cularly for mesothelioma, but some (Cullen, 1998; Stayner *et al.*, 1996) have regarded the extent of these differences as unimportant, particularly since chrysotile has been overwhelmingly the most commonly used fibre.

The interpretation of the whole body of evidence depends importantly on the interpretation of results from cohorts with predominantly chrysotile exposure together with a minority contribution—usually a few per cent—from amphiboles. As long as the difference in potency is not extreme these cohorts can be reasonably interpreted as indicating the risk of chrysotile exposure. But if the differences in potency are very substantial this is no longer the case. Furthermore, in this situation an additional source of error in the estimation of exposure will be introduced, since the measured exposure (mainly of chrysotile) will often be a poor proxy for the relevant exposure.

The data in this review suggest that order of magnitude differences in potency may indeed apply for mesothelioma, and probably also for lung cancer. The main reason this review differs from earlier similar reviews is in its use of the information from the amphibole mining cohorts in South Africa and Australia. The publication of mortality results from the South African mines seems to have gone almost unnoticed. The Australian cohort has been the subject of a series of publications with varying analytical approaches and varying results. One of these analyses gave a lung cancer risk from the cohort of around 1% per fibre/ml.yr, and this is the value that has been most usually quoted, but this is probably an underestimate due to incomplete follow up at older ages. This review is also the only one to have exploited the (admittedly uncertain) quantitative exposure information in the Massachusetts cohort.

Implications of the non-linear exposure response for mesothelioma

A non-linear relationship between the rates of pleural and peritoneal mesothelioma is more readily explicable if the cancer risk is proportional to some function of the concentration of fibres in the target tissue, rather than the simple number burden.

If concentration rather than number burden is the relevant parameter, then the possibility of a threshold type relationship becomes much more plausible, since if the effect depends on fibres acting together, there must presumably be some point at which individual fibres are simply too far apart to exert any joint effect. Of course, if the mechanisms of distribution of fibres within the lung and pleura are such that fibres tend to be delivered preferentially to particular areas—and there is evidence that this is the case in the pleura (Boutin *et al.*, 1996)—the effective threshold level may be very low. In any case such a threshold is unlikely to be a sharp cut-off. Random variations in the distribution of fibres in particular lungs, and differences in individual susceptibility will mean that the exposure response curve simply starts to descend more steeply from some point on the cumulative exposure scale.

Also, fibre concentration is the more plausible exposure metric for the production of fibrosis, so this interpretation is consistent with the link suggested by the HSE fibre review (and by other authors) between the two processes. It should be noted that the suggestion is not that tumours arise directly from fibrosis, but that both are products of an underlying inflammatory process.

If fibre concentration in tissue is the key risk measure, the extreme sensitivity in animal experiments to intra-peritoneal and intra-tracheal instillation of massive fibre doses is also readily explicable.

Combined with the knowledge of the much greater solubility of chrysotile in the lung, this may also explain why asbestos related diseases have only been clearly seen with heavy chrysotile exposures. If exposures are heavy and sustained a sufficient concentration of fibre in the lung may be maintained to trigger both fibrosis and malignancy. The extreme rarity of peritoneal mesothelioma in cohorts exposed to chrysotile alone may also be explained. If the route by which asbestos reaches the peritoneum is from the pleural cavity, it may well be that chrysotile fibres do not survive long enough in body tissues to make the journey in sufficient numbers.

Chrysotile and asbestos related malignancy

Smith and Wright (1996), showed a ranking of 25 cohort studies by proportional mortality from pleural mesothelioma and argued that since chrysotile was the primary exposure for two of the top 10 cohorts and present as part of the mix in six of them, and that the picture for crocidolite in terms of its presence in the mix was similar, while amosite was less evident than either of the other two fibre types, that chrysotile must therefore be similarly potent as a cause of pleural mesothelioma. What this argument ignores is any quantification of exposure. Without quantification it is very difficult to draw any conclusion about relative risk from a simple ranking by mesothelioma rate. In relation to the 25 cohorts identified in this review an equally pertinent observation might be that all of them involved exposure to one or other of the amphibole fibres. Smith and Wright also present arguments based on the relative levels of mortality from pleural mesothelioma and from excess lung cancer to suggest that there is only moderate difference between the potency of chrysotile and the amphibole fibres for causing mesothelioma—they suggest a factor of three or four. However this argument is based on the assumption that all fibre types are equally potent for lung cancer. If this review is correct in suggesting that this is not the case, these arguments are not valid.

Nicholson and Landrigan (1996), present similar