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EDITORIALS

Silicosis, Asbestosis, and Cancer of the Lung

The concept that members of occupations especially exposed to dust, particularly silica, have an unusual liability to cancer of the lung is an old one which is still held. Reliable epidemiologic data from various sources, however, show that pulmonary cancers are not excessively frequent among persons having occupational contact with coal[1-3] and silica dust [10, 15] and affected with anthracosis, silicosis, and anthracosilicosis, such as gold and coal miners. In fact, in radioactive ore miners with severe silicofibrosis in Schneeberg and Joachimsthal, who have a notoriously high frequency of lung cancer, the lungs are not often the site of such tumors.[13] Likewise, Bonser, Faulds, and Stewart[2] recently reported the existence of an inverse relation between cancer of the lung and siderosilicosis in English iron-ore miners. Merewether[10] noted that only 99 of 6881 cases of silicosis (1.32 per cent) were found to have carcinoma of the lungs on postmortem examination. In a series of 383 autopsy cases of silicosis in men 47 to 75 years old, lung cancer was present in only 7, *i.e.*, in 1.8 per cent against an expected rate of 9.9 to 12 per cent according to the age range and sex of the series.[14] Spörlein suggested on the basis of this evidence that an antagonism may exist between silicosis and cancer of the lung, especially since not a single instance of lung cancer was found among 187 men with severe silicosis.

The epidemiologic and pathologic evidence supporting a causal relationship between asbestosis and cancer of the lung, on the other hand, is quite substantial. Asbestos, a magnesium-iron silicate, mined on the North American continent and in South Africa, is incriminated in this respect.[3, 4, 6, 17] A total of 127 cases of asbestosis cancer of the lung are on record (United States, 21 cases; Canada, 6; Great Britain, 88; Germany, 12). Ten of the American cases were recently observed by O'Donnell[12] among 21 autopsy cases of asbestosis seen between 1940 and 1954 in a small community in Pennsylvania and occurring among employees of an asbestos textile plant.

The incidence reported for asbestosis cancer of the lung in autopsy series of asbestosis ranges from 7.5 per cent[9] to 50 per cent.[5] It is 15.5 per cent for a series of 738 autopsies of asbestosis with 114 lung cancers collected from the literature. According to Merewether, the male-female ratio of asbestosis cancer of the lung is at the low level of 2.45:1.

Asbestosis cancers show a diversity of histologic types. Among 56 cases, 29 were of squamous cell type, 15 were of the round cell–anaplastic variety, 7 were adenocarcinomas, and 5 were combination forms of squamous cell and adenocarcinoma. Asbestosis cancers follow the topographic pattern of asbestosis by involving often the lower lobes (four-fifths, according to Isselbacher, Klaus, and Hardy[7]). A multicentric genesis of cancer in the diffuse asbestotic lungs is not unusual. The exposure period to asbestos preceding and accompanying the development of asbestosis and cancer of the lung ranges from 6 months to 42 years. The lag between cessation of exposure and appearance of the pulmonary tumor may be

as long as 20 years. These tumors occur on an average at a somewhat earlier age than cryptogenetic cancers of the lung. The production of asbestosis cancers in experimental animals has not reliably been accomplished.[11]

It is uncertain whether a minimum of 170,000 dust particles per liter of air is a prerequisite for the development of asbestosis cancer in man and whether the inhaled particles must be above a certain size to be effective. Asbestosis cancer of the lung is a compensable occupational disease in Germany[13] and is notifiable with the Chief Inspector of Factories in England and Wales. In a Canadian case of occupational asbestosis cancer of the lung which was litigated, settlement was made in favor of the plaintiff. The available scientific evidence is adequate for recognizing asbestosis cancer of the lung for medicolegal reasons as an occupational disease. Since, at least in former years, industrial asbestos effluents caused local environmental air pollution, the possibility exists that in the absence of a history of specific employment of the deceased individual, asbestosis might be observed at autopsy because of former residence near an asbestos plant. Since asbestosis, like berylliosis, presents a characteristic histologic lesion, there should be no serious difficulty in identifying "neighborhood" cases of asbestosis and asbestosis cancer of the lung. Epidemiologic data available at present indicate that an increased liability to cancer of the lung is limited to the presence of asbestosis of the lung and does not extend to exposure to asbestos without the existence of a pneumoconiosis resulting therefrom.

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Medical Genetics

The science of genetics has made rapid strides during the past half century. Among the many applications of the recent advances in this field are those relating to human health and disease. That these applications are recognized as important is testified to by the results of a recent survey by Herndon[5] in which he reported that instruction in genetics is now given in 55 per cent of the medical schools of the American Association of Medical Colleges. The instruction varies from full-fledged courses to material included in didactic lectures.

Several thousand deviations from normality in man have been investigated from the genetic standpoint, and for several hundred of them a simple genetic basis has been reasonably well established. It is not a simple matter to confirm the genetic basis of a suspect trait, and precise technics are required for its establishment. A recent book by Neel and Schull[7] is particularly valuable for its discussion and evaluation of many of these technics.

Snyder, in his recent presentation to the medical section of the American Life Convention,[10] pointed out that not only are hereditary factors, or genes, being identified in man, but that much is known of how they act. The basic function of a gene is the development of a specific substance which determines the effect of the gene on the individual. This substance is, as a rule, an enzyme, and is responsible for the catalysis of a particular step in synthesis or degradation.

A mutation, which may derive from an inexact copying of the gene during its usual process of constructing a duplicate of itself in cell division, generally leads to a diminution or loss of activity in catalyzing the specific reaction that the unmutated gene accomplished. Thus, the mutated gene, which henceforth duplicates itself in its altered chemical form just as faithfully as the unmutated gene previously copied its original form, produces an enzyme dysfunction, and hence a physiologic or morphologic aberration.

The aberration may be striking and readily recognizable, as in phenylketonuria, in which the mutant gene fails to develop the enzyme which converts phenylalanine to tyrosine; in Tay-Sachs' disease, in which the mutant gene does not provide the enzyme required to oxidize sphingomyelin, or in glycogen disease, in which the phosphorylase needed to convert glycogen to glucose is not developed. On the other hand, the aberration resulting from the changed activity of the mutant gene may be only a slight deviation in physiologic activity underlying susceptibility, resistance, growth, or some other quantitative characteristic. In such instances the aberration may be appreciable only when several genes of this nature (polygenes) act cumulatively.