rence of disease, usually beginning more than 15 years after initial exposure. A synergistic effect between cigarette smoking and asbestos exposure is well demonstrated in the production of lung cancer (Table 4). Liddel (2001) noted that non-smokers have a higher relative risk due to asbestos than smokers, and the interaction between asbestos exposure and cigarette smoking is rather additive than multiplicative[8]. But Doll & Peto (1985) pointed out that this difference might be partially, and perhaps entirely, due to methodological artifacts, the most important of which was probably the misclassification of some current or ex-smokers as lifelong non-smokers[9]. For practical purposes, removal of either agent would be very effective. When the prevalence of cigarette smoking is very high in a country or area, smoking cessation programs should be promoted preferentially.

Merler, et al. (1997) reviewed the chemoprevention trials involving workers exposed to asbestos, and concluded that there were no practical tools for efficient, safe chemoprevention of asbestos induced respiratory malignancies[10].

Table 4. Combined effect of asbestos exposure and cigarette smoking on mortality of lung cancer (relative risk)

Study (Year)	As (+) Sm (+)	As (+) Sm (-)	As (-) Sm (+)	As (-) Sm (-)	Reference
Meurman LO (1979)	19.0	1.6	12.0	1.0	(4)
Hammond EC (1979)	53.2	5.2	10.9	1.0	(5)
McDonald JC (1980)	25.0	12.8	11.8	1.0	(6)
Morinaga K (1993)	48.3*	11.9*	4.1	1.0	(7)

As: asbestos exposure, Sm: cigarette smoking, * asbestosis

Mesothelioma

Mesothelioma is clearly associated with occupational and environmental exposure to amphiboles.

IARC (1973) concluded that mesothelioma is caused by exposure to crocidolite, and less frequently to amosite and chrysotile in the manufacturing and application industries, but no mesothelioma had been reported at a Finnish anthophyllite mine at the time[11]. Finnish miners exposed to anthophyllite seemed to have low risk of mesothelioma[12]. IPCS (1998) evaluated that exposure to chrysotile asbestos poses increased risk of mesothelioma in a dose-dependent manner[13]. Crocidolite has a far greater potency of inducing mesothelioma than chrysotile, but the difference of potency between amphiboles (crocidolite/amosite) and chrysotile ranges from 20 to 500 times according to the speculation of different researchers[9,14,15]. Crocidolite and amosite were banned in most countries, and chrysotile has not been used in industrialized countries (The Minister of Health, Labor and Welfare, Japan declared that chrysotile would be banned in the near future on June 28, 2002). These types of asbestos had been used for insulation and building materials in the past, and we cannot easily identify and differentiate them by appearance. Special regulation, task guidance, and training for removal or demolishing asbestos-containing materials is needed, and workers must use strict control measures. The lower the amount of asbestos exposure, the lower the risk of mesothelioma will be found. Mesothelioma is not linked with cigarette smoking.

A chemoprevention study (oral retinol) is ongoing[16].

Screening for asbestos-related diseases

Asbestosis

For detecting asbestosis, chest X-ray is useful for current workers or ex-workers in the manufactur-

ing and application industries. Computed tomography may be recommended for borderline findings of asbestosis. Lung function test may also be an indicator in the prognosis of asbestosis. Coutts II et al. suggested that a percentage of predicted FEV1.0 was of value in predicting death[17]. According to our experience in Osaka, the 10-year survival rate of asbestosis with radiological finding as ILO Grade 1 (1/0, 1/1, 1/2) was 48.7%[18]. This is probably too late for the screening for asbestosis by chest X-ray to prevent premature death for asbestos-exposed workers, because some of them may die from lung cancer or mesothelioma without radiological asbestosis.

Lung cancer

WHO's recent report (2002) states that screening for lung cancer has been attempted with X-rays and cytological examinations, but investigations have failed to establish its effectiveness[19].

An international expert meeting held in Helsinki (2000) concluded that a spiral CT screening for lung cancer is highly desirable to follow the results of the ongoing investigations in order to apply them quickly when scientifically valid[20]. However, both Japanese and ELCAP experience show that the vast majority found are adenocarcinomas, and about half of the low density ground-glass shadows in a Japanese trial showed no change in size after two years' follow-up; this supports the existence of an overdiagnosis bias and probable pseudodisease[21-24]. Early diagnosis will always appear to improve survival because of the volunteer effect, the zero-time shift problem (lead-time bias), and the preferential detection of slowly progressive disease (length-time bias)[25]. WHO's recent report mentions that randomized trials are required before this technique (low-dose spiral CT) is recommended for use[19].

Mesothelioma

In recent years, immunohistochemical staining and thoracotomy (including video-assisted thoracic surgery) are becoming popular. They involve fewer difficulties in the diagnosis of this rare disease, but there will surely be some cases which should be referred to the Mesothelioma Panel[26]. Although most mesothelioma originates from pleura, there are no clear health benefits in screening for mesothelioma like there is for lung cancer. Mesothelioma remains an incurable malignancy.

Surveillance of asbestos-related diseases

Surveillance of asbestosis, pleural plaques, and other pleural diseases may be beneficial for the workers and retired workers for compensation in their future. Lung cancer has multiple causes, and cigarette smoking is the leading cause, although some other lifestyle habits such as diet are also involved. So surveillance of lung cancer itself is not useful for controlling asbestos-related diseases. Surveillance of mesothelioma is very valuable, especially for those countries that have used only chrysotile, if possible. Currently, most industrialized countries have their own Mesothelioma Registers (Table 5)[27].

Table 5. Mesothelioma registers

Country	Name	Start year	Related organization
United Kingdom	Mesothelioma Register	1962	Medical Research Council's Pneumoconiosis Unit
		1966	Employment Medical Advisory Service, Department of Employment
Canada	Canadian Mesothelioma Registry	1965	McGill University
South Africa	Asbestos Tumor Reference Panel	1966	National Research Institute for Occupational Diseases
Netherlands	Mesothelioma Register	1968	Organization for Health Research TNO
France	Registre Francais des Mesotheliomes	1975	Le Ministeres de la Sante
Italy	Registro Italiano dei Mesotheliomi	1977	Institute of Pathology
Australia	Mesothelioma Register	1977	Support of Ad Hoc Committee on Asbestos of the National Health Research Council and New South Wales Dust Diseases Board

Morinaga K (1981) [27]

There are at least three reasons why such a specific cancer registry is needed. One of the reasons is that the diagnosis of mesothelioma should be based on histological specimens.

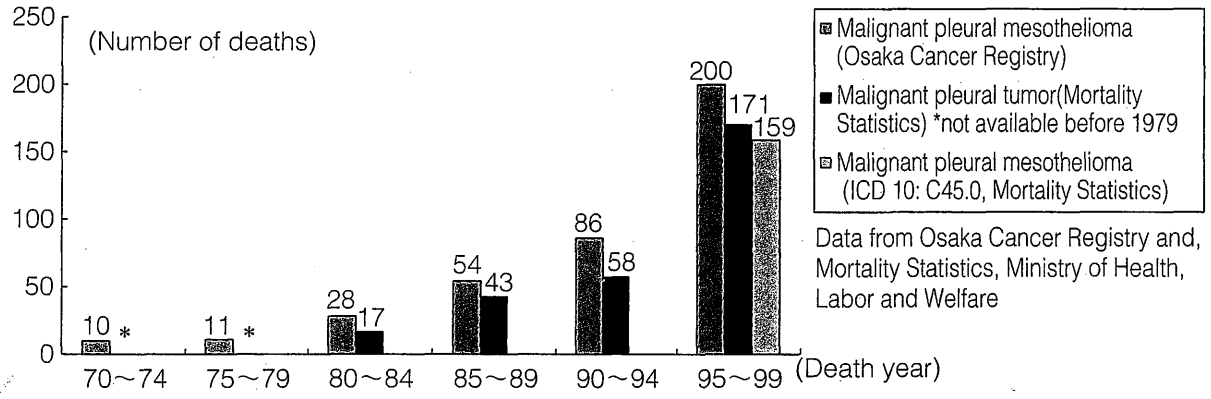

Figure 1. Number of deaths from pleural mesothelioma and pleural cancer in Osaka

The second is that a considerable number of cases of mesothelioma were found on death certificates with site of origin unknown. Figure 1 shows that the number of deaths from pleural mesothelioma/ malignant pleural tumor obtained by different sources in Osaka prefecture between 1970 and 1999. The number of death from malignant pleural mesothelioma on cancer registry is always greater than that of malignant pleural cancer or mesothelioma on death certificates.

The third is that death certificates and cancer registry cards do not carry sufficient occupational history, especially regarding asbestos exposure. Most Asian countries have population-based cancer registries now (Table 6), and it is recommended to establish a Mesothelioma Register where people have been exposed to chrysotile, separate from the cancer registries.

Table 6. Population-based cancer registries in Asian countries

Country	Area	Start year	Reference number
Japan	Hiroshima city	1957	(28)
	Nagasaki city	1958	
	Miyagi pref.	1959	
	Osaka pref., Aichi pref.	1962	
China	Shanghai	1963	(29)
	Tianjin	1978	
Singapore	nationwide	1986	(30)
Philippines	Rizal	1974	(31)
	Metro Manila and other cities	1978	
Taiwan	nationwide	1979	(32)
Indonesia	Semarang	1985	(33)
Thailand	Chiang Mai	1986	(34)
	Khom Kam	1988	
	Songkhla, Bangkok	1990	
South Korea	Seoul	1991	(35)
	5 large cities	1999	
Viet Nam	Ho Chi Minh	1993	(36)
Malaysia	Penag	1994	(37)
	Sarawak	1995	
	nationwide	1999	

Conclusion

Asbestosis is preventable with the controlled use of asbestos. Prevention of lung cancer is also possible by avoiding exposure to active and passive cigarette smoking. But mesothelioma, which is fatal and incurable at present, may occur 40 or 50 years after the first contact with asbestos. Sometimes the patient is not aware of asbestos exposure or has forgotten it. So, there is only one way to prevent the occurrence of mesothelioma, i.e., first prevention, to avoid exposure to asbestos.

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