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ASBESTOS-RELATED DISEASE - AN OVERVIEW, 1982

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Asbestos-related disease - an overview, 1982

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Introduction

This Symposium may prove to be a landmark in the history of asbestos use and asbestos disease. In this respect, it resembles the conference held by The New York Academy of Sciences in 1964. Unlike that meeting, however, the outcome is not necessarily sanguine nor broadly optimistic. We have come to a decision point, with several directions possible. Which are taken will, in considerable measure, be influenced by this meeting.

The New York Conference

Although the fibrogenic capacity of asbestos--potentially fatal-- had been increasingly studied since the 1920s and 1930s, it was not until the following two decades that the significance of cancer attracted broad attention. This, coupled with the exponential growth of the use of asbestos, spurred scientific inquiry. By 1964, accumulating data warranted critical review and in October of that year The New York Academy of Sciences convened an International Conference to consider what was known. The prospectives at that meeting were defined by its title "Biological effects of asbestos". The presentations largely focused on observations recently made in defined areas where additional scientific data could assist in clarifying scientific questions. Many had confidence that, with what was known and what would be studied, the disease hazard would be controlled. Scientific information would allow us to avoid hazard associated with this valuable material.

The Montreal Symposium

In the years since 1964, this optimism has been tempered. Asbestos disease has continued, and there is no unanimity that the conditions for its control have been achieved. The fact that this Symposium will address the question "Should the use of asbestos be continued?" is a measure of our past inadequacies, and current uncertainties.

This meeting will again be science-based. But it will, unlike 1964, have the additional responsibility of considering the economic, political, social, administrative, ethical problems associated with the continued and projected uses of asbestos. Perhaps we were remiss in New York in not addressing these problems more vigorously. Science was necessary, but not sufficient.

This Symposium, then, has a double responsibility: careful review of the scientific prospectives that have developed since 1964 and their translation into the use of asbestos without significant risk to human health.

Scientific perspectives, 1964-1982

Building upon and extending the scientific information that had become available by 1964, we have now achieved a useful overview of the scientific background against which the asbestos disease problem may be viewed. At the 1964 meeting, a number of questions were unresolved. Additional data were needed to fully characterize the nature and extent of the cancer risk, the influence of fiber dose and fiber type on such disease as would occur, the significance of non-occupational exposures, and how standards and controls could best be developed. Much information has been obtained, to help understand these critical issues. In addition, problems not predicted in 1964 have also been identified, and useful data obtained.

Spectrum of asbestos-associated disease

We now have a fairly good understanding of the spectrum of asbestos-associated disease, at least that which obtains with heavier exposure. Two cohort studies illustrate the extent of this knowledge. In the first, 17,800 asbestos insulation workers were registered on January 1, 1967 and followed to December 31, 1976, and included 166,853 man-years of observation. Table 1 summarizes their mortality experience during that decade. There was significant increased mortality of cancer of the lung, pleural and peritoneal mesothelioma, cancer of the esophagus, stomach, colon-rectum, cancer of the oro-pharynx and laryux, cancer of the kidney, and asbestosis. These data were based upon 2,271 deaths.

The experiences of a second cohort confirm this outlook, providing support from another epidemiolological direction. On January 1, 1943, there were 632 asbestos insulation workers in the New York-New Jersey locals of this Union. This group was followed to December 31, 1981, covering 14,547 man-years of observation. In the 39 years, 532 men died; this mortality experience thus covers almost the entire experience of this group. Table 2 demonstrates that 46 of the men died of asbestosis (approximately 8%). Far greater risks were deaths of cancer. Age, year and sex-specific data indicate that 63.9 deaths of cancer were to have been expected. Two hundred and thirty-eight occurred (45%). The major neoplastic risk was lung cancer. 15.7 were expected, 105 occurred (20% of all deaths). There were 50 deaths of mesothelioma (9%) and a modest but statistically significant increased risk of death of gastrointestinal cancer.

Both Table 1 and Table 2 indicate that the major concerns are lung cancer, mesothelioma, asbestosis and gastrointestinal cancer.

Populations at risk

By 1964, it was already clear that early emphasis on "asbestos workers" (asbestos miners, millers, asbestos products manufacture) was insufficient. Rather, hazards associated with product use vastly increased the number of people at risk of asbestos-associated disease. The insulation worker experience pointed to the construction industry; the reports by Harries and Stumpfus in 1968 added shipyard work as a major concern. Against this background, studies in a variety of trades expanded both the potential for disease and the necessity for controls--chemical plants, refineries, power production and utilities, transportation, ship repair and shipboard exposure, etc.

Further, utilizing mesothelioma as a marker and "signal" (the work of Cochran and Webster has been particularly telling in this regard), there was further emphasis on the likely importance of disease among family contacts and among those exposed in a number of environmental circumstances. Dr. W.J. Nicholson will discuss in this Symposium the results of his analyses concerning occupational populations exposed 1940-1980 in the United States; the number of people involved can only be described as huge. It will be valuable to have analyses made of exposed populations in other countries, to provide a global perspective in this regard.

Latency

Perhaps at the heart of our difficulties concerning asbestos-associated disease has been the long incubation period before important clinical evidence of such disease is noted. The "20 year rule" had been propounded for radiological asbestosis in 1964. It is clear that the same holds true for cancer, as well. Table 3 shows that little lung cancer or mesothelioma occurs in less than 20 years from onset of exposure. This is depicted in figures 1-3.

A corollary of this is that we learned the semantic difference between "duration of exposure" and "duration from onset of exposure". The two are by no means synonymous. With asbestos exposure of sufficient intensity, only short-term exposure is needed to yield long-term risk.

We have not yet learned how to loosen this iron grip of latency. In practical terms it means that the disease we are seeing now is the result of past exposure. By the same token, however, and important for this conference, is the fact that present exposure will result in future disease.

Low-level exposure

I'm not sure that this commonly used phrase is entirely appropriate; perhaps we should employ the more unwieldly "lower level exposure", since there is some contradiction in speaking of exposure as "low" when it produces disease and death. Further, we are not very confident about quantitation of "lower level exposure" since it was precisely in such circumstances that, in the past, few measurements were made.

This has been the case for family contact disease. When this phenomenon, heralded by Wagner's description of environmental mesothelioma in 1960, was documented by Newhouse in 1965, we had no information on what level of exposures might have been responsible for what was seen. Nicholson and Rohl in our Laboratory have made some measurements in recent years, but I believe that a valuable opportunity was lost after the New York meeting when extensive household asbestos exposure studies were not done. We would now know something at least about the lower limits of exposures associated with asbestos-associated disease.

Low-level exposure is sometimes used to characterize what has happened in occupational situations where exposure has been intermittent and indirect. These may not be the same as exposures in family contact circumstances, since the intensity of exposure on occasion can be more or less severe, albeit for short periods. It might well be that three hours in the hold of a ship where asbestos was being extracted could provide a much heavier lung burden than 10 years of residence in an asbestos worker's home.

Too, the general use of the phrase "low-level exposure" may not be at all pertinent to the levels of exposure that exist in ambient air and

experience of brake repair and brake maintenance workers, or sheet metal workers in the construction industry provide no necessary guide to evaluation of risk of the general population.

Selection within high risk groups

When it is said that one in five asbestos insulation workers dies of lung cancer, it is also implied that four in five don't. Similarly if one in 15 dies of mesothelioma, 14 do not. The reasons for such selection within groups at high risk have begun to be explored.

One factor that has been identified has been the importance of tobacco smoking, primarily cigarettes. Asbestos exposure by itself increases the risk of lung cancer, by about five times. However, since the risk of non-smokers is low, even such increase does not produce a very large number of cases of lung cancer. On the other hand, the same five times increase among cigarette smokers results in sharp multiplication of an already very high risk, resulting in a devastating lung cancer incidence. In one study (the 17,800 asbestos insulation workers mentioned above) in which the experience of more than 72,000 like men were used as a control, the rate for men who neither smoked cigarettes nor worked with asbestos was 11 per 100,000 per year. For non-smokers who worked with asbestos, it was 58. Among those who smoked, but were not asbestos-exposed, the risk was 112 per 100,000 per year and for those who had both exposures, asbestos and cigarette smoking, it was 601. The multiple factor interaction of asbestos and cigarette smoking pertains as well to cancer of the esophagus, cancer of the oropahryx and buccal cavity, cancer of the larynx but not to mesothelioma, cancer of the stomach or colon-rectum or cancer of the kidney. There may well be multiple factor interaction with other influences for a variety of asbestos cancers, but this has been little studied. One set of circumstances that can turn out to be of considerable importance is immunomodification: this is a subject of intense research at this time in our Laboratory.

Reversal of risk

During the cigarette smoking-asbestos exposure investigations, an important observation was made. Those asbestos workers with a history of cigarette smoking who stopped smoking, within 5-10 years had only one-half to two-thirds the lung cancer risk of those who continued to smoke. Data are not yet available concerning whether risk of oropharyngeal and buccal cavity cancer, laryngeal cancer, and esophageal cancer will show the same happy effect, but I anticipate that it will be so.

Cigarette smoking was also found to increase the risk of death of asbestosis, presumably by adding the emphysema-bronchitis burden of smoking to the pneumoconiotic effect of the dust. Here, again, it is likely that cessation of smoking will have an important beneficial effect.

This raises some very practical--and ethical--questions. It has been demonstrated that we can, at least in part, reverse the risk of lung cancer among individuals previously exposed to asbestos by cessation of smoking. Is it incumbent upon us to notify all those who we know have been exposed to asbestos to tell them of the added risk they have of death of lung cancer, compared to smokers in general, and of the potential of reversing that risk by smoking cessation?

Dose-response

Ample evidence has now been accumulated to indicate that an important dose-disease response gradient exists for asbestos, as for many other carcinogens. We will hear about this, I am sure, in some detail at this symposium. While the exact projections may be debated, it is clear that the less asbestos inhaled, the less the disease risk and, conversely, the more asbestos inhaled, the greater the risk. A corollary will be that avoidable exposure translates into avoidable disease.

An addendum to this subject has been added in recent years. We knew in 1964, and this has been confirmed since, that different exposed populations had variable disease outcome, as measured by mortality experience. One possible explanation was that different fiber types had different pathogenicity and after the New York Conference, the experience of populations exposed uniquely to one or another fiber type was sought. This was not easily come by in industrial circumstances, due to mixed exposures.

In our Laboratory, we have been able to obtain information on two fiber varieties. First, we have been investigating the experience of 1,663 men who were employed in an asbestos products factory in Paterson, New Jersey 1941-1954. A great deal of information demonstrated that amosite was the sole fiber used in this plant, apart from some minor amounts of chrysotile. Table 4 summarizes the experience of 582 men who began work 1941-1945 and were still alive 20 years later, and were followed prospectively from that point to 1978. It will be seen that their mortality experience was very much like that of asbestos insulation workers. Amosite, apparently, did not have a unique potential to result in other than the anticipated asbestos-associated diseases.

We have had the opportunity of investigating the experience of asbestos insulation workers in the New York-New Jersey area for two periods of time; one, in which employment began and continued when only chrysotile was used (before World War II) and a second group of men in the same union locals, in the same cities, doing the same work, employing the same work practices but exposed not only to chrysotile but potentially to amosite as well, which had by then been added to asbestos insulation materials. Tables 5-8 show that, for equivalent times from onset of exposure, no difference could be seen in the mortality experience of those exposed only to chrysotile or to chrysotile and amosite.

Unfortunately, we have no experience with crocidolite exposed populations in our Laboratory.

It may well be that the question posed in 1964 was much too restricted. The assumption was made that fiber type would be the major difference in explaining observed variations in the disease risk of various groups. It is now realized that exposure intensity certainly plays a very important role, perhaps a critical one. However, other factors may be of equal or even greater importance. I would go even further than Dr. McDonald (this Symposium) when he states that "While it is clear that, in experimental animals, fibres of different type but similar dimensions have much the same pathogenicity, various industrial processes could have a major effect on fibre size...." focusing, as he did, on the size of the inhaled fibers as a determinant of pathogenicity. Other changes besides those in size can occur in the fiber during its journey from the time it is extracted in the mine to its use in a variety of industrial processes. Dr. Langer will address this question here later. Dose response, then, may reflect not only the number of fibers inhaled, but various attributes such as fiber type, dimension, surface, structural alteration, etc.

Conclusion

When a death of asbestosis was observed in 1900 and recorded in 1906, it could not have been widely known. But it would have been difficult to overlook the serious potential of the dust when the careful clinical studies and surveys in the decade after 1914 found that asbestosis was common among exposed workers, and that deaths could occur. Despite this understanding, the 1930s, 1940s, 1950s went by with few precautions in trades in which there was asbestos exposure. Nor did accumulating scientific knowledge concerning the cancer potential of asbestos increase protective measures until the 1960s and 1970s.

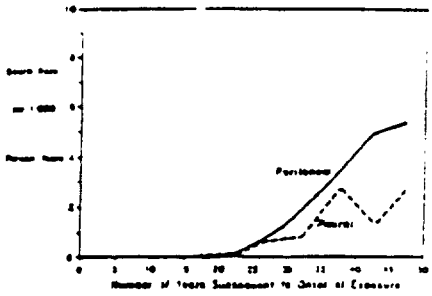
This Symposium again, as the meeting in New York in 1964, will still be science-based. However, it will also have the task of identification and resolution of industrial, economic, social, political and ethical questions. Thus, there will be debate concerning the dimensions of the disease legacy we now face as the result of our years

of failure--exactly how much lung cancer or mesothelioma or gastrointestinal cancer or cancer of the laryux or other cancers or asbestosis--in shipyards, the construction industry, transport, mines, factories, chemical facilities and refineries, power plants, insulation work or other trades. We will be asked whether levels of 10,000 or 2 million f/m^3 of air (0.01-2.0 f/ml) will protect people in the future and we will not be able to answer confidently because few measurements were made years ago to correlate with subsequent cancer experience. Still, we'll be able to give the key answer--that there is a "dose-response" for all asbestos disease--the more asbestos, the more risk, the less asbestos, the less risk.

But this discussion will not be able to answer the critical question--should the use of asbestos be continued--if evidence will not be available that it can be safety used. that there will be vigorous insistence on all feasible safety measures; not minimal controls but maximum capabilities. Would this prevent all asbestos disease? No--but it would avoid all that can be avoided, at least with what is presently known. It may well be that to do less than we can will prove unacceptable. Therefore, one perspective by which to judge this Symposium is that it has as its task the unique opportunity of deciding who will live, and who will die. It is this decision which will answer the question of whether or not asbestos should continue to be used.

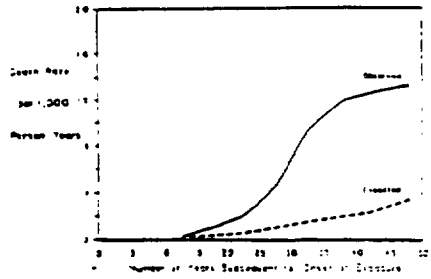
Deaths of mesothelioma

Fig. 1



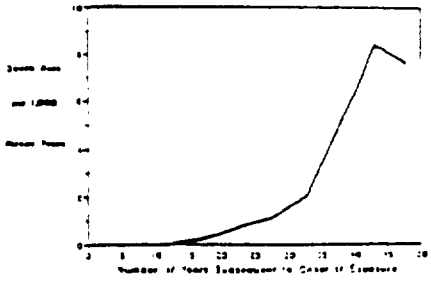
Deaths of lung cancer

Fig. 2



Deaths of asbestosis

Fig. 3



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