Raybestos Manhattan

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March 3, 1982

Dr. H. C. Lewinsohn
Perkin-Elmer
Main Ave.
Norwalk, CT 06856

Dear Hilton:

I have enclosed a draft review by Kevin Browne concerning lung fibre burdens.

The point relative to the disappearance of chrysotile fibers and mesothelioma (last paragraph page 8) is particularly interesting.

Sincerely,

John H. Marsh

am
enc.

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ASBESTOS INTERNATIONAL ASSOCIATION

(Limited by Guarantee)

68 GLOUCESTER PLACE, LONDON W1H 3HL

MEMORANDUM

MAR 2 1982

TO: Executive Committee

AIA/20/2/9/HAS

FROM: Director-General

25 February 1982

Measurement of Fibres in Lung

Dr. Kevin Browne, a member of the Medical Advisory Panel (and Medical Adviser to Cape Industries) has written a draft review of the literature on the measurement of fibres in the lung (attached).

Amongst other matters he points out the difference in measuring capabilities between electron and optical microscopes.

The paper refers to the huge numbers of all types of fibres which are lodged in the lungs of everyone. The dried lung of an average person not occupationally exposed to asbestos may contain about 100 million (100,000,000) fibres per gram. Since a dry lung weighs 200-300 grams this gives twenty to thirty thousand million (20 - 30,000,000,000) fibres per lung.

Further facts are that each lung contains 300 million (300,000,000) alveoli and that a fibre in an alveolus can be compared to a twig in a large room. (On the above figures there are 100 twigs per large room!)

The presence of such large "resident" quantities of fibres could be significant in the argument about lower limits and a cancer threshold.

If you have any comments or criticisms of the paper Dr. Browne would be very pleased to receive them at:-

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114 Park Street,
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T R Stack

Sir Neville Stack

Enc. 1

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copies to: MAP
DMAP
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The ATTRIBUTION of ASBESTOS-RELATED DISEASE by the ESTIMATION of LUNG FIBRE BURDENS

SUMMARY and CONCLUSIONS

The three major asbestos-associated diseases all occur independently of asbestos exposure. Interstitial fibrosis arises from many causes but in mild to moderate degree occurs as an incidental finding in 90% of urban dwellers. About one in 10 males in this country dies of lung cancer (the proportion is even higher among industrial workers); mesothelioma has been known as a malignant tumour long before the industrial use of asbestos and its incidence is of the order of 1 : 5-10,000 of all deaths unrelated to occupational asbestos exposure.

There is therefore a need of means to establish whether any particular case of these diseases is due to asbestos, and the amount of asbestos in the lungs is used as an indicator of exposure. But since no way has been found of implicating individual fibres directly in causation, asbestos can never be proved to have caused any individual case of one of these three diseases, i.e. to have been the necessary cause, but can only be shown to have been a sufficient cause if the lung burden of fibre in a particular case was comparable to other cases diagnosed on clinical grounds to be due to asbestos.

Sputum and bronchial lavage have been researched to try to demonstrate a relationship between lung fibre counts and exposure patterns, but both have severe limitations. Sputum, which is obtainable from some but not all subjects, contains coated fibres in only one-third of heavily-exposed subjects and may appear in subjects without any exposure, while little information is available about uncoated fibres. Lavage may provide extra information through the cellular content of the recovered fluid but its application is very restricted.

Much more work has been carried out in recent years on the fibre content of lung tissue obtained post-mortem. Coated fibres (asbestos or ferruginous bodies) are readily seen under the optical microscope, and ranges of counts have been put forward by various authors to distinguish subjects with occupational exposure from those without. Unfortunately, differences in technique and interpretation have been considerable, and the results obtained so far differ by more than an order of magnitude. Moreover, there are two additional objections to the use of coated fibres as an index. Firstly, chrysotile, accounting for 90% of industrial asbestos, is very rarely coated in the lung, so that counts only reflect amphibole exposure. Secondly, the proportion of fibres which is coated is not constant, but is related to fibre length, fibres under 10μ being rarely coated, while above 20μ a majority may be coated. Coating is also diameter-dependent, so that fewer finer crocidolite fibres may be coated than other amphiboles of comparable length.

Uncoated fibres may be detected under the optical microscope, using phase contrast, down to a diameter of about 0.2μ. This represents a proportion varying from about 5-15% of fibres visible by the electron microscope. An additional advantage of the electron microscope is that, with the aid of energy-dispersive X-ray analysis, individual fibres can be identified with a reasonable degree of accuracy, whereas no reliable identification is possible under the light microscope.

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The electron microscope has revealed the presence of large numbers of non-asbestos and non-commercial asbestos fibres in the lung, nearly all of which are undetectable by the optical microscope. Whereas it is probable that an optical count of commercial amphibole fibres will allow a reasonable estimate of the electron microscope count in most cases since the length distribution of particular types can be estimated, non-asbestos fibre counts appear to be unrelated to total optical counts, and such fibres as mullite may be present in very high numbers (e.g. 86 million fibres/gm of dried lung in one case).

In a majority of cases of amphibole exposure the history, combined with the optical count, could be expected to give an adequate indication whether the conditions have been sufficient to produce asbestos-related disease. However, even in these circumstances, there is great need to standardise methods of preparation and counting, comparably to what is being achieved in airborne fibre counting. In borderline cases the electron microscope may give additional information; but, if it is used, it is essential that an adequate sample is counted and each fibre identified - a very time-consuming process which, while it will reveal much higher numbers of fibres, is as likely to cast doubt on attribution of disease to asbestos as it is to confirm it. Again, it will be necessary to standardise techniques before these can be applied on any scale.

It must, however, be added that a recent study has suggested that only counts of fibres over 5μ long may show any relationship with disease, a finding which would receive support from implantation experiments. These have suggested that fibres $>8\mu$ long are the most important in the production of malignancy. Further research is clearly required on this point, but the ultimate outcome may possibly be to reinstate optical microscope counts as the final arbiter.

Chrysotile remains a problem. Recent work has confirmed beyond doubt that long chrysotile fibres disappear fairly rapidly from the lung, although short chrysotile fibres tend to persist in large numbers in the lungs of non-exposed subjects equally with exposed subjects (an alternative explanation of their persistence is that they are constantly being replaced from the environment). It is possible that this reflects the true rarity of chrysotile-related disease; certainly lung fibre counts are of little use at present in assessing the degree of chrysotile exposure and much more research is required on this subject.

Finally, it is perhaps worthwhile to view lung fibre burdens in perspective. The average lung in a person not occupationally exposed to asbestos may contain in the region of 100 million fibres per gram of dried lung, which may be increased 10-fold in those with industrial exposure. This figure has been quoted with alarm by politicians. But the average lung weighs 2-300 gm dry weight, and contains about 300 million alveoli. Many of the fibres are held in interstitial tissue and lymph nodes, but those in the alveoli are in average size comparable to a very small twig in a very large room, so that 50-100 would occupy negligible space; they would in any case merely take their place with the large numbers of non-fibrous particles which also routinely enter the lungs (for example the grains of American soil adhering to tobacco which enter the lungs of smokers of Virginian cigarettes with every inhalation, and which can be recovered if the lungs are lavaged).[1]

The average mineral content of the lung does not in any case correlate with the fibre count, demonstrating that mineral fibres are an insignificant fraction of the total content. The average mineral content is

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INTRODUCTION

Since the major types of pathology attributable to asbestos exposure, interstitial fibrosis, lung cancer and mesothelioma all occur in the absence of asbestos, there is need for criteria on which to decide whether any particular case has been caused by asbestos exposure.

The finding of asbestos fibre in lung tissue can never prove causation. Asbestos fibres, and even asbestos bodies, can be found in the lungs of every urban dweller [4,5], so that their mere presence does not prove potentially harmful exposure. Mild or moderate interstitial fibrosis is present in the lungs of 90% of urban, middle-aged males in the absence of occupational asbestos exposure[6] and is increased in smokers[7] and, despite Hourihane's[8] reference to the occasional finding of asbestos bodies in lung cancer tissue and of a fibre within a mesothelioma, it has not been found possible subsequently to repeat these findings sufficiently regularly to make them a basis for aetiology.

The distinction is of sufficient and necessary conditions. Fibre counts in the tissues of those believed to have died of asbestos-related disease may be related to their exposure. If their fibre counts are found to differ significantly from those in subjects without exposure, then, for any new subject coming to post-mortem, this difference in counts can be used as a yardstick to decide whether he had had sufficient exposure for asbestos to have been a cause of his disease. But if the identical disease also occurs in the non-exposed, asbestos can never on this basis be shown to have been a necessary condition, i.e. it can never be attributable with complete certainty.

It follows also that the yardsticks are constructed from counts obtained where the decision has already been made on clinical or epidemiological grounds as to whether the disease is asbestos-related, and any subsequent comparisons must be made with counts obtained by the same method. The point is important when optical- are compared with electron-microscope counts; one is only to be preferred to another if it provides better discrimination between the exposed and non-exposed; the fact that higher or lower counts are obtained is irrelevant.

METHODS

Three types of material have regularly been used for microscopic examination, viz.:

1. Sputum
2. Bronchial lavage fluid
3. Lung tissue obtained post-mortem.

(In special circumstances other material, e.g. pleural fluid or biopsy tissue, may be available, but these will not be discussed here).

In these biological materials, counting may be of either coated fibres (asbestos or ferruginous bodies) or uncoated fibres.

The examination may be carried out by optical microscope or transmission- or scanning electron-microscope (TEM or SEM).

1. Sputum

Sluis-Cremer[9] in 1964 demonstrated that asbestos-exposed subjects were more likely than control subjects to have ferruginous bodies (FB) in their sputum. Bignon, Sebastien and their colleagues[4] have taken this a step further by showing that numbers of FB in the sputum showed a relationship both to the degree of exposure and the numbers of FB found in lung tissue at subsequent post-mortem. However, both Sluis-Cremer and Bignon observed inconsistencies in the finding of FB, and this has since been confirmed by Gupta and Frost[10] in the course of examining sputum from over 5,000 subjects for the Johns Hopkins Lung Project. 33% of formerly heavily-exposed asbestos workers, 8% of currently lightly-exposed, 1% with some history of asbestos exposure and 0.3% of male smokers over 45 years with no exposure history produced sputum containing FB.

The French group has demonstrated uncoated fibres in sputum by TEM[11]. In one sample of sputum from a heavily-exposed person 700 coated and 100,000 uncoated fibres were found whereas, in a few subjects with moderate or doubtful exposure, numbers of coated fibres ranged from 0-10 and uncoated from 0-500,000. It was noted that in the latter groups most of the fibres were short chrysotile and there was a suggestion that these appear preferentially in the sputum. (Morgan[12] has shown that short amphibole fibres are cleared preferentially).

Unfortunately the impossibility of obtaining sputum from a large percentage of subjects has reduced its usefulness in epidemiological surveys. Apart from that of the French group who themselves point out the problems raised by their TEM findings, no work is apparently being carried out on uncoated fibres in sputum, while the presence or absence of coated fibres in the sputum of any one individual is of uncertain significance.

2. Bronchial Lavage Fluid

Bignon and his colleagues have used broncho-alveolar lavage in the study of lung fibre burdens[11, 21]. The French workers demonstrated a relationship between fibre count and exposure pattern in heavily-exposed asbestos workers. TEM counts in the lavage fluid increased from 5 million to 60 million as exposure increased up to 20 years, declining again to 5 million 12 years after exposure ceased. (Figures are for total counts in lavage fluid - 250 cc). They calculate that if the lavage fluid recovers all the intra-alveolar fibres (a very doubtful assumption), this represents only 1% of all the fibres retained within the lung parenchyma. The mean length of fibres recovered differed according to the method of recovery; in sputum the mean length, 5 μ, was almost identical with that of digested lung parenchyma (4.9 μ) while that from lavage fluid was only 3.3 μ. The authors speculate that while sputum may contain longer fibres deposited in the airways, the longer fibres, once inside the alveoli, tend to be entrapped in the interstitial tissues, while the shorter fibres are more easily cleared.

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The same group have also reported results of counting FB's in lavage fluid by light microscope and note discrepancies between numbers recovered and history of exposure. FB's were found in 88% of subjects with definite occupational exposure, in 14% of those definitely without, and in 42% of those whose history was inconclusive. Lavage has also been used by Haslam et al. at the Brompton Hospital for the diagnosis of asbestosis on the basis of cell counts[13].

But, since lavage is unacceptable as an investigation for wide application, it has limited the volume of data obtained in this way, and much more work remains to be done before its diagnostic usefulness can be established.

3. Post Mortem Lung Tissue

(a) Coated Fibres (Ferruginous Bodies)

FB's were described in great detail by Gloyne in 1931[14] and, since they are readily seen by optical microscope, many attempts have been made in recent times to use them as a quantitative index of exposure. There is general agreement about certain aspects:

- Asbestos bodies may be found in the lungs of all urban dwellers[4, 5]
- They almost always have an amphibole (often a non-commercial variety[15]) as the central core[4, 16, 17, 18]. Chrysotile is very rarely found, perhaps because of its tendency to break down into short, thin fibres
- They are almost always longer than 10μ[20].

Early attempts at quantification used smears of lung juice but, because of the inherent inaccuracy, this has been abandoned in favour of weighed portions of lung tissue. Certain facts about sampling and timing effects have been suggested:

- Morgan[20] has shown that the proportion of coated to uncoated fibres (by optical microscope) increases from 3% at the pleural surface of the lower lobe to 44% at the centre of the same lobe, a finding previously noted by Le Bouffant[18]. He has also shown that the longer the fibre, the greater the probability that it will be coated[12]. In the 10-20μ length-range coated and uncoated fibres are approximately equal in number; above this length coated fibres become increasingly more common than uncoated. Below 10μ coated fibres are rarely found
- Gylseth[19] has demonstrated numbers of coated fibres may differ by more than an order of magnitude in samples taken from different lobes within the same lung
- Bignon[4] has shown that the proportion of coated fibres increases with increasing lapse of time from the last exposure, suggesting that the longer the fibre stays in the lung, the greater the chance that it is coated

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- Churg has shown that in urban populations, where exposure is assumed to be at a continuous low level, there is no tendency for an increase in absolute numbers of FB. But cigarette smoking, perhaps by its adverse effect on lung clearance mechanisms, is associated with higher counts.

Despite these qualifications, figures have been published by various authors relating counts to degree of exposure. The list in Table 1 is representative rather than comprehensive.

Important differences in preparation of specimens may account for some of the differences in the figures. The early counts were mainly carried out using a counting chamber, while more recently the membrane filter technique has been used. Similarly the preparation of the tissue has been carried out by chemical and heat methods. These methodological differences are discussed in many papers, notably Ashcroft[22], Morgan[23] and Gylseth[24].

They would not, however, be sufficient to account for the major discrepancy between the ranges given by Churg and those of the authors. But Churg states that he only counts 'morphologically typical asbestos bodies', whereas Morgan counts all fibres with any evidence of coating. It is clear that if any comparability of counts is to be achieved between laboratories, rules for preparation and counting must be drawn up similar to those for airborne fibres.

Even with agreed rules of procedure, however, the two major problems remain. Firstly, as Le Bouffant and many others have pointed out, since the ratio of coated to uncoated fibres depends on the length distribution, unless this were constant (which of course it is not), a count of coated fibres can never accurately represent the total count. Secondly, since chrysotile is rarely coated, counts of coated fibres can never do more than indicate the degree of amphibole exposure.

Mention must also be made of the paradox described by Morgan[23]. Asbestos bodies have been described as the 'tombstones' of asbestos fibres, implying that, once coated, they cause no further harm. But if it is accepted that it is the long fibres which are responsible for the asbestos-related diseases, it is also true that the longer the fibre the higher the proportion which are coated and, on this assumption, rendered harmless, so that in some cases virtually all fibres over 20μ long are coated. One must then assume that the fibres start the pathological process before they are coated, and Morgan suggests that there is support for this in the fact that thin fibres are less readily coated than thick, and that crocidolite is more carcinogenic than the thicker amosite and anthophyllite.

(b) Uncoated Fibres

(i) The Optical Microscope

Table 2 gives the range of fibre counts found with the optical microscope by various researchers in recent years. Once again

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differences in technique have contributed to differences in results. Whitwell[25] modified the Ashcroft and Heppleston[22] technique and counted no fibres shorter than 6μ. Bossard[3] and Morgan both used phase-contrast microscopy, and both chemical maceration and dry ashing were used. Nevertheless, the figures are of the same orders of magnitude (the high count of 860 million fibres/gram of dried lung found by Morgan came from a Western Australian crocidolite miner) but they also show a considerable overlap between 'exposed' and 'non-exposed', as would in any case be expected, since exposure is a matter of degree and since lung clearance, which is influenced by many factors (e.g. smoking), must be taken into account as well as simple exposure.

(ii) The Electron Microscope

There are two major limitations to the optical microscope. Firstly, the resolving power is such that even using phase-contrast, fibres of less than 0.2μ diameter cannot be counted and, secondly, a decision on the identity of the fibre has to be made solely as morphology and in practice is wholly unreliable.

Morgan, with the best techniques available, claims to have been able to count by optical microscope 14% of the total number of fibres visible by TEM. Bossard[3] suggested a figure of 10%, while Pooley and Clark[26], in an analysis based on the size-range and identification of fibres counted, stated that the percentage of fibres seen on TEM, which could be counted by OM, was $<5\%$ for chrysotile, $<6\%$ for crocidolite and $<30\%$ for amosite. The main difficulty, however, is that, for reasons to be discussed, this percentage varies within very wide limits, so that no firm conclusions on absolute numbers can be drawn from OM counts.

With the TEM, and microprobe, energy-dispersive, X-ray analysis, it is now possible to identify each fibre counted with fair accuracy, and Le Bouffant[18], Gaudichet, Sebastien and Pooley[27], Churg[5] and others have listed many different fibres found by these methods. Pooley[28], for instance, has named 5 asbestos and 13 other fibrous phase minerals detectable in lung tissue, while Le Bouffant[29], quoting Pooley, refers to 31 different types, of which 12 are the most frequent and all but 2 are silicates.

A majority of these different fibres is too small to be seen under the OM. This may be important when OM and TEM counts differ by factors greater than those mentioned above, since a non-asbestos fibre may be responsible, which would not be an indication of asbestos exposure. It is also to be remembered that the work of Stanton[30] has suggested that fibres longer than 8μ are those most likely to induce malignancy, so that these smaller fibres may not be as important as their numbers might imply, although again the relevance of implantation experiments to the effects of inhalation in humans has still to be demonstrated.

Friedrichs and Otto[31], in an important recent paper, provide empirical evidence to suggest that the shorter fibres may be less relevant to the causation of disease. Using the scanning electron microscope without Edax identification of fibres, they evaluated the length and diameter distribution of fibres in 100 cases, which included normal lungs, cases of occupational and non-occupational mesothelioma and asbestosis. Their findings were that no discrimination between groups was provided by mean diameters, or by total fibre counts. When counts of fibres $<2\mu$, $>2\mu$ and $>5\mu$ were analysed, it was found that the area of overlap between the groups of non-exposed and exposed progressively decreased, suggesting that counting for the purpose of discriminating between these two groups should be restricted to the longer fibres.

(iii) The Problem of Chrysotile

The major problem revealed by the accurate fibre identification was that lung fibre counts could give no evidence of exposure to chrysotile, the asbestos fibre which accounts for more than 90% of world industrial consumption. Whitwell[25] pointed out that fibres counted by optical microscope are almost always amphibole, and with the TEM it became clear that long chrysotile fibres disappear rapidly from the lungs so that, even in workers occupationally exposed to chrysotile, the count of long fibres soon becomes indistinguishable from that of controls in most cases. Wagner and Pooley[6], in a comparison of occupationally-exposed cases and controls, found that the former had, on the average, 100 times as much amphibole in their lungs as the controls, but the amounts of chrysotile in cases and controls did not differ significantly. As they comment, a low chrysotile count may indicate little exposure, or high exposure terminating some years before death.

Rowlands, Gibbs and McDonald[32], in a TEM examination of lung fibre content of Quebec miners and millers, also found that chrysotile appeared to be removed from the lungs, while amphibole was retained. Tremolite is found around the chrysotile-containing ore of some Quebec mines but in 'extremely small' amounts. Yet it appeared in the lungs of miners and millers at post-mortem in amounts very similar to chrysotile. These authors did find a relationship between cumulative exposure and chrysotile count, but pointed out that they had not yet analysed the effect of different intervals between cessation of exposure and death and, since the people who worked longer at the mines are likely to have a shorter interval between cessation of exposure and death than those who left the mines earlier, this might account for the differences.

McDonald, McDonald and Pooley[33] also found equal quantities of chrysotile in lungs of North American mesothelioma cases and controls. A similar observation has been made for United Kingdom cases by Jones, Pooley, Clark et al.[34]. This finding may be due to the disappearance of chrysotile subsequent to the induction of the malignant process, but may alternatively indicate that chrysotile in humans rarely or never causes mesothelioma. (In

this connection the mounting evidence that asbestos acts as a promoter and not a complete carcinogen is relevant, since it is characteristic of promoters that continuous or repeated dosage is required for them to be effective. Amphiboles, by being retained in the lung, could operate in this way, whereas chrysotile might fail to do so because of its elimination or dissolution).

But simple elimination or dissolution do not completely resolve the mystery, since large numbers of chrysotile fibres, mostly of very fine-diameter (average perhaps of the order of 0.07μ[28]) are present in almost all subjects regardless of occupational history. Since chrysotile fibres do not persist as coated fibres to any extent, and since short fibres are cleared more efficiently than long[12], the large numbers of short chrysotile fibres found in almost all adult human lungs at post mortem is puzzling. A further curiosity is the distribution in the parietal pleura. Le Bouffant[18] and Sebastien[35] have shown that, while amphibole fibres are seldom found in appreciable quantities in the parietal pleura, it regularly harbours large numbers (up to 5 million/cc of fixed tissue) of short chrysotile fibres, these being particularly readily found in pleural plaques. Moreover, no correlation could be demonstrated between counts in the lung parenchyma and the parietal pleura.

(iv) Fibre Counts and Asbestos Exposure

Whitwell[25], using the optical microscope and a modified Ashcroft and Heppleston technique, found that even in mild cases of asbestosis over 1 million asbestos fibres could be found per gm. dried lung. Moreover, this increased with the severity of asbestosis, so that the mean for mild asbestotics was 4.7 million, for moderate cases 9.6 million and for severe cases 28 million. Since then 1 million fibres (optical count) has tended to be a guideline in deciding attributability of pathology to asbestos exposure. A guideline is particularly needed for mild asbestosis and for lung cancer, since it is now recognised that some degree of fibrosis of the lung is the rule rather than the exception in all urban males over 40. Wagner[6] has recently shown that, if fibrosis (or asbestosis) was graded 0-4 in increasing severity, 74% of a control series not occupationally-exposed had Grade 1 fibrosis and 16% had Grade 2, only 10% being classified as without. Lung cancer, even in heavy smokers, attracts compensation when an occupational history is accompanied by some fibrosis and, where this is mild and the occupational exposure limited, the fibre count may be the deciding factor.

Table 3 gives fibre counts now being established by transmission electron microscopy, and the important question is whether the different set of guidelines arrived at by TEM is an improvement on or merely an alternative to that provided by OM.

Apart from the fact that it is much more demanding in time and expensive equipment, the TEM has, as we have seen, one major advantage, namely its ability combined with Edax to identify individual fibres, and one disadvantage, namely that the sample examined is much smaller[35]. Sampling variations may in any case

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be important in borderline cases. Pooley, quoted by Rowlands[32], has stated that they may vary by a factor of 2, and Sebastien[36] that sampling-site differences may account for variations in the count of up to one order of magnitude.

Reproducibility has to be judged by the only inter-laboratory comparison published to date[27] (between Cardiff and Paris) which showed reasonable agreement, although for one sample out of three there was nearly 100% variation in the total count.

The best discussion on the use of OM counts in borderline cases and the additional information derived from the TEM is given by Seal[37]. He suggests that lesser degrees of asbestosis may occur with OM counts as low as 250,000 and says that the role of the TEM is far from clear. But in a series of illustrative cases he demonstrates how the TEM may help both to establish and to reject a diagnosis of asbestos-related disease. This occurs mainly through the establishment of the identity of the main fibres counted. For instance, in his first case, the OM count of 292,000 (right lung) and 425,000 (left lung) became a TEM count of 21 million, in itself unhelpful, but a finding of 49% of the fibres to be amosite weighed the scales in favour of an occupational causation. Another OM count of 500,000 gave a TEM count of 158 million, of which 65% were crocidolite. On the other hand, in a case with an OM count of 117,000 in one area and 306,000 in another, the TEM count was 50 million, of which 43% were mullite and only 26% commercial asbestos; the opinion in this case was that, despite 2 years' asbestos exposure 20 years previously, the microscopic fibrosis in this case was not occupationally-related.

A further extremely illuminating example comes from Jones' summing-up of one of the sessions at the 1979 Lyon Conference[38]. In stating how important it is to use the TEM where fibrosis is found in the absence of asbestos fibres under OM he refers to 2 cases in which no fibres or bodies were detectable under OM yet significant concentrations of chrysotile fibres were identified by EM, and he says how important it is that such examples are recognised for compensation purposes. However, he then has added, in a footnote, that further investigation showed the fibres to be mullite and not chrysotile! Mullite is a fibrous aluminium silicate possibly produced by the thermal transformation of clay[29] through the heating of bricks, and may appear in lungs in large numbers (86 million/gm in one count[27]), its mean dimensions being about 1μ long and 0.1μ diameter. Non-industrial asbestos fibres are also very common and Churg[5], in an examination of the lungs of non-occupationally-exposed urban dwellers, found non-asbestos fibres 4 times as numerous as asbestos, with the latter consisting mainly of short chrysotile fibres. Commercial amphiboles (amosite and crocidolite) accounted for less then 4% of total amphiboles and less than 1% of all asbestos fibres.

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TABLE 1

	Coated fibre counts and some equivalents (fibres/gm dried lung)					
	OPTICAL MICROSCOPE				ELECTRON MICROSCOPE	
	Coated fibres		Uncoated fibres			
	Non-exposed	Exposed	Non-exposed	Exposed	Exposed	Non-exposed
GROSS 1970[39]	300 - 4,000	70,000-191,000,000				
DAVIS & GROSS 1973[40]	27 -31,000		500 - 170,000			150,000-6,600,000
ASHCROFT 1973[41]	0-4,000,000					
ASHCROFT & HEPPLESTON[22]		62,000-192,000,000		138,000-684,000,000		
FONDIMORE & DESBORDES 1974[17] *	93%<250	100%>2,500				
SEBASTIEN 1977[36]	540-1,400	1,500-2,400,000		1,700-19,000,000		
CHURG 1977[15] *	<1,000	1,000-100,000				
GYLSETH 1981[19]		1-2,000,000 +x			100,000- + 2,300,000	
MORGAN 1980[23]	0-500,000	1,000-11,500,000				
1981[20]		10,000-47,000,000		400,000-850,000,000		

* Estimated on the basis of wet lung figures x 10.

+ Scanning electron microscope.

x 2 subjects only.

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TABLE 2

Optical counts of uncoated fibres

Fibres/gm dried lung

	Non-exposed	Exposed
BOSSARD & RUTTNER[3]	360,000-4,500,000	700,000-720,000,000
WHITWELL[25]	0-200,000	20,000-70,000,000
MORGAN[20]		800,000-860,000,000
ASHCROFT & HEPPLESTON[22]		138,000-684,000,000

TABLE 3

Fibre counts by TEM - fibres/gm dried lung

	Non-exposed	Exposed
DAVIS & GROSS[40]	153,000-6,750,000	
GYLSETH[42]	100,000-2,300,000	-490,000,000
CHURG & WARNOCK[5]*	8,000,000	
BIGNON et al[11] +	up to 100,000,000	1,000,000->100,000,000
JONES, POOLEY et al[34] X		
chrysotile	10% > 10,000,000 20% < 100,000	20% > 10,000,000 40% < 100,000
amphibole	35% > 1,000,000 20% < 100,000	15% > 100,000,000 5% < 100,000
WAGNER, POOLEY et al[6] X		
chrysotile	20% > 10,000,000 10% < 1,000,000	30% > 10,000,000 20% < 1,000,000
amphibole	20% 1-10,000,000 40% < 100,000	20% > 100,000,000 15% < 1,000,000
non-asbestos	1,000,000-100,000,000	1,000,000-1,000,000,000
ROWLANDS, GIBBS & McDONALD[32] (Quebec miners & millers)		
chrysotile		4% > 100,000,000 25% < 1,000,000
tremolite		11% > 100,000,000 38% < 1,000,000
non-asbestos		0% > 100,000,000 18% < 1,000,000

* Estimated on the basis of wet lung figures x 10. These figures are based on counts of asbestos fibres multiplied by 5 to correct for non-asbestos fibres (the author's figure).

\+ Asbestos only. Estimated on the basis of wet lung figures x 10.

X Figures derived from graphs and therefore approximate only.

REFERENCES

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1. Bernard J, Gee L, Fick Jr. RB. Bronchoalveolar lavage. Thorax 1980, 35, 1-8.

2. Nagelschmidt G. Some observations of the dust content and composition in lungs with asbestosis, made during work on coal miners pneumoconiosis. Annals of the New York Academy of Sciences 1965, 132, Art 1, 64-76.

3. Bossard E, Stolkin I, Spycher MA, Ruttner JR. Quantification and particle size distribution of inhaled fibres in the lung. Biological effects of Mineral Fibres (ed Wagner JC) 1980, 1, 35-41.

4. Bignon J, et al. Review of some factors relevant to the assessment of exposure to asbestos dusts. The Use of Biological Specimens for the Assessment of Human Exposure to Environmental Pollutants 1979, 73-108, (IOEH 4851).

5. Churg A, Warnock ML. Asbestos fibers in the general population. American Review of Respiratory Disease 1980(November), 122(5), 669-678, (IOEH 5263).

6. Wagner JC, Pooley FD, Berry G, Seal RME, Munday DE, Morgan J, Clark NJ. A pathological and mineralogical study of asbestos-related deaths in the United Kingdom in 1977. Inhaled Particles V (ed Walton H) - in press.

7. Weiss W. Cigarette smoking and diffuse pulmonary fibrosis. Am Rev Repir Dis 1969, 99, 67-72.

8. Hourihane O'B D. A biopsy series of mesotheliomata and attempts to identify asbestos within some of the tumours. Ann N. Y. Acad Sci 1965, 132, Art 1, 647-673.

9. Sluis-Cremer GK. Asbestosis in South Africa - certain geographical and environmental considerations. Ann N. Y. Acad Sci 1965, 132, Art 1, 215-234.

10. Gupta PK, Frost JK. Cytologic changes associated with asbestos exposure. Seminars in Oncology 1981(September), 8(3), 283-289, (IOEH 5580).

11. Bignon J, et al. Measurement of asbestos retention in the human respiratory related to health effects. National Bureau of Standards Special Publication 506. Proceedings of the Workshop on Asbestos: Definitions and Measurement Methods held at NBS, Gaithersburg, MD 1977(Jly 18-20) issued Nov. 1978, 95-119, (IOEH 5177).

12. Morgan A. Effect of length on the clearance of fibres from the lung and on body formation. Biological effects of Mineral Fibres 1980,1,329-335.

13. Haslam PL, et al. Bronchoalveolar lavage in pulmonary fibrosis: comparison of cells obtained with lung biopsy and clinical features. Thorax 1980, 35, 9-18.

14. Gloyne SR. The formation of the asbestosis body in the lung. Tubercle 1931, 12, 399-401.

15. Churg A, Warnock ML. Correlation of quantitative asbestos body counts and occupation in urban patients. Archives of Pathology and Laboratory Medicine 1977(December), 101, 629-634, (IOEH 5122).

16. Pooley FD.. Asbestos fibre in the lung and mesothelioma a re-examination of the Malmo material. Acta path microbiol scand, section A, 1973, 81, 390-400, (IOEH 3994).

17. Fondimore A, Desbordes J. Asbestos bodies and fibers in lung tissues. Environmental Health Perspectives 1974, 9, 147-148, (IOEH 4085).

18. Le Bouffant L, et al. Observations on asbestos fibres and on various mineral formations in the asbestotic lungs(French). Mul Resp Supplement 2, 1976, 4, 121-140, (IOEH 4510).

19. Gylseth B, Baunan R. Topographic and size distribution of asbestos bodies in exposed human lungs. Scand J Work Environ Health 7 1981, 190-195(IOEH 5597).

20. Morgan A, Holmes A. Concentrations and characteristics of amphibole fibres in the lungs of workers exposed to crocidolite in the U.K. gas-mask factories, and elsewhere, during the second world war. British Journal of Industrial Medicine (in press).

21. Gaudichet A, Sebastien P, Bientz M, Jaurand MC, Atassi R, Bonnaud G, Bignon J. Amiante et lavage broncho-alveolaire. Mal Resp 1978, 6, 345-351.

22. Ashcroft T, Heppleston AG. The optical and electron microscopic determination of pulmonary asbestos fibre concentration and its relation to the human pathological reaction. J Clin Path 1973, 26, 224-234.

23. Morgan A, Holmes A. Concentrations and dimensions of coated and uncoated asbestos fibres in the human lung. British Journal of Industrial Medicine 1980, 37, 25-32.

24. Gylseth B, et al. Analysis of inorganic fiber concentrations in biological samples by scanning electron microscopy. Scand J Work Environ Health 7 1981, 101-108, (IOEH 5592).

25. Whitwell F, et al. Relationship between occupations and asbestos-fibre content of the lungs in patients with pleural mesothelioma, lung cancer, and other diseases. Thorax 1977, 32, 377-386, (IOEH 4575).

26. Pooley FD, Clark NJ. A comparison of fibre dimensions in chrysotile, crocidolite and amosite particles from samples of airborne dust and from post-mortem lung tissue specimens. Biological effects of Mineral Fibres, 1980, 1, 79-86.

27. Gaudichet A, et al. Identification and quantification of asbestos fibres in human tissues. Biological effects of Mineral Fibres 1980, 1, 61-68.

28. Pooley FD. A report on investigations into the type and quantity of fibres in cases of mesothelioma and in controls in the U.K. Proceedings of Asbestos Symposium Johannesburg, South Africa (ed Glen HW), 3-7 October,1977, 83-84.

29. Le Bouffant L. Physics and chemistry of asbestos dust. Biological effects of Mineral Fibres 1980, 1, 15-33.

30. Stanton MF, Layard M. The carcinogenicity of fibrous minerals. Workshop on Asbestos: Definitions and Measurement Methods (NBS Special Publication 506) 1978, 143-151.

31. Friedrichs KH, Otto H. Fibers in human lung dust samples: a scanning electron microscope study. American Industrial Hygiene Association Journal 1981, 42(2), 150-156, (IOEH 5296).

32. Rowlands N, Gibbs GW, McDonald AD. Asbestos fibres in the lungs of chrysotile miners and millers - a preliminary report. Inhaled Particles V (ed Walton H) - in press.

33. McDonald AD, McDonald JC, Pooley FD. Mineral fibre content of lung in mesothelial tumours in North America. Inhaled Particles V (ed Walton H) - in press.

34. Jones JSP, Pooley FD, et al. The pathology and mineral content of lungs in cases of mesothelioma in the United Kingdon in 1976. Biological effects of Mineral Fibres 1980, 1, 187-199.

35. Sebastien P, et al. Asbestos retention in human respiratory tissues: comparative measurements in lung parenchyma and in parietal pleura. Biological effects of Mineral Fibres 1980, 1, 237-246, (IOEH 5420).

36. Sebastien P, et al. Topographic distribution of asbestos fibres in human lung in relation to occupational and non-occupational exposure. Inhaled Particles IV Part 2 (ed Walton) 435-446.

37. Seal RME. Current views on pathological aspects of asbestosis (the unresolved questions and problems). Biological effects of Mineral Fibres 1980, 1, 217-235.

38. Jones JSP. Discussion summary. Biological effects of Mineral Fibres, 1980, 1, 377-381.

39. Gross P, et al. Fibrous dust particles and ferruginous bodies (methods for quantitating them and some results from the lungs of city dwellers). Arch Environ Health July 1970, 21, 38-46, (IOEH 3331).

40. Davis JMG, Gross P. Are ferruginous bodies an indication of atmospheric pollution by asbestos? Biological effects of Asbestos (IARC) 1973, 238-242.

41. Ashcroft T. Epidemiological and quantitative relationships between mesothelioma and asbestos on Tyneside. J. Clin Path 1973, 26, 832-840, (IOEH 4016).

42. Gylseth B, et al. Inorganic fibers in lung tissue from patients with pleural plaques or malignant mesothelioma. Scand J Work Environ Health 7 1981, 109-113, (IOEH 5593).