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Dear Wendell:

I have carefully reviewed the cataloging of medical literature relating to lung cancer as an asbestos health effect, prepared by Phil Enterline. I will attempt to provide you with my thoughts on extending the factual chronology given in the Enterline material to the interpretation of medical significance as might be perceived by medical practitioners. Please bear in mind that these comments are highly judgmental and it is quite likely that others working in this field might have substantially different interpretations.

First, it is important to recognize that since 1935 when the first suggestion was made that carcinoma of the lung may be associated with asbestosis, the strength of the evidence supporting this association in the medical literature has gradually increased. From 1935 until approximately 1940, the literature contained primarily case reports of lung cancer in patients who also had asbestosis determined at autopsy. During this period, editorial comment in major medical journals was tentative, at best, in support of this association, and in 1938, the Journal of the American Medical Association doubted a causal relationship while the British Medical Journal in an editorial suggested the "possibility" that such an association may exist. The literature during that time continued to be confusing, particularly as it was still suggested in some quarters that silicosis also carried an excess risk for the development of lung cancer (an association which has subsequently been shown not to be present). During this first five or six year period, one might conclude that the association between lung cancer and asbestosis was at best "possible" and essentially constituted a suggestion which subsequently led to further investigation.

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From 1941 until approximately 1949, a number of reviews appeared in the literature addressing the question of this association. Some rather weak experimental evidence suggested that asbestos exposure in animals resulted in lung carcinogenic effects. During this period, it was further reported that "pre-malignant" histologic changes were found in cases of asbestosis and several references were made in the medical literature to the acceptance in Germany of the association between lung cancer and asbestosis for compensation purposes. In 1947, an attempt was made to compare prevalence of lung cancer in workers dying with asbestosis with the expected number in the general population coming to autopsy. These results were not conclusive, but an excess of lung cancer with asbestosis was suspected. During this period, the evidence in favor of a causal association was slightly stronger but the association would still have to be classified as "possible".

The next relevant time period which I have selected is from 1949 until 1955. This period began when Meriwether, the Chief Inspector of Factories in the U.K., published his annual report with the finding that cancer of the lung or pleura occurred in 13% of individuals found to have asbestosis at autopsy. This compared with a risk of 1.3% in individuals with silicosis. Also, in 1949, an editorial in the Journal of the American Medical Association accepted the association between asbestosis and lung cancer. As you undoubtedly know, the JAMA is the most widely read journal among medical practitioners in this country. In 1951, Gloyne found 14% of individuals with asbestosis had pulmonary cancer in an autopsy series, confirming the findings of Meriwether. Also, around this time, attention was directed to an increase in the female to male ratio for lung cancer in individuals with asbestosis, as compared to the general population, again supporting an occupational association. In 1953, Harriet Hardy and colleagues published two case reports in the American Journal of Medicine with the conclusion that the causal association is highly likely. I mention this because the American Journal of Medicine has been widely read by physicians specializing in internal medicine. It is also of some interest, but perhaps not entirely relevant to the present discussion, that in 1953 and 1954 the suggestion was made that pleural and peritoneal mesotheliomas respectively were associated with asbestos exposure, these reports appearing in the German literature. During this time period, I would conclude that the medical literature might lead the reader to the opinion that the association between asbestosis and lung cancer was now "probable".

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Finally, the last time period is 1955 until the present. This phase, of course, began with the publication by Richard Doll using the most valid epidemiologic techniques up to that time to investigate a causal association, i.e., a cause-specific mortality study of workers with defined employment in a specific plant. He found that employees of this asbestos textile factory had approximately ten times the risk of developing lung cancer than members of the general population. He suggested that this risk was confined to those individuals who also had asbestosis. Also, in 1955, editorials in the British Medical Journal, Lancet, and American Journal of Clinical Pathology accepted this association as did the author of the most prestigious book on occupational medicine, Donald Hunter. It would be my judgment that since 1955, the causal association can be considered "proven" or "definite".

Up to the present time, there continues to be some difference of opinion concerning the question of whether the lung cancer risk is limited to individuals with asbestosis or is present in those only with asbestos exposure. The primary reason for this uncertainty is because the definition of asbestosis is highly variable and on one extreme might be based on thorough histologic examination with the whole lung available, and on the other might depend on several clinical, radiographic and physiologic criteria. My judgment at present is that it is probable that the level of asbestos exposure necessary to result in a detectable excess risk for developing lung cancer is also a dose which is likely to produce diffuse changes of pulmonary fibrosis (asbestosis). However, the evidence of asbestosis may not be clinically or radiographically apparent.

I hope this discussion is useful. You will of course appreciate that the time periods indicated above are arbitrary. I would be most pleased to discuss any of these opinions with you or to provide clarification where required.

With kindest regards,

Sincerely yours,

Hans Weill, M.D.

HW:nc
cc: Mr. Guy Gabrielson
Mr. Robert Mereness

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