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THE ASSESSMENT OF EXPOSURE IN TERMS OF FIBRES

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Abstract—see p. 409.

INTRODUCTION

THE purpose of this paper is to examine the 'exposure' component of 'exposure–response' relationships used in epidemiological studies of chrysotile workers. Because the main diseases under investigation, lung cancer and mesothelioma, usually occur decades after first exposure, estimates of exposure levels in such studies have depended on historical measurement methods and data.

In the late 1960s, a belief that the direct measurement of fibre concentrations would be more appropriate for controlling exposures to fibrous dusts than previously available methods, led to decisions, almost worldwide, to express worker exposures as the number of fibres per ml of air ($f\,ml^{-1}$). A new method, the membrane filter method, was introduced (MF). In this method fibres were defined as particles with an aspect ratio 3:1 or greater and length greater or equal to 5 μm. The samples for analysis were collected on membrane filters which were rendered transparent and fibres were counted using phase contrast microscopy. The sampling and counting methodology continues to evolve.

The impact of this world-wide harmonization is evident when it is recognized that there have been no studies of the relationships between exposure to chrysotile and long-term health effects in which exposure has been based directly on counts of fibres using the membrane filter method. This leads to several questions relating to the extent to which the only available scientific data can be used to derive risk estimates based on exposures expressed as number of fibres per ml. Perhaps the crucial question is:

—Can the 'indices of exposure' based on past measurement methods be converted to reliable estimates of fibre exposures based on the membrane filter–phase contrast microscopy method currently used to monitor workplace chrysotile concentrations?

The validity of an exposure index is determined by its ability to predict disease incidence. This means that regardless of the index a meaningful dose–response relationship would enable any dust or fibre index to be used for control purposes as long as the methodology remained sufficiently sensitive and reproducible. This is the situation for all dusts where the actual component or parameter of the dust responsible for the disease is not known. In the case of chrysotile, it is not known whether the parameters of the dust responsible for asbestosis are those likely to relate to lung cancer, nor is it known whether the fibre sizes derived from experimental systems as predictive of mesothelioma risk are the ones which might be most predictive of this tumour occurrence in humans. It is known that the dusts associated with chrysotile will vary between production facilities, processes and industrial sectors where the chrysotile is used. The dimensions of fibres may also vary. While such differences may exist, the issue is whether differences are of practical significance. A key question which arises under such circumstances is:

—Are the indices of exposure used in epidemiological studies, in particular of lung cancer and mesothelioma, in one industrial sector directly comparable to those in other sectors and, if not, can they be rendered comparable taking into account etiological factors?

ASSESSMENT OF EXPOSURE FOR EPIDEMIOLOGICAL PURPOSES

While tissue analyses (Sebastien *et al.*, 1989) and other methods such as magnetic lung scans (Cohen *et al.*, 1981) have been applied in attempts to quantify exposure to chrysotile, the most usual method of deriving exposure indices has involved work histories and past measurements of airborne dust concentrations. It is this approach that will be examined below.

CUMULATIVE LIFETIME EXPOSURE

Cumulative lifetime exposure is the sum of the products of time spent on each job and the concentration of dust associated with that job for the working lifetime of the individual. This index of exposure provides a method of dealing with variations in concentrations with job or over time, and can take care of changes in working hours, etc. It is the index of exposure used in the main cohort mortality studies of chrysotile workers.

Methods to measure exposure intensity, which distinguish duration and level, have been rarely applied. However recently Vacek and McDonald (1991) using data for tremolite-exposed vermiculite miners found that risk was absent at low concentrations, increased rapidly as concentrations increased, and levelled off at high concentrations. They noted that this was "a feasible relation that was not evident when risk was modelled as a function of cumulative exposure". Liddell has recently conducted analyses using intensity estimates for chrysotile exposures in the Quebec mining and milling industry (Liddell, 1994).

EPIDEMIOLOGICAL STUDIES

In the HEI-AR report (HEI-AR, 1991), it was noted that there were only three cohorts in which substantial excess lung cancer risks had been observed and where reasonably extensive historical dust measurements existed, from which individual exposures could be estimated. These cohorts were employed in the Quebec chrysotile mines and mills (McDonald *et al.*, 1980b), the Rochdale (U.K.) textile plant (Peto *et al.*, 1985) and the South Carolina (U.S.) textile plant (Dement *et al.*, 1982; McDonald *et al.*, 1983). The British Friction Industry study was noted as having extensive exposure data available (Berry and Newhouse, 1983; Newhouse and Sullivan, 1989) but there was in essence no excess lung cancer mortality. Individual exposure estimates have also been used in studies of asbestos cement workers (Hughes and Weill, 1980) (also, Albin, personal communication, 1992).

DUST AND FIBRE MEASUREMENTS AND THEIR RELATIONSHIPS

Canada and the United States

Dreesen *et al.* (1938) used impingers to measure dust concentrations in studies of exposure and health effects in asbestos-exposed workers in the United States. As a result of this early work, threshold limit values based on counts of particles collected in the midget impinger were adopted. Thus, prior to about 1964, all asbestos measurements in Canada and the United States involved the use of impinger methods (in particular the midget impinger), and all studies of exposure–response depended on these measurements.

Basically, the midget impinger collects particles in specially designed impingers containing water or iso-propyl alcohol. Particles in an aliquot of the liquid are allowed to settle for a known period of time in a cell of known depth and the number of particles in a known area is counted at $\times 100$ magnification. Concentrations are reported in million particles per cubic foot (mppcf). In the Canadian mills, the method applied was essentially that approved by the Asbestos Textile Institute (Asbestos Textile Institute, 1963). Its sensitivity was adequate in the years when concentrations were high, and because larger samples can be collected it may have sufficient sensitivity to reflect differences at very low chrysotile dust concentrations. However it is a relatively short-term instrument, is difficult to use for personal monitoring and is not specific for fibres.

While between 1964 and 1968 the midget impinger continued to be used, the membrane filter method was under development. This early method involved methods of clearing, mounting and counting filters which were considerably different from those used now. Measurements using a membrane filter method began routinely in the early 1970s. At that time, observers in Canada used either the USPHS Method (Edwards and Lynch, 1968) or the method published by the British Occupational Hygiene Society (Lane *et al.*, 1968).

Estimates of exposure in Canadian mines and mills

Based on midget impinger counts (MI). Cumulative exposure estimates (mppcf-years) were developed based on the jobs, areas in which jobs were performed and measurements made using the midget impinger method (Gibbs and LaChance, 1972). Exposure estimates were based on 4152 systematic midget impinger measurements made in the mines and mills by the same person between 1948 and 1966. He noted which samples were representative of exposures and which were made for control purposes and always recorded the actual concentration when the exposure limit was exceeded. Thus this environmental data base was of a quality better than most. Measurements from other sources such as government reports, insurance companies, mining companies and others were consulted and data gathered when necessary using surveys by the research team. The distribution of measurements were such that it was possible to obtain a reasonable estimate of the concentrations associated with most jobs and work areas on an annual basis. As measurements covered periods before and after the introduction of major dust controls, dust concentrations in the earlier years could be estimated. The basic technology for fibre extraction has not changed over the years and reductions in levels of dustiness coincided with the introduction of dust control measures. In addition to the mill samples, 3096 dust measurements were made between 1944 and 1966 in the factory included in the Quebec studies (GIBBS and LACHANCE, 1972).

Membrane filter fibre exposure equivalents. The conversion of midget impinger (MI) particle concentrations to membrane filter (MF) fibre exposures for the mining industry was first examined in a series of 87 side-by-side midget impinger counts and membrane filter samples (GIBBS and LACHANCE, 1974). Most of these impinger samples were counted by the same person who had counted the 4000 or more midget impinger samples in the mills since 1948. This series of samples included impinger counts mainly in the range 5–10 mppcf but included five in the range 10–35 mppcf. After logarithmic transformation of both variables the overall correlation was 0.45 for the 56 samples with more than one fibre per field. The predictive value of this relationship was only 13% better than a conversion obtained at random. However, examination of MF/MI ratios by job-site and by mine suggested that much of the variation may be due to substantial differences between mine-sites and between different operations in the mills. Although the number of samples was small, it can be noted that the overall lowest mean ratio by mine and by process was 1.7 and the mean ratios for most mine-sites and for other operations were 4.5 or above. A further series of 623 side-by-side MI and MF samples collected by Gibbs (DAGBERT, 1976) also showed a poor overall relationship. Dagbert claimed a significant association between the logarithmically transformed MI and MF concentrations but the correlation was only 0.44. Thus it is clear that there is no single overall conversion factor that can be applied to the mine and mill data. However, there were definite patterns with MF/MI ratios increasing from the predominantly dust-generating operations such as drilling and crushing to fibre-releasing operations such as fibre screening and bagging, and Dagbert found a reasonably strong relationship between MF and MI counts for some areas such as around fibre and rock screens.

In a case-control study of lung cancer mortality of Quebec miners and millers conversion factors were derived for individual jobs using 10 205 particle counts and 11 819 fibre counts made in that industry (MCDONALD *et al.*, 1980a). The results of all side-by-side samples, and the mean and median MI and MF concentrations in various areas in various years were used to establish a conversion factor for each particular work area. It was assumed that the same conversion factor had applied throughout the history of the plant. The application of these job-specific conversion factors resulted in an overall conversion factor, based on the mix of the occupations of cases and controls, of 3.64. The results of various other analyses resulted in overall conversion factors of the same order of magnitude, 3.67, 3.57, 3.46 and 3.44 f ml^{-1} per mppcf (LIDDELL *et al.*, 1984).

Using the mean values from the side-by-side samples Dagbert calculated that the overall mean ratios for all concentrations at or above 0.1 f ml^{-1} were greater than 2. The 95% confidence intervals for the ratio for all samples analysed were 0.58 $(MI)^{0.68}$ and 55.7 $(MI)^{0.68}$. The lower confidence intervals were 0.28 $(MI)^{0.75}$ for mining; 3.52 $(MI)^{0.77}$ for rock screening and 6.43 $(MI)^{0.65}$ for fibre screening. These 95% confidence intervals would suggest that an overall 'conversion factor' of approximately 3, based on all jobs held by persons in the Quebec chrysotile cohort, is not unreasonable. If a factor of 3 were applied to some of the high concentrations reported in the mills, such as 100 mppcf, the airborne fibre concentration would be 300 f ml^{-1}. This is a very high average concentration by modern standards, but quite believable when concentrations in 1971–1972 were as high as 130 f ml^{-1} (GIBBS and LACHANCE, 1972) and even in 1975 were reported to range up to 57 f ml^{-1} (NICHOLSON *et al.*, 1979). PARSONS *et al.* (1986) calculated MF/MI ratios in a Newfoundland mine by year from 1969 to 1974. Their lowest ratio was 7.0 based on pit measurements. This is higher than reported by Gibbs and LaChance in Quebec, even for some of the fibre operations.

Although at very low concentrations, MF/MI ratios may be erroneously elevated because of errors in the impinger and fibre counts, and this is suggested by the Quebec mine and mill data, the consistently high ratios of fibres to particles in all studies of fibre–particle relationships indicate that fibre exposures in the mining and milling industry may have been higher than previously considered probable. This suggests that risk for miners and millers, if anything, may have been overestimated.

Estimates of exposure in the U.S. textile industry

In the early 1960s a method using a membrane filter was developed for fibre counting (LYNCH and AYER, 1966). Using this method, AYER *et al.* (1965) carried out a comparison of membrane filter counts and midget impinger counts in the textile industry. Interestingly they noted at that time that the membrane filter method was not being proposed as a substitute method for the midget impinger. They reported that overall for the textile industry 1 million particles per cubic foot was equivalent to 6 f ml^{-1}, but were consistent with others attempting to find an overall conversion factor in noting that ratios varied considerably with process.

DEMENT *et al.* (1982) studied mortality from lung cancer in a U.S. asbestos textile plant and calculated individual cumulative fibre exposures. The plant studied used chrysotile asbestos from Canada and Rhodesia, 200 pounds of crocidolite yarn from 1950 to 1972 and a small amount of amosite experimentally in the late 1950s (McDONALD *et al.*, 1983). The basis for their exposure estimates were 5952 environmental measurements between 1930 and 1975. All samples prior to 1965 involved the use of the midget impinger. Between 1965 and 1971 membrane filter samples were also collected by the company, by its insurance carrier, by the U.S. Public Health Service and by the State Board of Health. In order to derive a MF/MI conversion factor there were 120 paired impinger–membrane filter samples collected in 1965 and 986 simultaneous samples by these two methods in 1968–1971. Their data suggested a conversion factor of about 3 for all textile operations except preparation. The ratio, based on stepwise linear regression, appeared to be about 8 for the preparation area. It was assumed that these ratios applied throughout the history of the plant.

The report by DEMENT *et al.* (1982) did not provide information on whether or not samples were personal samples, nor on the distribution of locations at which the side-by-side samples were taken. Counts of fibres in this instance were made at a time when the membrane filter was in its developmental phase. Compared to other studies of fibre:particle relationships, this study revealed remarkably narrow confidence intervals around the conversion estimates. Except for the preparation area workers a single conversion factor was used to convert particle to fibre counts. If there has been little exchange of workers between preparation and other jobs, the shape of the dose–response relationship would be expected to be very similar regardless of whether exposures were expressed in million particles per cubic foot or in f ml^{-1}. A later independent study of the same plant by McDONALD *et al.* (1983) in which exposures were calculated as million particles per cubic foot years (mppcf-years) confirms this. They also found a very steep slope for the relationship between lung cancer and exposure expressed in mppcf-years. The risk of lung cancer appeared to be about 50 times that of workers in the Quebec chrysotile mining industry.

Asbestos-cement industry

Data for the asbestos-cement industry have also shown that no single conversion factor can be used for all areas. However a good correlation between particle and fibre counts has been reported at high dust concentrations and poor correlation at low concentrations (HAMMAD *et al.*, 1979).

The U.K.

In the U.K., all measurements prior to 1960 used a thermal precipitator (TP) in which all particles were counted. For the purpose of epidemiological studies (PETO *et al.*, 1985) and standards development (LANE *et al.*, 1968) factors were used to convert past particle counts with this instrument to counts using the long running thermal precipitator (LRTP) which was used 1960–1966 and involved counts of fibres. Counts by this latter method were considered comparable to those using the membrane filter method which came into use in the mid-late 1960s.

There was no contemporary (1960–1961) parallel sampling to establish the relationship between STP particle counts and LRTP fibre counts, so BOHS compared the 1960 STP results with 1961 LRTP results for a conversion factor of 38:1 (WALTON, 1982). Measurements in 1977 showed the ratio of the TP to the membrane filter method then in use to be 14:1. Walton suggested that this might be the result of counters changing to an eyepiece graticule as this had been shown to increase counts of chrysotile by a factor of about 2 (HSE, 1979).

PETO *et al.* (1985), using counts made since 1951 and work histories of British textile workers, calculated individual exposure indices. As noted above the exposure estimates in fibre terms involved conversions from past exposures and some of the same assumptions about the past as were used in the United States and Canadian studies. While this textile plant has been considered as a chrysotile plant, a total of 10 322 short tons of crocidolite were purchased between 1932 and 1968 some having been purchased in all but 2 years. This may explain their mesothelioma experience but is unlikely to account for the apparently high lung cancer risks.

The validity of exposure assessments for the Quebec mines and mills, and Charleston textile plant

The apparently large difference in risk between miners, cement and friction workers and textile workers raises questions about their relative exposures. For example, the HEI-AR (1991) report suggests that, because the confidence intervals around the Quebec mining conversion factors are large, it is not possible to conclude that there is a 50-fold difference in risk between the textile and mining populations. This inference is incorrect. If in the most improbable circumstance, the lower 95% confidence conversion factor of 0.58 $(MI)^{0.68}$ were to apply this would account for only about a 5-fold difference and as the confidence intervals in the textile industry was about 2 when a factor of 3 was used the combined effect would not result in the same overall risk estimates.

Some important information which strongly supports this viewpoint has been forthcoming from lung tissue studies. SEBASTIEN *et al.* (1989) analysed the concentrations of chrysotile fibres in the lung tissues of Quebec mine and mill workers and Charleston textile workers. They found that the ratio of chrysotile fibre concentrations in the lung tissues of miners to those in Charleston textile workers, matched for duration of exposure and time from last exposure to death, were higher than the coresponding ratios of estimated exposures based on impinger counts. Measurement of tremolite in tissue led to a similar conclusion.

These results indicate that in terms of fibres the estimated exposures of the Quebec miners and millers relative to those of textile workers at the Charleston plant may have been even greater than estimated in the epidemiological studies.

Present day vs older membrane filter methods

As there has been considerable evolution in the membrane filter counting method since 1968 (WALTON, 1982), it seems likely that concentrations measured using the latest membrane filter method would be substantially higher than those recorded in the late 1960s. This change in the U.K. was estimated to be about a 2-fold increase (HSE, 1979) but methods have been modified further since then. The trend towards taking personal samples has also been suggested to increase the recorded concentrations 2-fold. However the impact remains controversial (PETO *et al.*, 1985). Thus it remains unclear as the extent to which past methods will have underestimated exposures compared to the more recent methods. There is no doubt that inter- and intra-observer errors have been greatly reduced over the past 20 years.

In the U.K., the results for the Long Running Thermal Precipitator LRTP were considered to be directly comparable to those of the membrane filter method. However published data in support of this assumption are limited and might also be questioned in view of the evolution in the membrane filter method.

COMPARABILITY OF EXPOSURE INDICES BETWEEN SECTORS

Does a concentration of 1 mppcf or 1 f ml^{-1} in one industry mean the same as 1 mppcf or 1 f ml^{-1} in another? This is a very complex question. It is self-evident that there will be qualitative differences in the chrysotile fibre and associated contaminants in different mines and in different industrial sectors. The addition of oils in the textile industry has been raised as a possible etiological factor. The issue is whether these differences are important. Two which may be important will be examined.

(a) *Tremolite and mesothelioma*

MCDONALD *et al.* (1992) fitted the Quebec chrysotile mining and milling data to the exponential mortality model (LIDDELL, 1988):

$$\text{Annual incidence per unit of population} = b \times (\text{years since first exposure})^{3.2}$$

and obtained values of the factor (b) of 0.1×10^{-8} for the miners and millers at Asbestos and 0.24×10^{-8} based on Thetford Mines data. Tremolite exposures have been considered to be greater in Thetford Mines than at Asbestos and McDonald *et al.* suggested that tremolite exposures were sufficient to affect the risk of mesothelioma in the two mining areas. This conclusion is supported by the fact that fibrous tremolite is commonly found in the lungs of some of the Quebec miners and millers (SEBASTIEN *et al.*, 1989).

The possible presence in the airborne dust of another substance which may be responsible for all or part of the health risk under study presents a problem. While the overall risk of lung cancer or mesothelioma can be determined in relation to the various exposure indices, these indices do not make it possible to distinguish the contribution by fibres or by dust other than chrysotile to risk. This may be adequate for assessing or controlling lung cancer and pneumoconiosis risks, but as fibrous tremolite may be an important factor in explaining the mesothelioma risks for chrysotile miners and millers there is an urgent need for the following.

(i) Information on the distribution of mesothelioma by mine and a determination of whether the fibrous tremolite in the lungs of miners or millers accumulated as the result of long-term low-level exposure to tremolite or high exposures at some time in the past. This involves a detailed review of the work histories of cases and of the geology of mines worked in the past.

(ii) Information on the relationship between the burdens of fibrous tremolite in the lung and quantitative assessments of the exposure to airborne fibrous tremolite necessary to produce those burdens. Such information may be obtained from studies of vermiculite workers exposed to tremolite fibres if dimensions and other characteristics are similar to those in Quebec.

At present the concentrations of tremolite in the air of chrysotile workplaces are not known and may be difficult or impossible to measure. However, combining information from the tremolite-exposed vermiculite miners and millers or from other tremolite-exposed industrial workers, with that for the Quebec chrysotile miners and millers, may provide answers. It may be possible to develop exposure indices which reflect the percentage of tremolite which must have been present in the airborne chrysotile dusts to result in the lung burdens of tremolite measured in the lungs of the chrysotile miners and millers. This may reveal what proportion of mesotheliomas in Quebec mills might reasonably be related to tremolite exposure. More importantly it would lead to an understanding of mesothelioma risks in terms of chrysotile containing different percentages of tremolite. Such information may be relevant only to the mining industry, as studies to date, such as that in the friction industry (BERRY and NEWHOUSE, 1983), provide no convincing evidence of chrysotile-related increased risks of mesothelioma in downstream industries.

(b) *Fibre dimensions*

Measurements of fibres in lung tissues by SEBASTIEN *et al.* (1989), based on small numbers, showed that there was a higher proportion of long fibres in the lungs of the Charleston workers than in the lungs of miners and millers. As such differences may not be discerned without a detailed study of the longer fibres (as most of the fibres counted are short), real quantitative differences in the long fibre exposures are not known.

Measurements of the dimensions of fibres in the air of the Quebec mills and in the same textile plant as studied by SEBASTIEN *et al.* (1985) showed that in the textile industry the variation in size distribution with process is quite large and that the percentage of fibres observable by transmission electron microscope and longer than 5 μm was as high as 21% in carding and 24.5% in ring and gang spinning (Gibbs, unpublished data). This contrasts with 1.3% in mining and 4.1% in bagging fibre in a mill (GIBBS and HWANG, 1980). Unfortunately studies in the textile industry have not indicated whether or not the excess lung cancer mortality is evenly distributed; if it is, this might permit the issue of fibre-characteristic differences to be addressed by weighting fibre exposure indices by process.

It should be noted that the proportion of fibres longer than 5 μm decreased to less than 9% in beaming and weaving. For other industrial sectors dimensional data on which to base such comparisons are limited. In fact they may be less needed, as in those instances differences in lung cancer risks between sectors have not been large and mesothelioma risks have generally been accounted for by occupational crocidolite or amosite exposures.

CONCLUSIONS

At the beginning of this paper two questions were posed.

—Can the 'indices of exposure' based on past measurement methods be converted to reliable estimates of fibre exposures based on the membrane filter–phase contrast microscopy method currently used to monitor workplace chrysotile concentrations?

—Are the indices of exposure used in epidemiological studies, in particular of lung cancer and mesothelioma, in one industrial sector directly comparable to those in other sectors, and if not, can they be rendered comparable taking into account etiological factors?

The answer to the first question is clear. There are considerable uncertainties associated with all fibre estimates. These uncertainties may be less for the U.K. friction material manufacturing study where past conditions were simulated (SKIDMORE and DUFFICY, 1983). Nevertheless, the pattern of exposure–response for the British and the U.S. textile workers with exposure estimates derived from completely different data sets are similar. The results of analyses of fibres in lung tissues from miners and millers and from textile workers also indicate considerable consistency in findings, and indeed that exposures in terms of fibres may have been even higher (and risks lower) in the Quebec mines and mills than predicted by the exposure indices used.

It has been well established that cumulative exposures based on impinger counts relate reasonably well to lung cancer mortality in several sectors of industry (McDONALD *et al.*, 1980a,b, 1982; DEMENT *et al.*, 1982; HUGHES and WEILL, 1980). Likewise converted fibre counts with all their uncertainties have also been shown to relate to the risk of lung cancer both in North America and in the U.K. This suggests that both were appropriate. However the uncertainties in the MF/MI conversion ratios make the risk–unit fibre exposure less certain than those based on unconverted exposure data.

While existing data suggest that there are differences in the quality of dusts to which workers in different sectors are exposed, explanations for differences between the lung cancer experience in the textile industry and that in other chrysotile sectors demand more careful scrutiny of qualitative factors (e.g. associated oils, etc.) and exposure assessments, taking into account fibre-dimensional data and especially those relating to long fibres.

Combining data from tremolite-exposed workers such as those in vermiculite mines may provide a means of deriving realistic estimates of risks of mesothelioma associated with chrysotile containing various levels of fibrous tremolite.

[For the discussion of the issues raised in this and the other allied papers see pp. 411–412.]

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