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Invited Editorial

Unfinished Business: The Asbestos Textiles Mystery

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It would be naive to hope, let alone suggest, that in consequence of the recent papers published in Annals on the Quebec chrysotile cohort—the most recent in this issue—that peace may now break out between the warring factions of 'chrysophiles' and 'chrysophobes' (see McDonald and McDonald, 1997). There are encouraging signs, nevertheless, that the distance between the two camps is less than it used to be; it now seems fairly widely accepted that the carcinogenicity of the amphiboles, crocidolite in particular, is appreciably greater than of chrysotile and that contamination of the latter by fibrous tremolite may well have a disproportionate effect. There is also probably general agreement that the very high risks of lung cancer among workers in the manufacture of asbestos textiles have yet to be convincingly explained. This gap in knowledge is serious for until the mystery is resolved the future industrial use of mineral fibres—natural or man made—must be subject to a nagging uncertainty. We would be wise therefore to examine this question in some detail.

The problem first came to light in 1983 with the publication in that year of two independent cohort mortality studies (Dement *et al.*, 1983a part I; Dement *et al.*, 1983b part II; McDonald *et al.*, 1983a) with closely similar findings on exposure response for lung cancer among employees of an asbestos textile plant in Charleston, South Carolina. This was the plant, incidentally, from which an autopsy on an employee gave the first evidence of a link between asbestosis and lung cancer (Lynch and Smith, 1935). The study by Dement *et al.*, was of a cohort of 1261 white males employed for one month or more between 1940 and 1975. There were 35 deaths from lung cancer before the end of 1975 for a SMR against US rates of 1.50; 29 of the 35 occurred twenty or more years after initial employment (SMR 3.39). The study of McDonald *et al.*, was of a cohort of 2545 men, black or white, employed for one month or more between 1938 and 1958 followed to the end of 1977 by which time there had been 66 deaths ascribed to lung cancer. The overall SMR was not calculated but among men employed twenty years or more there were 59 lung cancer deaths; taking account of race, the SMR against South Carolina rates was 2.00. The differing constitution of the two cohorts, and of the mortality rates used for reference were quite sufficient to explain the relatively minor difference in lung cancer SMRs.

Of greater importance was the fact that in both studies exposure response relationships were investigated with almost the same results. Not surprisingly the exposure estimates used in the two studies were also similar since both had essentially the same base, namely over 5000 impinger samples taken since 1930 by the Metropolitan Life Insurance Company (1930–1939), the US Public Health Service (1968–1971) and the company itself from 1930 onwards. Dement *et al.*, 1983a, (part I) estimated the relevant exposure levels to range from 3 to 78 fibres/cc with typical levels well above 10 fibres/cc, although these estimates were all obtained by conversion from dust particle measurement (mpcf). Apart from the preparation area where a conversion factor of 8 was used, 2.5 was applied elsewhere. In the study of McDonald *et al.*, no conversion from particle to fibre counts was attempted. Instead, for comparison of the two studies, both SMRs and RRs (relative risks) were calculated in relation to accumulated exposure (mpcf.y) for white men only, 15 years or more from first employment. The resulting relationships were essentially linear and expressed by quite similar equations, thus:-

Dement *et al.*, $RR = 1 + 0.069$ mpcf.y; McDonald *et al.*, $RR = 1 + 0.051$ mpcf.y

Apart from very small amounts of amosite acquired for experimental purposes in the late 1950s and less than 2000 lbs of crocidolite yarn imported annually at one location from the early 1950s until 1972, only chrysotile, mainly from Thetford Mines, Quebec, but

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also from Rhodesia, was used in the plant during the relevant period.

That these findings were specific to asbestos textiles manufacture and probably to chrysotile is supported by two other cohort studies in this industry. In parallel with the Charleston survey, another very similar in design was made at a plant in Mannheim, Pennsylvania, owned by the same company, which used mainly chrysotile but also small quantities of amosite and crocidolite (McDonald *et al.*, 1983b). The exposure response relationship for lung cancer mortality at Mannheim ($RR = 1 + 0.051$ mpcf.y) was virtually identical to that in Charleston ($RR = 1 + 0.059$ mpcf.y) but, whereas only one death from mesothelioma was observed in the latter, at least 14 were noted in the former. Less easily compared with these two investigations of American textile plants was that by Peto *et al.* (1985) of the textile factory at Rochdale. This factory which also used mainly Canadian or Rhodesian chrysotile, but an important amount of crocidolite in addition, gave very similar findings for both lung cancer risk and mesothelioma incidence to those from Mannheim.

At the time of publication of these various studies it was immediately clear that the slope of the exposure response lines for lung cancer in the textile industry was some 50 times steeper than that observed in Quebec chrysotile miners and millers where exposures were very much higher and for whom an equation of $RR = 1 + 0.016$ mpcf.y for lung cancer risk had been estimated (McDonald *et al.*, 1980). Various possible explanations were considered of which the main were errors in exposure estimation in mining and milling and/or textile manufacture, differences in fibre size distributions, differences in smoking habit, and conceivably the effect of mineral oils sometimes used in textile plants for spraying to reduce dust and to facilitate spinning. However, with the possible exception of the last mentioned, none of these explanations seemed capable of reducing the difference in risk to below 10 fold. In contrast, it was evident that the mystery applied to lung cancer only; certainly at Charleston where no important amount of commercial amphiboles were used, the one case of mesothelioma in over 500 deaths from all causes (2/1000) was entirely in line with the 10 cases from nearly 5000 deaths from all causes (2/1000) in the Quebec cohort (McDonald *et al.*, 1980).

Since the discovery of the problem in the early 1980s, additional information has come to light which has done more to clarify the mystery than to explain it. It is now fairly clear, for example, that so far as chrysotile exposure is concerned, textile manufacture is the exception; available data for asbestos cement and friction products manufacture all approximate to that for mining and milling (Hughes, 1994). The mortality experience of both the Charleston cohort (Dement *et al.*, 1994) and Quebec cohort (Liddell *et al.*, 1997) have been updated and if anything estimates of lung cancer risk in the former have increased and in the latter decreased (see also Stayner *et al.*, 1997). On the other hand, there were now two mesothelioma deaths out of 1259 from all causes (2/1000) in the Charleston cohort compared with 38 of 8009 (5/1000) in the Quebec cohort (McDonald *et al.*, 1997). More revealing, however, are two investigations using lung burden analysis. In the first of these (Sébastien *et al.*, 1989), 161 lung tissue samples taken at necropsy from cohort members—72 from Charleston and 89 from Thetford Mines, Quebec—were analysed by transmission electron microscopy. Statistical analyses of asbestos fibre concentration in lung tissue, with allowance for duration of employment and time from last employment to death, indicated that the Quebec/Charleston ratios for chrysotile concentrations were even higher than those for estimated dust exposure (mpcf). After allowance for the fact that the proportion of tremolite in dust was estimated to be higher in Thetford Mines than in Charleston, the Quebec/Charleston ratios for tremolite were much the same as for chrysotile. Altogether over 4000 chrysotile and tremolite fibres were identified and their length and width measured. With the exception of tremolite fibres over 20 μm in length, the distributions of lengths and widths for both fibre types were closely similar for the two cohorts. Of 175 tremolite fibres from Charleston, 4 (2.2%) were longer than 20 μm compared with only 1 of 405 (0.2%) from Thetford—a difference easily due to chance.

The other fibre burden study, published very recently (Green *et al.*, 1997), entailed the analysis of lung tissue taken at autopsy from 54 members of the Dement cohort from Charleston and, for comparison, 34 other autopsies adequately matched for sex, age, hospital and year of death. The geometric mean concentration of chrysotile fibres per microgram of dried lung was higher in cohort members (33.45) than referents (6.71) and, of tremolite, much higher (3.56 vs. 0.26). There was also some evidence in the asbestos workers that fibre concentration was related to a score of fibrotic changes graded on tissue sections, with tremolite providing a better prediction of fibrosis than chrysotile. In the absence of denominators and times since last exposure and obvious uncertainty about the representativeness of this small series, further interpretation is difficult.

In summary, then, we have strong and consistent evidence that in terms of exposure response the risk of lung cancer, but not of mesothelioma, was much higher—perhaps 50 times higher—in textile workers than in workers in mining and milling, or in the manufacture of asbestos cement or friction products, for all intents and purposes all exposed only to commercial chrysotile. There is nothing to suggest that the estimates of cumulative exposures in the relevant cohorts were seriously in error although questions of peak exposures and fibre size distributions in ambient air have not been examined. There remain two hypotheses, neither of which are well supported, the first concerning fibre length and the other the use of min-

eral oil spray. If fibre length is responsible then the recent evidence (McDonald and McDonald, 1997) that the carcinogenicity of commercial chrysotile largely depends on its tremolite content must be taken into account. From the findings of Sébastien *et al.* (1989), it is clear that the dust to which textile workers were exposed contained relatively lower proportions of tremolite than that experienced by mine workers. Of course, this might not be true of very long tremolite fibres (i.e. $>20\,\mu m$) so a study to evaluate this possibility has now been initiated. Acceptance of this hypothesis, however, would have two implications: first, that long fibres determine the risk of lung cancer but not of mesothelioma; second, that such fibres are specific to the textile process since they would otherwise surely have been present in sufficient quantity in the much higher airborne dust levels of the Quebec mills. The mineral oil hypothesis also has its problems. Spraying was not used in the Rochdale plant until 1974 and it seems probable that persons employed before then were already at high risk of lung cancer. In the Charleston plant, an attempt was made by Dement *et al.* (1994) to assess risk among employees in relation to probable level of oil contamination. This analysis showed only a twofold difference at most but, as oil spray was applied very early in the process, the extent to which levels of exposure were correctly assigned is open to doubt. It has also been stated that mineral oils have not been shown to induce lung cancer in workers exposed to machining oils (Stayner *et al.*, 1997). It is known, however, that cheap oils of varying quality and purity were used, and there is evidence that some such oils have probably caused lung and skin cancer in both the UK and the USA (IARC, 1987).

Thus we are left with an unexplained mystery of very considerable scientific and practical importance which directly affects the future use of both natural and manmade mineral fibres. The question was identified epidemiologically 15 years ago and despite further studies remains unsolved. Without a far greater contribution from physical scientists—including occupational hygienists—on qualitative and quantitative differences in the nature of the relevant exposures and of experimental toxicologists in testing potential hypotheses, the question may never be answered.

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