Epidemiologic Studies of Air Pollution*

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There is no dearth of data on this subject. That it may be inadequate for the purpose of proving cause and effect in regard to disease and air pollution is not to be denied, but its sheer mass almost overwhelms us. The problem is one of analyzing these data properly and viewing them in an appropriate perspective. We are dealing with many factors—multiple variables, multiple substances and combinations of substances, and, quite possibly, multiple and variable responses—which require more than the simple association which has provided us with so many of the leads and "proofs" that serve so well with a single infectious disease agent and the more acute disease reaction it provokes.

Morbidity and mortality data can serve two purposes. First is to give some idea of the magnitude of the problem in regard to the amount of disease present which is suspected to be associated with air pollution. These are descriptive data—somewhat equivalent to the morphologic description of the anatomists. Thus, one finds that chronic bronchitis in Great Britain is the third leading cause of death and the leading cause of disability and absenteeism.

Similarly, one finds that some of these types of respiratory illness, such as lung cancer, chronic bronchitis, and emphysema, are more frequently present in urban areas, and that in general, the rate present is in direct proportion to the population of the area. Air pollution, too, generally is greater in proportion to city size.

Deaths from lung cancer have twice the rate in metropolitan areas in the United States as compared with the national aver-
this implies that smoking, by itself, is not the sole factor influencing the occurrence of lung cancer. Stocks of England, has utilized lung cancer data and air pollution measurements in which he has shown a strong association of lung cancer and bronchitis with 3, 4-benzpyrene, and to a lesser extent, 1, 12-benzoepylene found in community atmospheres. In further studies in 23 localities, he has shown that for 13 trace elements found in urban air, lung cancer is associated strongly with beryllium and molybdenum, with arsenic, zinc, and vanadium showing a weaker association. For bronchitis, molybdenum appears to be the most important element, while for pneumonia, beryllium emerges as the most important one.

Already in this discussion, I have begun to overlap with the second use of some of these statistical data, that is, the comparative approach. This entails the adjustment of rates between groups or areas in regard to their geographic, ethnic, smoking, social, economic, and occupational backgrounds, and their comparison in regard to time. In California, an almost four-fold increase in emphysema deaths between 1950 and 1957 has been reported by Breslow and Goldsmith. The national data show a similar increase in this period.

The increase in emphysema appears to be continuing (Fig. 2 and 3) and is even more rapid than the striking and rather terrifying increase in lung cancer.

Greenburg and his associates have recently reported the findings of 220 excess deaths which occurred in New York City in 1953, associated with a temperature inversion and increased air pollution. This, the first example found in the United States that is similar to the famous London smog episodes, is evidence of the acute effects of air pollution on health.

There are some who would say that these data, along with many other studies not mentioned here, would constitute "proof" of the relationship between air pollution and adverse health effects such as lung cancer and emphysema.

At the same time, others would question the usefulness of such data at all, pointing out that they have many pitfalls. These critics state that such data may not be

![Figure 2](http://journal.publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/21378/ on 06/26/2017)
complete; all deaths may not be reported; all illnesses do not result in death (or may not result in death directly, and therefore, may be ignored in reporting); faulty diagnosis may give an erroneous picture of the actual cause of death; and other factors such as treatment, surgical skill, the patient's susceptibility to resistance may change the pattern of death.

I believe such data can show associations and provide leads which require further study. Facts must be observed, developed, and used; hypotheses alone are insufficient.

Thus, in the studies conducted by the Division of Air Pollution of the Public Health Service, more and more emphasis has been placed on studies utilizing direct controlled observation, which although susceptible to statistical analyses, have not been dependent on data less well controlled and objectively gathered. I am speaking of the surveys, field studies, and epidemiologic approaches which have been conducted by our staff, or through our support, by persons at universities and state and local health departments.

The largest epidemiologic study under-taken by our Division was done in cooperation with Vanderbilt University, the state and local health departments, and the University of North Carolina. This was a survey of Nashville, Tennessee entailing a huge air sampling program, the interview by questionnaire of some 3,000 families, and the pulmonary assessment of selected groups of patients and individuals. An overwhelming amount of data has resulted from that study, and already some of this has been rewarding.

Zeidberg and co-workers\textsuperscript{54, 5b} reported recently on 84 out-patients, 49 adults and 35 children, under treatment for chronic bronchial asthma. It was observed that the asthmatic attack rate in these individuals, as reported by them on a daily basis, varied directly with the level of sulphation in the residential environment. Sulphation was measured by a technique which gives an integrated summary of the amount of sulphur dioxide, sulphur trioxide and related compounds present in the atmospheric environment. For the adult asthmatics, the rate was three times as high in those living in high pollution areas compared to those
in the low. No consistent difference was noted by sex, but there was a higher attack rate for adults as compared to children. The pollution levels present in the three areas examined in this particular phase of the study were all moderate or low and consistent with those found in other cities of similar size in the United States.

Further analysis of these patients, for 27,440 person-days of observation, showed that attack rates on days with high versus low sulphur dioxide values were significantly different (Fig. 4). In this case, measurements were made for sulphur dioxide directly on a 24-hour basis. The attack rates were significant at the 5 per cent level; rates observed one day following a rise in pollution were even more significant. In these studies the influence of temperature, humidity, and barometric pressure on the asthmatic attack rate could not be demonstrated, but wind velocity showed an inverse relationship. This latter probably could be explained on the basis of the wind’s role in dispersing air pollutants.

I wonder if some of our apparent “drug failures,” our “untreatable” cases, relapses, exacerbations and unexplained variations—often ascribed to emotional as well as to other uncontrollable factors—may not be related to variations in the sulphur dioxide content of our environments. How many of us have observed days on which we had a larger than usual number of calls from our asthmatic patients, or observed more patients with cough and wheezing? How many of us thought of the environmental factors that might be the common denominator affecting the entire group?

I would like to emphasize that these studies now indicate the direction of the laboratory work which is necessary to provide the basic and objective measures needed. A device for screening was needed. In venereal disease studies, blood tests had served as an epidemiologic tool; in tuberculosis, the tuberculin test and the x-ray had played this role; in malaria, the blood film had worked. Now we saw the need for pulmonary function tests to help measure objectively the variations in persons exposed to air pollutants.

Spicer, Jr. and colleagues, of Baltimore used such tools. Further, he had realized that the variation in his patients’ conditions seemed related to some common external factors. He has now reported a study in which daily pulmonary function tests, including gross spirometry, airway resistance and compressible FRC (functional residual capacity) were determined in the body plethysmograph. These patients gave clinical history of cough productive of sputum almost daily during the winter months, for better than two years; physiologically they demonstrated evidence

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<th>Pollutant</th>
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<tr>
<td>DUSTFALL tons/sq. mile/month</td>
<td>26</td>
<td>83</td>
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<tr>
<td>SULFATION mgm/100 cm³/day</td>
<td>0.6</td>
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<td>SUSPENDED PARTICULATE MATTER µgm./M.²</td>
<td>109</td>
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of a moderate degree of obstructive airway disease. Spicer's data have shown that the patients become "better and worse together." In view of the non-homogeneity in the group, this "togetherness" strongly suggests that they are influenced by something they have in common, yet because of their out-patient status, they presumably have no common factor other than the general environment. The patients' changes from bad to worse were associated with increases in sulphur dioxide, particulate air pollutants, and on occasion humidity. It was observed that many of the changes in respiratory function varied so much from day to day—in the same patient—that the single series of tests usually done by the physician gave little reliable information as to the true condition present.

Spicer and associates' have concluded that there is no simple cause and effect relationship with any pollutant, but rather, that there seems to be a complex problem involving combinations of factors with subtle variations around the theme of environmental changes.
In another study, conducted by the Public Health Service in association with the Pennsylvania State Department of Health and with the participation of Prindle and co-workers and the assistance of Wright and his associates, pulmonary function tests and x-ray films were obtained and questionnaires studied on some 85 per cent of the population over age 35, in two villages.

In this case, one village had approximately 3.2 times as much sulphur dioxide on a continuous basis as the other (Fig. 5). In addition, there was several times more particulate matter in the polluted village. Pulmonary function tests performed included average airway resistance, maximum breathing capacity, one and three second timed vital capacity, residual volume, and total vital capacity (Fig. 6). This project, primarily designed as a methodologic study to assess the usefulness of these various pulmonary tests in field surveys, has not only demonstrated that these tests can be applied in the field and that they can discriminate between persons and groups, but it shows that in the village with high air pollution, the large majority of tests showed deviations from the normal more frequently. At this time, it is not possible to arrive at a "diagnosis" on the population as a whole, but it is possible to say that on the basis of the physiologic criteria the average values deviate from the normal and that there appear to be more individuals present in the polluted city whose deviations tend toward disease-conditions.

These epidemiologic approaches appear to be most fruitful as clues for laboratory investigations. The observation has frequently been made that the rising incidence of lung cancer might well be associated with previous episodes of influenza. A recent study reported by Wiseley and colleagues illustrates this.

They infected a selected strain of mice with influenza virus and observed that those who survived had a slightly increased cancer rate as compared to normal controls (Fig. 7). However, the cancer incidence was increased many-fold by the further exposure of these animals to an artificial smog consisting of ozonized gasoline. This, to my knowledge, is the first example of the production of a true epidermoid-type carcinoma in the lungs of animals by such a technique. Interestingly, the sex incidence of the animals was 29 males compared with nine females. This incidence is similar to that found in humans and certainly cannot be the result of differing occupational or smoking habits in the test animal.

I now come to my earlier question raised in regard to the problem of demonstrating cause and effect. The kinds of diseases and "agents" with which we are faced in this, and many other environmental problems, do not lend themselves to the use of Koch's postulates. We are not concerned with transmissible agents which may be grown on artificial media and transferred from one subject to another. We, therefore, must establish new criteria, and I would like to suggest to you that these might be: (1) statistical evidence that a disease or condition exists in the population; (2) epidemiologic evidence of the association between this disease or condition and a certain factor or factors present; (3) laboratory demonstration that this factor or factors can produce a condition in experimental subjects—similar to that found in the population; and (4) the ultimate demonstration that protection from this factor or factors will lessen the amount or severity of the disease conditions present.

If these postulates are sufficiently rigorous and acceptable, then I submit that with some of the data presently existing we are well on the way to establishing "proof" that air pollution can and does adversely affect human health.

**Summary**

Supplementing existing data which indicate an association between disease and air pollution, new epidemiologic studies provide evidence on the relationship of malignant neoplasms of the lung to air pollution, the distribution of deaths resulting from
emphysema and the apparent increase in this disease, the relationship of asthmatic attack rates to air pollution as measured by sulphur dioxide, and the effects of air pollution exposure on pulmonary function in a normal population.

Since epidemiologic studies cannot provide "cause-and-effect" proof, the author postulates that they must be supplemented by laboratory and other studies to strengthen the evidence. In order to establish "proof" that air pollution adversely affects human health, one must have: (1) statistical evidence that a certain disease condition exists in the population; (2) epidemiologic evidence of the association between this disease condition and a certain factor or factors present; (3) laboratory demonstration that such factors can produce a condition in experimental subjects similar to that found in the population; and (4) the ultimate demonstration that protection from such factors will lessen the amount or severity of the disease condition.

RESUMEN

En apoyo de los datos que indican una asociación entre la enfermedad y la polución del aire, nuevos estudios epidemiológicos proporcionan la evidencia de la relación entre las neoplasias malignas del pulmón, la polución aérea, la distribución de las muertes que resultan del enfisema y el aparente aumento de esta enfermedad, la relación de ataques asmáticos con la polución aérea medida de acuerdo con el contenido del aire en dióxido de azufre, y los efectos de la exposición a la polución aérea sobre la función pulmonar en una población normal.

Puesto que los estudios epidemiológicos no pueden dar prueba de "causa y efecto", el autor sostiene que deben ser completados por estudios de laboratorio para respaldar la evidencia. A fin de establecer "pruebas" de que la polución aérea afecta adversamente la salud humana, debemos tener en cuenta: (1) evidencia estadística de que ciertas condiciones patológicas existen en la población; (2) evidencia epidemiológica de la asociación entre esta enfermedad y ciertos factores presentes; (3) demostración por el laboratorio de que tales factores pueden producir una afección en sujetos experimentales similar a la encontrada en la población, y (4) la demostración final de que la protección contra tales factores disminuirá la cantidad o la gravedad de la enfermedad.

RESUMÉ

Des notions complétant ce qu'on sait déjà sur les rapports entre l'état pathologique et la pollution de l'air et de nouvelles études épidémiologiques apportent la preuve du rapport qui existe entre les néoplasies malignes du poumon et la pollution de l'air. C'est la répartition des décès dus à l'émphysème et l'augmentation apparente de cette affection, la relation entre le taux des crises d'asthme et de la pollution de l'air mesurée par l'anhydride sulfureux et les effets de l'exposition à l'air pollué sur la fonction pulmonaire chez des sujets normaux.

Puisque des études épidémiologiques ne peuvent apporter la preuve "cause à effet", l'auteur émet le postulat qu'elles doivent être complétées par des études de laboratoire et autres pour renforcer la preuve. Pour prouver que la pollution de l'air a des effets toxiques sur la santé de l'homme, on doit avoir:

(1) la preuve statistique qu'un certain état de maladie existe dans la population;
(2) la preuve épidémiologique de l'association entre cet état de maladie et la présence d'un certain facteur ou de certains facteurs;
(3) la démonstration au laboratoire que de tels facteurs peuvent produire un état pathologique semblable à celui constaté chez des individus étudiés à titre expérimental;
(4) la démonstration finale selon laquelle la protection contre de tels facteurs diminuera la quantité ou la gravité de l'état pathologique.

ZUSAMMENFASSUNG

In Ergänzung bereits vorliegenden Materials, das auf einen Zusammenhang zwischen Erkrankung und Luftverunreinigung hinweist, geben neue epidemiologische Untersuchungen Beweise für die Beziehung bestätigender Neubildungen der Lunge mit der Luftverunreinigung, für die Verbreitung der Todesfälle infolge Emphysems und der offenen Zunahme dieser Krankheit, für die Beziehung der Häufigkeit asthmatischer Anfälle zur Luftverunreinigung, mißt man diese an ihrem Gehalt an Schwefeldioxid, und schließlich für die Wirkungen der Exposition gegen Luftverunreinigung auf die Lungenfunktion einer normalen Bevölkerung. Nachdem epidemiologische Untersuchungen keinen Beweis für Ursache und Wirkung liefern können, stellt der Verfasser die Forderung auf, daß sie durch Untersuchungen im Laboratorium und anderer Art eine Unterstützung erfahren müssen, um die Beweiskraft zu verstärken. Um Sicherheit darüber zu bekommen, daß die Luftverunreinigung die menschliche Gesundheit ungünstig beeinflußt, bedarf es (1) statistischer Beweise, daß ein bestimmter Krankheitszustand in der Bevölkerung vorliegt; (2) epidemiologischer Beweis für die Verknüpfung dieses Krankheitszustandes und eines oder me-
A METHOD OF DEMONSTRATING SITE OF PERFORATION OF THE ESOPHAGUS

No undesirable effects have resulted from swallowing a Ryle's tube, nor was there any difficulty in passing the tube to the stomach. There might be some objection to passing a tube in a case of suspected rupture of the esophagus for fear of enlarging the tear, but it is felt that this is a theoretic objection and has not been borne out in practice in this small series. It must be remembered that the patient with a torn esophagus, though deprived of food and fluid by mouth, does continue to swallow considerable quantities of saliva and the accurate localization of a rupture may be a life-saving procedure. However, sutures in the esophagus are renowned for their weakness and in postoperative esophago-enterotomy cases, where a leak is suspected, it may well be advisable to pass a tube. Many surgeons, however, pass a tube at the time of operation and this could be employed. The tube method allows much more time for observation and suitable films to be taken, especially in the upper part of the esophagus, through which a bolus passes rapidly.


A CASE OF LEIOMYOSARCOMA

A case of leiomyosarcoma is described. Twenty-nine cases have been described in the literature and the present case is the 30th. The patient was a woman, aged 54, pregnant; the tumor grew rapidly and the patient died within six weeks. The tumor originated from the left upper lobe bronchus and infiltrated the whole lung, the parietal and the diaphragmatic pleura, and the pericardium; there were secondary deposits in the para-aortal and abdominal lymph nodes, and the lymph nodes of tracheal bifurcation. At necropsy, gross examination did not identify the type of tumor: it was classified on microscopic examination.