The silica carcinogenicity issue in Japan

In the opinion of this writer, the recent action by the Japanese government amending relevant laws designating lung cancer as a compensable complication of pneumoconiosis is a big step towards improvement. Pneumoconiosis victims who develop lung cancer will be compensated under the national compensation plan. In Japan, there are currently an estimated 12 000 pneumoconiotics officially recognised as “administrative level (AL) 2.3 or 4 (1 stands for ‘no pneumoconiosis’)” who would be potential beneficiaries. Prior to the amendment, compensation was restricted to lung cancer cases complicating pneumoconiosis of only AL 4 (and AL 3, limiting the number of compensated cases to less than 30 per year. With the inclusion of lung cancer as one of the six designated complications of pneumoconiosis, compensation coverage is extended to essentially all pneumoconiotics (AL 2 or higher), with entitlement to additional benefits, for example, surviving family members’ pension, if a pneumoconiotic develops lung cancer and dies of it. The amendment therefore came as a blessing to pneumoconiotic victims and families, and was welcomed by the media.1 Despite the positive implications, however, I would like to express here reservations regarding some aspects of the 2002 Final Report (Report)2 of the Expert Committee (Committee), convened by the Ministry of Health, Labour, and Welfare (MHLW) (of which KT was member), which laid down the basis for the amendment.

My criticism is specifically aimed at the refutable stance taken by the Report towards the carcinogenic risk of crystalline silica (silica). Although the Committee was convened “in consideration of the judgment by the International Agency on Research on Cancer (IARC)” to classify silica as a carcinogen, and its subsequent endorsement by the Japan Society of Occupational Health,3 the Committee ultimately concluded that: (1) epidemiological studies do not support silica carcinogenicity but indicate increased risk of lung cancer among pneumoconiotics; (2) neither animal or mutagenicity studies support silica carcinogenicity; and (3) pathological findings suggest that carcinogenesis is triggered by fibroproliferative changes of lung interstitial tissue, alveolar structural reforma-
tion, and repair of DNA damage. The third point was advanced as a possible underlying mechanism in line with the assertion of epidemiological studies that, although the risk of lung cancer is evident, it is confined to those who develop pneumoconiosis (from which silicosis cannot be separated). Pneumoconiosis was thus judged to be a necessary condition for lung cancer among silica exposed workers. Hence, silica remains outside the sphere of carcinogenic substances regulated by the MHLW, even though the MHLW took into serious consideration the designation of silica as a carcinogen by the IARC and JSOH.

The Committee’s assertion of epidemiological studies relied on a meta-analysis of epidemiological studies evaluating: (1) overall lung cancer risk among silica containing dust exposed (dust exposed) workers (18 studies);2 7 weighed pooled risk = 1.32; 95% CI 1.24 to 1.39); (2) lung cancer risk among dust exposed workers shown separately for non-silicotics and silicotics (eight studies);2 8, 11, 18, 21, 23–26 weighed pooled risk for non-silicotics = 0.97; 95% CI 0.84 to 1.14; and (3) lung cancer risk among pneumoconiotics (13 studies);2 5, 11, 18, 19, 23–26 weighed pooled risk = 3.71; 95% CI 3.45 to 3.99. It was thus deduced that lung cancer risk is slightly increased among dust exposed workers, but not among non-pneumoconiotics, whereas lung cancer risk is apparent among pneumoconiotics (which could not be explained by bias or smoking). Further, combined with the aforementioned negative assertion on animal and mutagenicity studies, the Committee drew the conclusion that “there is no evidence to support the carcinogenicity of silica itself”, and “further findings are needed for judgment”.

The most serious problem with the reasoning behind this position is the reliance on eight epidemiological studies showing lung cancer risk separately for non-silicotics and silicotics. It is obvious that few of these studies were designed to specifically address the issue of dissociating risks between non-silicotics and silicotics, with the notable exception of the study by Checkoway and colleagues,19 in which lung cancer risk was detected in relation to cumulative exposure among non-silicotics. In the remaining studies where such data were lacking, most authors acknowledged the possibility that the exposure profile of subjects was represented by the status of fibrosis, so the presence/absence of silicosis should be regarded as a marker of high/low cumulative exposure. The argument that silicosis is, but silica itself is not, a risk factor for lung cancer cannot be advanced from a pooled risk calculated for the non-silicotics in these studies. Furthermore, such arguments tend to underestimate the fact that the distinction between the presence/absence of fibrosis is arbitrary because fibrosis occurring at microscopic levels often eludes radiographical detection. The fairly limited scope of the available epidemiological literature warrants that the silica carcinogenicity issue be treated in perspective, combining findings from the spectrum of silica exposed subjects, including non-silicotics and silicotics. The rebuttal of the animal and mutagenicity studies as failing to provide evidence of silica carcinogenicity only lessens the scientific credibility of the Committee’s argument.

Finally, I reiterate that significant progress has been made administratively in Japan to provide improved opportunities for follow up of pneumoconiotic victims and better compensation if and when these develop lung cancer. Needless to say, such action falls into the realm of secondary and tertiary prevention. Further steps should be taken to reevaluate silica carcinogenicity and incorporate it into administrative measures aimed at primary prevention.

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References
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NOTICE

The Faculty of Occupational Medicine, Silver Jubilee celebration conference, Thursday, 29 January 2004

The Faculty of Occupational Medicine has scheduled their Silver Jubilee celebration conference for Thursday, 29 January 2004 at the Royal College of Physicians in London.

Keynote speakers include Professor Malcolm Harrington CBE, Emeritus Professor of Occupational Medicine at the University of Birmingham; the leading oncologist of international repute, Professor Karol Sikora, once Chief of (and still Adviser to) the World Health Organisation Cancer Programme; and the management “guru”, Christine MacNulty from the United States.

The aims of the conference will be to consider key human and medical issues relating to occupational medicine today; and explore potential advances over the next quarter century. The conference is expected to attract around 300 Faculty members and their colleagues, including occupational physicians; and senior human resource managers in large and small public and private sector organisations.

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