekly observations of the individual subjects are much more important than his physical condition before and after the trial period. Nevertheless, the clinical assessments were made as complete as possible.

The most important part of the pilot study was to determine and record at frequent intervals changes, however slight, in the patients' well-being. The success or failure in this effort depends largely upon such observations. The patients were asked to maintain a diary recording the occurrence or exacerbation of 12 symptoms. These were selected principally to elicit any unusual irritation of the upper respiratory tract and to record the day-by-day state of the cardiorespiratory system. Some were included to test the validity of the record.

Visiting nurses recorded the pulse, temperature, and respiratory rate, checked the diary, and noted any relevant change in the environment. To reinforce the subjective findings, they made certain objective measurements of lung function at predetermined intervals. If such epidemiological investigations of air pollution are to be pursued properly in the future, simple portable tests, readily adaptable to field requirements, must be developed. This has been given much thought, and some work has been done. Much more work is required, and we believe that this pilot study will be justified by indicating fruitful approaches to this question alone. However, the following were selected arbitrarily for objective measurements.

Timed vital capacity. The proportion of the total vital capacity expelled in 1, 2, or 3 seconds can be determined readily by the Gaensler vital-

ometer. For this investigation, we believe that a single interval will be sufficient but the most informative of the three will be chosen after preliminary trials with each subject.

Oximeter. In spite of many known sources of inaccuracy, the oximeter test of blood oxygenation has proved useful for following the progress of patients if cross-checked by simultaneous arterial puncture and gas analysis. In this study where variability from time to time was all-important and the other errors were not critical, it offered the advantage of being independent of patient cooperation, but the value of the observations is questionable.

Respiration. The maximum inspiratory and expiratory pressure test, not yet adequately evaluated, was included because of the rapidity and ease of use in the patient's home. It furnished some information on the relative contribution of viscous and elastic components of the lung to the total resistance and served as an index of patient variation.

Measurement of the Environment

Pollutants. We selected the American Iron and Steel Institute (AISI) automatic smoke sampler to estimate the concentration of air contaminants. This device gives an indication of the atmospheric concentration of "smoke" by aspirating air through white filter paper. Transmission of light through the spots obtained was used as a crude index of the amount of pollution in the patients' environment.

Temperature and humidity. Temperature and humidity were recorded by an 8-day automatic thermohygrograph. The temperature was obtained by a bimetallic unit and the humidity by a bundle of human hairs, each operating individual recording pens. These instruments were checked at weekly intervals by more accurate psychrometers and readjusted if necessary.

Location and servicing. Since the protocol required that the patient's environment be continuously sampled, these mechanisms were enclosed in a soundproof box, placed in or near the bedroom. Although the noise level was not great, the need to protect the instruments and to insure the patient against the possible irritation induced by the constant hum and periodic clicks, forced the development of an elaborate cabinet. It also seemed wise to fuse all circuits to avoid damage to the home or instrument wiring. The nurses checked and serviced the devices at each visit. The machines recorded for a week.

Other measurements. Although smoke was chosen as a crude index of the pollution faced by the patient, it is not to be inferred that it is the only, or even the principal, injurious component. Four Wilson sequence samplers were obtained to ascertain the extent of correlation between SO_2 (or total acid) and the concentration of smoke. This is a satisfactory instrument, but it is not entirely suitable for home installation because of the noise of the pump and the need for daily servicing. Therefore, they were used only in carefully selected locations. There was reason to assume that, except in the neighborhood of a major effluent, the levels of smoke and SO_2 would correlate reasonably well in Cincinnati.

The observations were adjusted to the community measurements of the United States Weather Bureau, the Cincinnati bureau of smoke inspection, and the Public Health Service Robert A. Taft Sanitary Engineering Center. High volume samples were obtained at five points. There were 20 dustfall stations and 3 smoke samplers in regular operation. These records of the external air in Cincinnati were correlated with the household observations.

Statistical Analysis

The technique of multiple linear regression will be used to evaluate the results. A separate regression analysis will be performed for each of the pulmonary function tests and for certain groupings of the subjective symptoms. We assumed that the value of each of these tests and symptoms can be represented by a model of the form

$$Y_i = B_0 + B_1 X_1 + B_2 X_2 + \ldots + B_{47} X_{47} + E_i$$

where Y_i is the ith observation of one of the tests or symptoms; and X's are certain reduced variates identifying lapse of time, patient, and environmental conditions at the time of measuring Y_i or during the preceding week; and E_i is the observational error. The effect of time will be removed by a second order polynomial; the effect of absolute differences in patient's

level of response will be removed by the corresponding terms in the model for each patient; and relevant environmental conditions are also represented in the model. In the light of these considerations it seems reasonable to assume that the E_i will be normally and independently distributed so that the usual tests of significance can be used. This assumption, of course, can and will be checked.

The sums of squares and cross-products for the variates will be obtained by punch-card equipment, and the resulting matrix will be manipulated with aid of electronic calculation.

Results

It is far too early to report or speculate about the observations. During the course of this initial study, an enormous number of observations were made, and the analyses, as have been indicated, will not be simple nor quickly made. Even this aspect of the project is considered essentially experimental and will require trial with various approaches.

Study Extension and Continuation

From the experiences of the past year, it is obvious that a determined effort should be made to obtain or develop simpler and more sensitive and objective methods for the assessment of respiratory efficiency. For example, the weight of the instruments, particularly the vitalometer, is at the upper limit. Also, it is essential to find a means for measuring the diffusion component of the respiration mechanism in the patient's home. Several other techniques are available, but each must be modified to meet the peculiar requirements of field investigations.

In view of the importance of eye irritation as a symptom in certain situations, we believe it is worthwhile now to consider the development of a quantitative objective method of measuring this reaction to air contaminants. Tentative steps have been made in this direction, but apparently a great amount of careful work will be required.

Furthermore, the continuous recording of the concentrations of particles of respirable size with the AISI samplers in the patient's home, if feasible, should be supplemented by measurement of gaseous acids. Only a brief trial of the Wilson sequence sampler was carried out in this pilot study. Also, no satisfactory method of silencing has been developed, and this defect, coupled with the need of frequent servicing, limits their use in human habitations.

Summary

The desirability for expanding investigations dealing with the many problems of atmospheric pollution has been accepted by all. They rank among the most important challenges remaining in the field of public health today. The immediate need for safe and practical disposal of airborne wastes and for rational controls cannot be ignored by the community, its industries, or the public health agencies.

Many of the proposed solutions are controversial because the reactions of man on exposure to common air contaminants at the low concentrations customarily found have not been described unequivocally. Lacking acceptable clinical evidence either pro or con, reasonable and rational control procedures cannot be instituted. Additional and more detailed epidemiological studies relating the reactions of man to this hazard are urgently needed.

We have outlined the pilot study now in progress in Cincinnati, in which the atmospheric pollution exposure of the subjects has been measured specifically and the effects of various concentrations have been sought in those individuals most likely to show measurable changes. In the event that an association between pollution and well-being is demonstrated, the methodology for further studies can be described easily. It may even be possible to institute an alarm system based on the behavior of cardiorespiratory or other sensitive patients followed in this way. On the other hand, with the precise measurements employed, a failure should have greater significance.

This approach is only one of many; it may succeed or it may fail. However, until human disease can be shown to be related to community air pollution in an acceptable fashion, the controversies regarding the degree and kind of control for air contaminants will continue.

RECENT BIBLIOGRAPHIES AND REPORTS

Campbell, I. R., Christian, M. R., and Widner, E.: Classified bibliography of publications concerning fluorine and its compounds in relation to man, animals, and their environment including effects on plants. Cincinnati, Ohio, Kettering Laboratory Library, Department of Preventive Medicine, University of Cincinnati, 1950.

Davenport, S. J.: Bibliography of Bureau of Mines publications dealing with health and safety in the mineral and allied industries. Washington, D. C., U. S. Bureau of Mines, 1946, 190 pp.

Davenport, S. J., and Morgis, G. G.: Air pollution: A bibliography. Bureau of Mines, Bull. 537. Washington, D. C., U. S. Government Printing Office, 1954, 448 pp.

Heimann, H., Brooks, H. M., Jr., and Schmidt, D. G.: Biological aspects of air pollution. An annotated bibliography. Washington, D. C., U. S. Public Health Service, 1950.

Jenkins, G. F.: Air pollution bibliography. *In* Air pollution abatement manual. Washington, D. C., Manufacturing Chemists' Association, Inc., 1952, ch. 12, manual sheet P-13, pp. 1–57.

Kramer, H. P., and Rigby, M.: Cumulative annotated bibliography on atmospheric pollution by smoke and gases. Am. Meteorol. Abstr. 1: 46–71 (1950).

Roth, H. P., and Swenson, E. A.: Air pollution: An annotated bibliography. Los Angeles, School of Medicine, University of Southern California, 1947.

COMPREHENSIVE ARTICLES

Adams, E. M.: Physiological effects. *In* Air pollution abatement manual. Washington, D. C., Manufacturing Chemists' Association, Inc., 1951, ch. 5, manual sheet P-6, pp. 1–28.

Batta, G., Firket, J., and Leclerc, E.: Les problemes de pollution de l'atmosphere. Paris, Masson and Cie, 1943.

Beaver, Sir Hugh, and others: Interim report of the Committee on Air Pollution. London, Her Majesty's Stationery Office, 1953.

Bloomfield, J. J.: Health implications of air pollution. Proc., Air Pollution Smoke Prevention Association of America, 1950, pp. 76–81.

Drinker, P.: Atmospheric pollution. Indust. and Engin. Chem. 31: 1316–1320 (1939).

Gilliam, Alexander G.: Some aspects of the lung cancer problem. Mil. Med. 116: 163–174, March 1955.

Hemeon, W. C. L.: Scientific boundaries in air pollution studies. Am. Indust. Hyg. A. Quart. 14: 35–40, March 1953.

Johnstone, H. F.: Properties and behavior of air contaminants. *In* Lectures presented at the inservice training course in air pollution, Feb. 6–8, 1950, University of Michigan School of Public Health. Ann Arbor, The School, 1950, pp. 17–25.

Kehoe, R. A.: Air pollution and community health. Proc., First National Air Pollution Symposium, Nov. 10–11, 1949, Stanford Research Institute, Stanford University, Calif., The Institute, 1950, pp. 115–120.

Lanza, A. J.: Health aspects of air pollution. Combustion 21: 56–57, January 1949.

Larson, G. P.: Medical research and control in air pollution. Am. J. Pub. Health 42: 549–556 (1952).

Logan, W. P. D.: Fog and mortality. Lancet 1: 78 (1949).

Marsh, A.: Smoke. The problem of coal and the atmosphere. London, Faber and Faber, 1947, pp. 72–73.

McCabe, L. C., Mader, P. P., McMahon, H. E., Hamming, W. J., and Chaney, W. L.: Industrial dusts and fumes in the Los Angeles area. Indust. and Engin. Chem. 41: 2486–2493 (1949).

McCord, C. P.: The physiological aspects of atmospheric pollution. *In* Lectures presented at the inservice training course in air pollution, Feb. 6–8, 1950, University of Michigan School of Public Health. Ann Arbor, the School, 1950, pp. 7–11.

McDonald, J. C., Drinker, P., and Gordon, J. E.: The epidemiology and social significance of atmospheric smoke pollution. Am. J. Med. Sc. 221: 325–342 (1951).

New York Academy of Medicine: Report of the Committee on Public Health Relations: Effect of air pollution on health. Bull. New York Acad. Med., 2d series 7: 751–775 (1931).

Russell, W. T.: The influence of fog on mortality from respiratory diseases. Lancet 2: 335–339 (1924).

Stanford Research Institute: Report of the Committee on Studies to Determine the Nature and Causes of Smog: The smog problem in Los Angeles County. Los Angeles, Calif., the Western Oil and Gas Association, 1954.