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AIR POLLUTION AND ASBESTOS CARCINOGENESIS: INVESTIGATION OF POSSIBLE SYNERGISM

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INTRODUCTION

Recently, we presented evidence derived from the investigation of two groups that multiple etiological factors may be of importance in the pathogenesis of lung cancer.

In the first investigation, we analysed the mortality experience of 370 New York-New Jersey asbestos insulation workers between 1963 and 1967 (Selikoff et al., 1968). These men all had long periods of occupational exposure to asbestos and were the survivors of a group of men who had been found to have a death rate from lung cancer which was approximately six times that expected for 1943-1962 (Selikoff et al., 1964). Their smoking histories were recorded in 1963. When observed prospectively, it was found that their lung cancer death rate was still extraordinarily high, but that the excess deaths were limited to those asbestos workers who also had a history of cigarette smoking. Of 87 men without such history, no lung cancer deaths occurred during the period of observation. On the other hand, among the 283 who had smoked cigarettes regularly, three lung cancer deaths had been expected, and 24 occurred. It was concluded that asbestos exposure greatly increased the risk of lung cancer from cigarette smoking and that an asbestos worker who smoked cigarettes had 92 times the risk of dying of lung cancer, compared to men who neither smoked cigarettes nor worked with asbestos.

These observations were later confirmed in a prospective study of 17,800 asbestos insulation workers in the United States and Canada from 1967 to 1971. Of these men, 9590 had a history of regular cigarette smoking, while 2066 did not (although 609 of them had smoked

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pipes and/or cigars). Among the 2066 non-cigarette smokers, 5.
from lung cancer were expected over the period of observation;
occurred. On the other hand, among the cigarette smokers, 25.0
from lung cancer were expected, and 134 occurred (Hammond & Sel
1973). We again concluded that employment in asbestos insulati
greatly increases the lung cancer risk for cigarette smokers, b
it was uncertain whether such employment significantly increase
risk of lung cancer among non-smokers.

In another study, the lung cancer experience of over one mi
men and women enrolled in a prospective epidemiological investi
in late 1959 and early 1960 by the American Cancer Society was
examined (Hammond, 1966). The subjects lived in 121 counties o
sizes and types, ranging from strictly rural areas to the most
populated cities. Special attention was given to areas conside
have severe general air pollution. All subjects answered detai
questionnaires, including questions on place of residence, occu
exposures and smoking habits. It was of interest to find that
between the ages of 30 and 64 who lived in cities or metropolit
areas, 29% said that they were or had been occupationally expos
air pollutants. Of equal interest, and perhaps contrary to the
popular image, farmers between the ages of 30 and 64 also state
they were so exposed: 53.8% indicated that they had had such ex
usually in the form of dust from fertilizers or vapours from ir
cides.

It had previously been found (Hammond, 1966) that lung can
deaths were uncommon among men who never smoked regularly: onl
deaths were recorded among 95,849 men with a total of 358,254
years of exposure to risk, i.e., a lung cancer death rate of c
0.14 per 1000 man-years. Of this small group of deaths, some
was attributed to occupational exposure, and the residue was c
ed perhaps to be due to general air pollution. However, this
was so small that it was felt that it would be virtually impo
to determine whether or not this was so. Altogether, the evi
interpreted as suggesting that multiple etiological factors c
of importance in lung cancer (Hammond & Selikoff, 1970).

The data in the second study did not appear to indicate
general air pollution *by itself* significantly increased the
lung cancer, and it was doubted that general air pollution w
rise to such a level as to present a significant risk of lun
to the non-smoker. Indeed, if it did, it was considered tha
cancer would then probably be the least of our worries. On
hand, the experiences of the asbestos workers in the first
suggested that multiple factors could be of importance in t
of lung cancer: certain occupational air pollutants and per
some degree, general air pollution could increase the risk
rette smokers.

PRESENT STATUS

We observed the 11,509 asbestos workers from January 1, 1967 to December 31, 1974. During this time (covering 66,523 person-years of observation), 1385 deaths occurred from all causes; 301 died of lung cancer, and 312 died of other malignant neoplasms, thus, 613 men (44.3%) died of one or another cancer. In addition, 109 died of asbestosis.

We are now analysing the observed and expected numbers of deaths among the workers in each of the 84 cities, taking age, year, sex and smoking habits into account. This is being done for the following categories: total deaths, all causes; total cancer, all sites; lung cancer; all 'asbestos disease' (lung cancer, pleural mesothelioma, peritoneal mesothelioma, cancer of oesophagus, stomach, colon, rectum); and asbestosis.

Recorded measurements of the listed air pollutants are also being analysed; for each air pollutant, the 84 cities being investigated have been divided into four ranks, ranging from high to low, by geometric averages of the recorded values. We are then analysing to determine whether there are variations in the ratios between observed and expected numbers of deaths in the several mortality categories and whether such variations will show any consistent pattern in relation to the concentrations of air pollutants in the cities concerned.

LIMITATIONS OF THIS STUDY

This investigation inevitably suffers from a number of significant constraints which should be recognized Firstly, while we enrolled the entire membership of the insulation workers' union on January 1, 1967, this cohort was clearly a survivor population, and we have no way of knowing if those who either left the union or died before 1967 were in any way different from those we observed prospectively between 1967 and 1974.

Secondly, while our data include the effect of long asbestos insulation employment [in which exposures changed comparatively little between 1935 and 1975 (Selikoff et al., 1965)], we have no information concerning concentrations of air pollutants before 1967 in the cities studied. Since the effects of air pollution on health may not be seen before a long period of clinical latency (as in the case of asbestos exposure), measurements between 1967 and 1974 may not represent a true index of such influences. Even if the relative standings of the 84 cities were the same in the past, as may well be, this is unlikely to have been the case for the individual pollutants, in view of changes in types of fuel consumption, automobile use and industrial outputs.

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Measurements of air pollutants are also encumbered by important uncertainties, since relatively few sites are sampled in any one city, and such sites were certainly not selected with the study population in mind. Even though the sites accurately reflected the ambient air in which the men worked, for two-thirds of the day an unstudied proportion of tne men may have been in quite different environments, at their homes. Moreover, their occupational environments may have had varying influences, since they were employed in such diverse settings as power plants, refineries, chemical facilities, boiler-rooms, construction sites for schools and commercial buildings, etc.

It should also be appreciated that while correlations were made with concentrations of air pollutants, the possible influence of other urban factors cannot be excluded.

Finally, and perhaps most important, it may materialize that the size of the population available for study is too small to provide statistical reliability in our analyses. Obviously, the addition of a third variable (air pollution) to the other two factors (asbestos exposure and cigarette smoking) greatly increases the sample size necessary, unless the effect is a very powerful one.

COMMENT

There are formidable difficulties in obtaining information concerning the hypothesis that carcinogenic agents in urban air may act to augment the carcinogenic potential of other factors such as cigarette smoking or occupational carcinogens. Nevertheless, the question is an important one since, should this be the case, even low concentrations of carcinogenic air pollutants might be of significance.

We have approached the problem by investigating the possibility that air pollution in the US may increase the carcinogenicity of asbestos. In doing this, we have sought to take into account a second neoplastic agent known to have an influence in the etiology of asbestos lung carcinogenesis, i.e., cigarette smoking. This factor is also an extremely important variable in any study concerning urban air pollution and lung cancer.

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