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COMMENTARY

Cigarette Smoking Does Not Produce or Enhance the Radiologic Appearance of Pulmonary Fibrosis

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Because the chest X-ray is utilized as the principal clinical diagnostic method for recognizing pulmonary fibrosis, it is obviously important to know whether cigarette smoking over a prolonged period induces changes in the lung X-ray that resemble those of fibrosis. Does cigarette smoking induce X-ray changes that resemble or could be confused with the changes caused by pneumoconiosis, including asbestosis?

It has been reported by Weiss [1967] from an examination of photofluorograms taken for the primary purpose of detecting tuberculosis that cigarette smokers had more prominent bronchovascular markings, which extended to well within the peripheral one-third of the lungs. There are serious difficulties in interpreting this information. First, the X-rays were photofluorograms, ie, 70 mm or miniature films, and the films were interpreted without using standard (ILO) criteria for pneumoconiosis. These criteria have excluded linear and bronchovascular markings since before 1959. In the initial study, 1,000 such photofluorograms were examined from a population that was 81% white and 55% women and included 393 nonsmokers and 527 smokers. Using the definition of increased bronchial and vascular marking and their extension into the periphery, 4.2% of all current smokers had changes, and 14.3% of 98 smokers of more than 20 cigarettes per day showed such findings, compared to 1.5% or 6 of 393 nonsmokers.

In a follow-up study of 2,825 adults surveyed by the same author [Weiss, 1969], questionnaires and expirograms were obtained as well as the 70 mm photofluorograms. Forty of these subjects had roentgenographic evidence of diffuse fibrosis using a somewhat extended definition from that employed previously; namely, the abnormality was defined as bronchial vascular markings that appeared to be more prominent than would be expected in a normal person after considering the degree of pulmonary expansion and the technical quality of the film, and that linear markings extended well into the periphery of the lung. A clear relationship of this finding to age was reported in both males and females

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with no examples of X-ray findings before age 24, 0.6% at ages 25–44, 1.4% at 45–64, and 3.3% over 65. Only 5 of 839 nonsmokers had these findings versus 35 of 1,860 smokers for a difference of 0.6% vs 1.9%.

Serious problems with the methods make definite conclusions from these studies impossible. First, extension of bronchovascular marking more peripherally does not define diffuse interstitial fibrosis, so the relevancy of such observations might be seriously questioned. Second, the small densities or irregular opacities which occur in asbestosis, measuring 1.5 to 3 mm on standard (14″ × 17″) X-rays, are often a problem in visual detection. Their recognition is much more difficult when film size is reduced. Third, in addition, the emulsion grain decreases the possible resolution of fine densities in small films. Such differences in resolution may account for the fact that only half of a sample of the 70 mm films read as fibrosis were thought to be fibrosis when 14″ × 17″ films on the same subjects were examined. Fourth, only 75% of the diagnostic impressions on 70 mm readings were confirmed by the original interpreter on a second reading. If one were to apply these errors of interpretation to the differences between cigarette smokers and nonsmokers, the frequencies would be decreased by approximately two-thirds, and the differences between the groups would disappear.

The author of these two studies suggests that they confirm radiographically the microscopic changes described by Auerbach et al [1967, 1970] in the lungs of cigarette smoking men and those produced experimentally in dogs, which consisted of alveolar septal fibrosis and thickening around tiny blood vessels. This suggestion overlooks 2 to 3 orders of magnitude difference in resolution between the optical microscope and the chest radiograph, which is even greater for the photofluorogram. Thus this line of reasoning is irretrievably flawed. Actually Auerbach et al [1963, 1967] observed epithelial metaplasia in airways and microscopic collections of cells with some irregular alveolar wall thickening which was not microscopically advanced. The resolution of linear infiltrates microscopically on tissue sections is obviously much greater than for chest X-rays. Clearly, findings from histological examination of lungs can not be inferred or transferred to the chest X-ray. Difficulties in extrapolation would be magnified if applied to miniature chest X-rays.

In view of these findings, which lead to serious questions about attributing to cigarette smoking any of the alterations observable by X-rays, and a failure to apply internationally agreed upon criteria for the diagnosis of asbestosis by chest X-ray [ILO, 1980], it is difficult to interpret a further study by the same author [Weiss, 1971]. The possible interaction of cigarette smoking and asbestos in the production of pulmonary fibrosis was studied in 142 workers in a chrysotile textile mill. There were 98 workers (73 smokers and 25 nonsmokers), and 14″ × 17″ chest X-rays were taken. The definition of fibrosis was "fine linear densities more prominent than normal, and/or bronchial vascular markings in pulmonary parenchyma especially in the peripheral third of the lung fields." In short, the definition used for diffuse fibrosis in the previous studies was again not that agreed upon by the ILO [1980], which refers to irregular opacities of sizes from below 1.5 mm up to 10 mm. Such opacities are not "connected" to the bronchovascular markings.

This study was small. There were no data given about the date of initial exposure to asbestos, but the individuals can be divided roughly by using their ages into three groups; those under 20 years from initial exposure, 20–30 years, and greater than 30 years. Examination of the 20–30-year group showed that when these small numbers are further divided into subgroups, by smoking and years of asbestos exposure, that the numbers in the groups become inconclusively small. Thus, the statement that 74% of the cigarette

smokers with a 20 years or more exposure to asbestos and 20 pack/years cigarette smoking had fibrosis represented 14 of 19 workers, whereas in the nonsmoking group, 6 of 14, or 43% had fibrosis. However, among the smokers with asbestos exposure as a group, irrespective of pack/years, 16 of 28 or 57% had fibrosis, not a statistical difference from the 43% in nonsmokers. In a more recent study of 88 workers in two asbestos products manufacturing plants, Weiss and Theodos [1978] reported a cigarette smoking-asbestos pulmonary fibrosis relationship in one factory but not the other. Chest X-rays were read to a consensus by both authors using ILO criteria. Clearly the numbers are so small with only ten nonsmokers in the positive factory that the differences have no statistical significance. Opposite conclusions—ie, no effect of cigarette smoking on radiographic signs of asbestosis—were reached in a larger study of 383 subjects by Samet et al [1979], who showed that the regression coefficient for increasing radiographic score against increasing asbestos exposure was the same for 58 nonsmokers, 11 past smokers, and 207 present smokers. This comparison emphasizes the hazards of inferences from small numbers.

A careful study using the same format as that of Samet et al [1979] showed no influence of cigarette smoking upon the prevalence of coal workers' simple pneumoconiosis, which was increased in a linear fashion by cumulative exposure to coal dust in 20 British collieries. Not only were the shapes of the probability curves identical for smokers and nonsmokers, but the prevalence of pneumoconiosis was similar, 30.2% in 2,675 smokers and 29.8% in 704 nonsmokers. The only other study on the other side of the issue was that of a small group of 92 women over 35 years of age employed at a New Jersey hospital. Age and cigarette smoking appeared to increase both the linear (bronchovascular) and nodular (bronchovascular on end?) markings in chest radiographs [Jacobsen et al, 1977]. However, there was no control for obesity and the breast shadows particularly in obese women made judgment concerning these shadows in the lower and mid-lung fields most difficult. In light of these problems, to attribute the changes observed solely to cigarette smoking is unjustified.

Thus, there is no substantial evidence that would support the suggestion that cigarette smoking acts additively or synergistically to produce pulmonary fibrosis that is visible on chest radiographs. Furthermore, there is no animal experimental evidence to show that cigarette smoking produces fibrosis. The data reported by Auerbach et al [1967, 1970] in studies of smoking beagles showed emphysema and small airways disease, not fibrosis.

At the moment it thus seems clear that a connection between cigarette smoking and diffuse pulmonary fibrosis visible by chest radiographs rests on sketchy evidence, using inadequate categorization of inadequate chest X-ray, and extrapolations from microscopic fibrosis in human and cigarette smoking beagles' lungs to accentuated bronchovascular markings visible on chest X-rays. Furthermore, repetition of the findings was not possible, and attempts by the same authors to verify fibrosis on 14″ × 17″ X-ray showed changes of the type described in only half of the X-rays thought to be positive on photofluorographic examination. Moreover, the markings are clearly different from the irregular opacities in the distal lung fields in asbestosis. Furthermore, efforts by others to show any causal relationship between cigarette smoking and pulmonary fibrosis have produced negative results. The answers to the questions: 1) Does cigarette smoking produce pulmonary fibrosis as judged by the chest radiograph, and 2) does cigarette smoking contribute to the fibrosis due to asbestos or coal workers' pneumoconiosis? is no to both.

The suggestion that fibrosis could be yet another effect of that ubiquitous pollutant cigarette smoke has been accepted by some without critical consideration. Critical anal-

ysis not only provides no support for this thesis but provides adequate reasons to bury the suggestion.

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