human carcinogen, or a cocarcinogen, and/or potentiator of cigarette smoke and/or other factors.

The Influence of Fiber Type and the Nature of Exposure on Biological Response

After the 1964 New York Conference (5), the UICC working group on cancer urged study of "the relationship of dust dosage (including concentration and duration of exposure) and the composition and physical state of the dust to the incidence of asbestosis, carcinoma of the lung, mesothelioma and other cancers." In other words, 2 areas were identified for urgent future research: (*1*) to establish whether dose-response relationships exist between exposure and biologic response, and (2) to establish whether the composition and physical state of the dust affects these dose-response relationships.

In the ensuing 11 years, health scientists throughout the world have gathered data in support of the first hypothesis, namely, that a dose-response relationship exists for all of the responses listed (asbestosis, carcinoma of the lung, other cancers, and, probably, mesothelioma). Furthermore, this holds for all types of fiber and for all types of exposure investigated. The evidence has been already summarized in table 4.

It has proved more difficult to investigate the second hypothesis, that composition and physical state of the dust influence the responses, because this requires the comparison of dose-response curves for different fibers, or for the same fiber under different exposure conditions, e.g., mining and milling compared to manufacturing. Even animal studies in which exposure can be relatively well controlled are inconclusive about the relative fibrogenicity of different fiber types (62, 224) although differences in carcinogenic potential have been shown (224). Epidemiologic studies in man in different occupationally exposed groups suggest differences between fibers, and between exposures, in terms of their carcinogenic potential both for lung cancer (table 6) and for mesothelioma (224); however, it is usually impossible to establish to what extent these can be explained by differences in exposure levels and associated factors, such as cigarettes and other co-carcinogens. Furthermore, exposures to one fiber type only are rare (usually in mining), and most production workers have mixed exposures (224). For instance, table 8 summarizes data collected in Quebec asbestos workers, exposed only to chrysotile fibers. Even in these results, which show a dose effect for all responses, there are between-area differences, particularly for radiologic changes, for men of the same stock and working the same geologic deposit, and with exposure calculated using the same type of index. Given these between-area differences, to what extent, if any, are these dose-response curves applicable to other working populations?

Criteria for comparability require that both the dose and the response be measured in a similar fashion and that the populations compared have equivalent susceptibility. Enough has already been said to indicate that even if the first 2 criteria were met, virtually nothing is known about the factors accounting for susceptibility, much less whether it is possible to measure them in practice. The only comparison attempted was inconclusive, because mortality was assessed by fundamentally different techniques (figure 5). Thus, it is not possible to deduce from this comparison whether, indeed, there is greater risk for production workers compared to miners (figure 5, upper panel) attributable to differences in the nature of the exposure, an interpretation for which there is little scientific justification, or whether the risk is comparable for both groups, but the scaling (figure 5, lower panel) requires appropriate adjustment.

Despite the difficulties in making between-study comparisons, a consensus has emerged, outlined in a carefully reasoned paper by Kleinfeld (224), and in the conclusion of the Advisory Committee on Asbestos Cancers (7, p. 341). It is believed that there are gradients in the mesothelioma-producing potential, related to fiber type (greatest with crocidolite, less with amosite and with chrysotile, least with anthophyllite) and to occupation (e.g., for amosite, greatest in insulation workers compared to miners). Gradients in fibrogenic capability of the different fibers, less clear, may also be present, with crocidolite leading chrysotile, whereas gradients in lung cancer risk may be more closely related to the nature of the exposure, with production leading mining, at least for chrysotile.

To date, the best explanation of these gradients in biologic potential is that developed by Timbrell (7, p. 295), namely, that biologic activity relates to the degree of penetration and deposition in the lung (see also figure 6). Thus, the greater mesothelioma potential of crocidolite compared to amosite, anthophyllite, and chrysotile, could be due to its smaller fiber size and its other aerodynamic properties, which permit greater penetration and deposition. Similar-