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POSSIBLE ETIOLOGIC FACTORS IN LUNG CANCER*

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The annual number of cancer deaths in the United States is steadily increasing, but this is due in large measure to the growth and aging of our population. After adjusting for age, it is seen that the cancer death rate among females has been going down since about 1936. We have reason to believe that this is attributable to a combination of more effective therapy and earlier diagnosis made possible through public health education. On the other hand, among males age-adjusted cancer death rates are rising.

Most of this increase, however, is due to the surprisingly rapid increase in deaths from cancer of the lung. A few decades ago the occurrence of bronchiogenic carcinoma was seldom observed but by 1942 it claimed the lives of 8,800 Americans. Only ten years later it is estimated that 21,000 of our people died of this cause. The most alarming fact is that the upward trend shows every indication of continuing.

For the present, at least, the problem is more serious among men than among women. About 2,200 women died of lung cancer in 1942 and 3,600 in 1952. By comparison, the lung cancer death figures for men were 6,600 in 1942, increasing to 17,400 in 1952. The highest incidence rates in males occurs in age group 60 to 70 and in females in age group 70 to 80. Most authorities are under the impression that almost all the increase has been in epidermoid type of carcinoma.

City dwellers seem to have a much higher incidence of these tumors than do inhabitants of rural districts. Among males, the death rate is more than twice as high in urban areas than in rural

* Condensation of the paper presented by Dr. Hammond at the meeting of the Association.

areas. However, it should be noted that these figures are based upon death certificate reports. The possibility exists that the differences noted above are due to errors in diagnosis and errors in specifying place of residence which combined may perhaps result in under-reporting in rural areas.

There is evidence that some cases of lung cancer have resulted from the exposure of industrial workers to dust or vapors containing such substances as arsenic, nickel, chromate, asbestos, radioactive substances, and coal tar fumes. However, there is little indication that occupational exposure to such substances has caused many cases of lung cancer in the United States. It seems most unlikely that industrial exposure could account for any large proportion of the lung cancers now occurring.

To account for the tremendous increase in this type of malignant neoplasm it seems that we must look for some factor, or combination of factors, which affect the general population rather than only a few highly specialized occupational groups. Furthermore, it would seem logical to be most suspicious of certain factors in the environment to which the public has been increasingly exposed during the last several decades. In addition, we might look for substances to which city people are more heavily exposed than country people and to which males are more exposed than females. We must also remember that there may be a delay time of as much as twenty years between exposure and clinical appearance of the disease.

Since we are dealing with a disease of the lungs, most attention has been given to substances which are inhaled. Among the numerous factors which have been suggested, at one time or another, the following four stand out most prominently.

Coal tar and certain oils contain chemical agents of known carcinogenic properties capable of producing cancer in experimental animals. The concentration of exhaust fumes from automobiles has been increasing greatly ever since 1900; practically the entire population is exposed to some degree; and city dwellers are more heavily exposed than country dwellers. However, this does not necessarily explain the question of sex difference.

The same can be said of the dust from tarred roads which is increasing and contains known carcinogenic agents.

Air pollution in the form of dust and fumes from coal and oil furnaces as well as from certain industrial processes has become a first rate nuisance in many communities, and the degree of exposure is greater in the urban than in the rural populations.

The three suspects named above are all being intensively studied in laboratories but the real question is whether or not the concentrations actually inhaled by human beings are sufficient to cause cancer of the lung, and this can only be discovered by epidemiologic studies on human population groups. Such investigations are both very difficult and very costly, but several are now getting under way. It will probably be a number of years before the results are known—and in the meantime the lung cancer death rate continues to rise.

By far the greatest attention has been given to a fourth factor, namely tobacco smoking. On the face of it this seems to meet most of the requirements for a first rate criminal suspect. The consumption of cigarettes has been increasing dramatically ever since World War I. The habit, as an almost universal custom, started first among men and spread to women at a later date. The tarry products of tobacco smoke have been used to produce malignant tumors when rubbed on the skin of experimental animals. However, I must add that such circumstantial evidence alone should not necessarily lead to a conviction and that other more direct evidence has been accumulating in recent years.

In 1928, Lombard and Doering of the Massachusetts State Health Department conducted a study in which patients were questioned about their smoking habits. A larger percentage of heavy smokers was found among patients with cancer of the buccal cavity than was found among other groups. No mention was made of lung cancer, probably because it was a relatively rare disease at that time.

The next significant study was made by Raymond Pearl of the Johns Hopkins University in 1938. By quite a different method of investigation he obtained evidence which seemed to indicate that heavy smoking produces an appreciable shortening of life expectancy. The volume of material was not sufficient to make an analysis by cause of death. After an initial period of excitement resulting from this surprising report, interest in the subject diminished.

In 1945, the results of a second study of smoking in relation to cancer were published from the Massachusetts State Health Department. This time they found a much larger percentage of heavy smokers among lung cancer patients than among other groups.

By 1950, the lung cancer death rate had increased to such proportions that it stimulated a renewal of interest in the problem and in that year the results of five major and independent studies were published. All of these investigations were conducted by the same method as that used in the original Massachusetts study. This is known as the historic method of investigation. All of them showed that upon questioning, a larger percentage of lung cancer patients report a history of heavy smoking than do control series of persons who do not have lung cancer. However, the order of magnitude of the correlation differed considerably between the studies.

For certain technical reasons, some investigators—myself among them—are not convinced that the methods of procedure used in these studies can be counted upon to yield valid, unbiased results. Most particularly, I am uncertain whether the order of magnitude of the correlation is so small as to be of only academic interest or so large as to be of great practical importance. Principally for this reason we are undertaking a very large-scale investigation of the problem using an entirely different method of approach. It may be described as the follow-up method as distinguished from the historic.

Between January and June 1952, volunteer researchers of the American Cancer Society obtained smoking histories on 204,000 white men between the ages of 50 and 69. Each of these men is being followed at annual intervals. For each death reported, the cause is ascertained from the death certificate. The first follow-up was done about a year ago and the volunteers successfully traced 99.4 per cent of the men originally questioned. If this efficiency can be maintained, we should have enough information to yield a conclusive answer in about one and one-half to two and one-half years from now.

Although our major concern is lung cancer, an analysis will be made for all major causes of death. Perhaps the most im-

portant finding will be the effect, if any, of smoking on the general death rate. If cigarette smoking proves to be seriously harmful, it is fair to assume that the tobacco companies will undertake research to discover the injurious ingredients and remove them from the product; otherwise at least some people may decide to give up the habit.

It is entirely possible, and indeed seems not unlikely, that a combination of factors rather than a single factor is responsible for the increasingly high death rate from lung cancer. Until the final answer is found, all reasonable possibilities should be investigated. The problem is much too serious to risk concentrating all our efforts on a single line of investigation even though at the moment it may appear to be the most promising.

PRESIDENT BONNETT — Thank you, Dr. Hammond.

The number of persons applying for insurance and giving a history of a nervous disorder or current nervous manifestations is increasing daily. Perhaps as a result of the unprecedented recognition of psychiatry by the armed services during the war, a general acceptance somewhat later by the medical profession, and now by the population in increasing numbers, people are willing to admit that they are "nervous" and to seek help. When psychiatric treatment is admitted on an application, we are frequently at a loss as to its significance or to the real nature of the disturbance. Until all of our examiners are basically trained in psychiatry, we shall continue to have this growing problem.

Fortunately, the death rate is not excessive, but we do have the problem of separating from among numerous applicants with nervous manifestations those who are potential suicides and those who are not. Those who are not are almost certainly standard risks. Dr. Peter G. Denker is well known to this audience. He has an excellent insurance background and is keenly aware of this problem. We are particularly fortunate in having him here to discuss, "The Evaluation and Classification of Neuropsychiatric Disorders."

Dr. Denker is Assistant Professor of Clinical Neurology at Cornell University Medical College, and an old friend of most of us here. It is good to welcome you back, Dr. Denker.