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Review Article

Asbestos-Related Lung Cancer and Mesothelioma in Japan

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Abstract: In Japan, crocidolite had been used for asbestos cement pipe and spraying, and amosite had been used for building board and spraying. These two types of asbestos had stopped to use in Japan in the late 1970s. An extreme increase in imported asbestos (all 3 commercial types) was observed between 1960 and 1974. In 1960, 77,000 tons of asbestos were imported, and reached the peak as 352,316 tons in 1974. This extreme rise of asbestos imports corresponds with the recent rapid increase in mortality of malignant pleural mesothelioma. Between 1995 and 1999, an estimated mean annual death from pleural mesothelioma was about 500. The annual number of compensated occupational respiratory cancers due to asbestos exposure has also been increasing. Up to the end of March 2000, 162 cases with malignant mesothelioma and 197 cases with lung cancer were compensated. As for lung cancer, epidemiological studies are scanty in Japan. Limited environmental data of the working places in asbestos textile factories suggests that heavy asbestos exposure in the past made deaths from respiratory diseases. Less asbestos exposure will enable exposed workers to survive enough to reach cancer age. Even now smoking rate among males in Japan are over 50%. So lung cancer deaths caused by the interaction between smoking and asbestos exposure will be continuing.

Key words: Asbestos, Lung cancer, Mesothelioma, Asbestos body, Case-control study, Historical cohort study, Japan

Introduction

Since 1978, asbestos induced lung cancer and mesothelioma was prescribed as occupational cancer by the Ministry of Labor, Japan[1, 2]. The criterion of lung cancer and mesothelioma with asbestos exposure was shown in Table 1. Up to the end of March 2000, 197 cases of lung cancer and 162 cases with malignant mesothelioma (pleura, peritoneum) were compensated as occupational asbestos-related cancers. Since 1997, asbestos was the leading causal agent for occupational respiratory cancer, the second was hexavalent chromium (140 lung cancer and 24 upper respiratory tract cancers), the third was coke oven emissions (162 lung cancer), the forth was arsenical compounds (74 lung cancer and 2 skin cancer), and the fifth was bis(chloromethyl)ether (18 lung cancer)[3]. The rapid increase in asbestos-related cancers was observed in recent years (Table 2). Of course, this number is surely underreported, but probably reflects the real increase of asbestos-related lung cancer and mesothelioma in the occupational asbestos exposed workers.

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Table 1-1. Criteria for occupational lung cancer due to asbestos exposure

Case No.1 Lung cancer with radiological asbestosis (with more than 1/0)
among the workers occupationally exposed to asbestos
Case No. 2 Lung cancer without radiological asbestosis
Both (a) and (b) are needed
(a) More than 10 years of occupational asbestos exposure history
(b) One of the medical findings mentioned below is needed
Pleural plaques on chest X-ray fillm
Asbestos bodies in sputum
Asbestos fibers, asbestos bodies in the lung tissue obtained from TBLB, BAL, biopsy, or autopsy
Case No. 3. Lung cancer without the case No. 1 and case No. 2
Relatively short but heavy exposure working history with medical finding case No. 2 (b)

Since 1978, Japan

Table 1-2. Criteria for occupational mesotheliomas due to asbestos exposure

1. More than 5 years of occupational asbestos exposure history
2. One of the medical findings mentioned below is needed
(a) Radiological findings of asbestosis (with more than 1/1)
(b) Pathological findings such as diffuse interstitial fibrosis,
hyaline plaques, asbestos fibers or asbestos bodies in the
lung specimen obtained from autopsy, et al.

Table 2. Number of compensated cases with lung cancer and mesothelioma due to occupational asbestos exposure by 5 periods

Year	Lung cancer	Mesothelioma	Total
–1980	18	1	19
1981–1985*	17	4	21
1986–1990*	36	28	64
1991–1995*	49	50	99
1996–2000*	77	79	156
Total	197	162	359

*from April 1 to the end of March, 5 years' interval.

Background of Asbestos-Related Cancers in Japan

It was in 1880s that raw asbestos and asbestos products had been imported to Japan[4]. The first asbestos factory was founded in Osaka in 1886 and began to manufacture asbestos packing and other insulation materials[5]. A skilled maker of Japanese tabi (pair of socks) in the southern part of Osaka devised manufacturing of asbestos textile using a little amount of cotton mixed with asbestos fibers in 1910. Since then, most of asbestos textile (yarn, cloth, etc.) had been manufactured in Osaka. At the beginning of 20th century, the use of asbestos had extended to the battle shipbuilding, the installation of military facilities, boiler making, brake lining of trains and so on. During World War II, raw asbestos could not be imported from foreign countries, and the Japanese military had been eagerly looking for asbestos mine in Japan[6]. A lot of small asbestos mines had been in operation, and raw asbestos mined near Dailin in China was also used. Anthophyllite in Kyushu was also mined and used[7]. But, the quality of these asbestos fibers was not good, and the quantity was not so abundant. So, all asbestos mines in Japan had been closed before 1972. At present, only one mill is recovering short chrysotile fibers (less than Class 8) in the dump, which has been used for as the mixture in board, tiles, paint, lubricating oil, asphalt, and adhesives.

After World War II, especially during the rapid growth period from the late 1950s to the early 1970s, industries such as iron and steel, construction, and pharmaceuticals grew quickly, and the household electrical products industry and the petrochemical industry developed. With this economic growth, the use and the amount of asbestos rapidly expanded. Asbestos was necessary for the electric power industries, shipbuilding, and heavy chemicals industries for heat treatment and the efficient use of energy. Asbestos filter was also used for electrolyte in chemical industries especially for manufacturing ammonium sulfate for getting a lot of rice. Spraying asbestos for ceiling, wall and iron frames in the buildings and railroad cars began since 1957, and became popular in the construction building. The

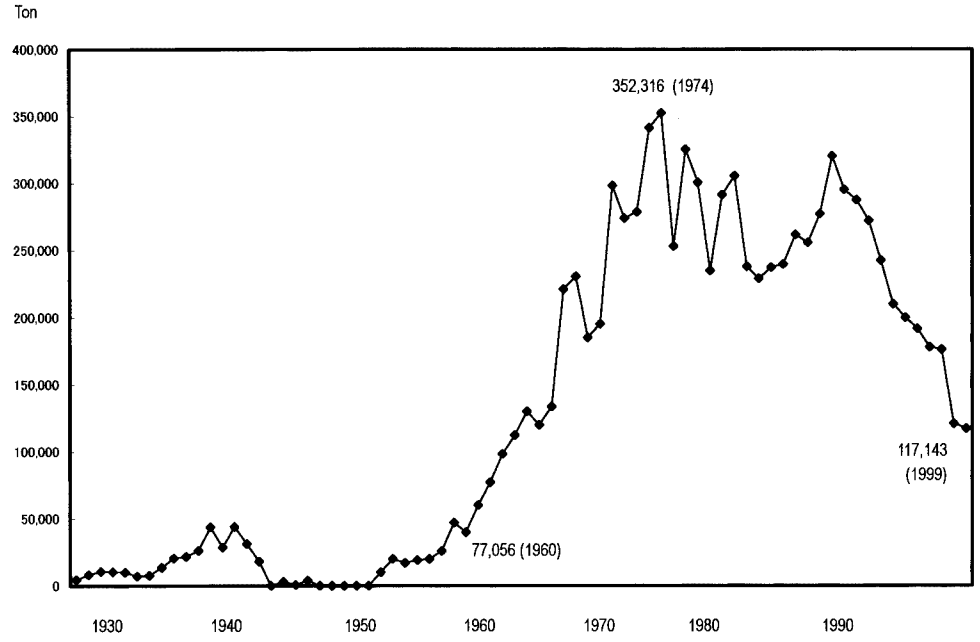

Fig. 1. Asbestos imports in Japan

Revised Ordinance on the Prevention of Hazards due to Specified Chemical Substances prohibited spraying asbestos since September 30, 1975[8]. During 1971 to 1974, about 62,000 tons of asbestos had been consumed for spraying. Rockwool containing less than 5% of asbestos was used for spraying till 1980. All three types of commercial asbestos; chrysotile, amosite, and crocidolite had been used for spraying. Asbestos cement pipe had also been produced in several factories. Crocidolite had been used mainly spraying and cement pipe, but this type of asbestos was stopped to use and import since 1976. Building materials containing asbestos started to be produced since the early 1950s, but the rapid increase was observed between 1965 and 1975. In 1960, 25 million sheets of asbestos slate were used, and in 1970, nearly 100 millions of these sheets were used[9]. Both chrysotile and amosite were used for slates and boards. Since 1975, more than 85% of imported asbestos was used for manufacturing asbestos containing boards and slates. Crocidolite and amosite were prohibited to use or import since April, 1996 by Law, but these two types of asbestos had been used widely in Japan, and people will be continuing to be exposed, especially when demolition or maintenance of the buildings.

Raw asbestos had been imported under the permission of General Head Quarter (GHQ), but since the autumn of 1963, free trade of raw asbestos and asbestos products began. This is one of the reasons why the import of raw asbestos had been increasing rapidly around this year (Fig. 1). This situation is different from the developed European countries. In 1960, nearly 77,000 tons of asbestos was imported, and about 4.6 times of tons of asbestos in 1974. After 1986, the importation of asbestos has been decreasing, and its amount was 117,143 tons in 1999.

Lung Cancer

Sukegawa *et al.* conducted a health survey of screening for asbestosis among mainly asbestos textile workers in 18 factories located in Osaka prefecture and one factory in Nara prefecture between 1937 and 1940[10, 11]. A total of 1,024 workers were screened, and 65 cases with definite asbestosis were found. At that time, one male worker with 14 years' exposure duration was found to have a sign of asbestosis as category 1 on his chest X-ray. In 1960, lung cancer was found in his right lung field[12]. This was the first case of lung cancer with occupational asbestos exposure reported in Japan. Sera *et al.* presented 10 cases of lung cancer among asbestos textile workers in Sennan district, the southern part of Osaka prefecture[13]. There were nearly 80 small-scale asbestos factories in this district around 1960s. Matsuda *et al.* showed 16 cases (15 males and one female) of lung cancer with asbestosis[14]. The location of these tumors was classified into 2 cases as central, and 14 as peripheral. In 4 cases, tumor was found in the upper lobe, 9 in the lower lobe, and one in the middle lobe. Histological subtype was divided into 5 cases of squamous cell type, 3 cases of adenocarcinoma,

4 cases of large cell and 4 cases of mixed types.

Since 1980s, lung cancer cases among shipbuilders were reported in Kure and Yokosuka. Kishimoto *et al.* examined asbestos bodies in the lungs of 158 consecutive autopsied cases between 1984 and 1986 in Kure Kyousai Hospital[15]. Among 158 cases, 51 were lung cancers. More than 100 asbestos bodies/g wet lung were found in 36 cases with lung cancer. They had all definite history of asbestos exposure as a worker in a shipyard. The latent period between the initial exposure and the death from lung cancer was 27 years on average ranging from 15 to 48 years. Katayama also studied asbestos bodies in the lung of 124 cases with lung cancer, 97 cases with hepatocellular carcinoma, and 115 controls (excluding serious respiratory diseases) between 1979 and 1988 in National Kure Hospital[16]. His conclusion was that more than 65% cases with lung cancer might be highly exposed to asbestos, and that 40% of cases with hepatocellular carcinoma or other controls might also be exposed.

Yokosuka was in the same situation as Kure. In both cities, naval dockyards had been located. Miura *et al.* presented a series of lung cancer cases with asbestos exposure[17].

Tachiyama *et al.* also examined asbestos bodies in the surgically resected lung of 84 cases with lung cancer and found more than 30 bodies/g wet tissue in 29 cases (35%), 8–30 bodies/g in 23 cases (27%), and 0.2–8 bodies/g in 32 cases (38%)[18]. Asbestos bodies were detected in all cases when 5 g of wet lung tissue was examined.

Mesothelioma

In Japan, the International Classification of Diseases, 9th Revision was adopted for coding the underlying cause of death on death certificates between 1979 and 1994, and the 10th Revision has been used since 1995. During the 5 years from 1995 to 1999, 1,753 (1,367 males, 386 females) cases were coded as C45.0 (mesothelioma of pleura), 254 (155 males, 99 females) as C45.1 (mesothelioma of peritoneum), 27 (17 males, 10 females) as C45.2 (mesothelioma of pericardium), and 72 (55 males, 17 females) as C45.3 (mesothelioma of other sites). A total of 542 cases for males and 233 for females were coded as C45.9 (mesothelioma unspecified), which equaled to nearly 40% of the number of deaths from pleural mesothelioma for males and about 60% for females, respectively. Most of unspecified mesothelioma was pleural in origin according to our experience in record linkage with death certificates and population-based cancer registry cards[19, 20]. So, we estimated

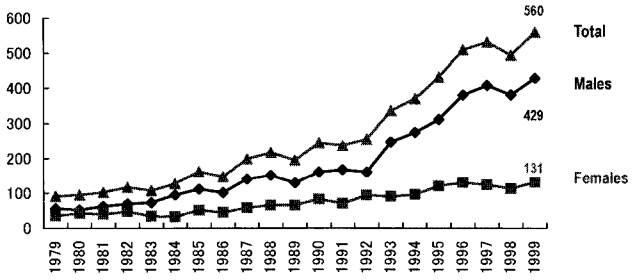

Fig. 2. Estimated annual number of death from pleural mesothelioma in Japan (1979-1999)

the number of deaths from pleural mesothelioma as follows. Between 1995 and 1999, total deaths from pleural mesothelioma were calculated as the number of death from pleural mesothelioma (C45.0) plus the number of deaths from unspecified site of mesothelioma (C45.9). Between 1979 and 1994, it was calculated as 1.4 times of the number of deaths from pleural tumor (ICD9: 163) for males and 1.6 times for females. Figure 2 shows the estimated annual number of deaths from malignant pleural mesothelioma from 1979 through 1999. An estimated mean annual death from pleural mesothelioma was 506 between 1995 and 1999. A steep increase was observed in males since early 1990s, as compared with the gradual increase in females.

The trend of the incidence of mesothelioma during 1977 to 1984 using population-based cancer registries (8 prefectures and 2 cities) was observed[21]. The incidence (/ million/year) of malignant mesothelioma was steadily increasing for both sexes: 0.89 (1977–78), 1.02 (1979–80), 1.47 (1981–82), 1.80 (1983–84) for males, and 0.35, 0.53, 0.70, 0.74 for females. The age-adjusted incidence using World Population was 0.7 (1977–81), and 1.4 (1981–86) for males, and 0.3 (1977–81) and 0.5 (1982–86) for females[20].

It was in 1973 that the first case of malignant peritoneal mesothelioma was reported in Japan[22]. He had been engaged in the manufacturing insulation materials and suffering from asbestosis. In the next year, a case of pleural mesothelioma with asbestosis was reported[23]. Both patients lived in Osaka prefecture.

Several studies on the asbestos bodies or naked fibers in the lung tissue of malignant mesothelioma were conducted.

Morinaga *et al.* examined the asbestos fibers content in the lung of 23 cases with malignant mesothelioma that reviewed by Osaka Mesothelioma Panel[24]. In 19 cases, asbestos fibers were found using semi-quantitative evaluation by transmission electron microscope (TEM). Amphibole fibers were detected in 13 cases with mesothelioma, but in 6 cases only chrysotile was found.

Kishimoto *et al.* presented 8 cases of pleural mesothelioma with definite asbestos exposure in Kure Kyousai Hospital between 1984 and 1986[25]. Seven cases were exposed to asbestos in the dockyards during World War II, and only one case was exposed initially after 1950. They added further 4 cases of these malignancies with definite asbestos exposure[26]. The latent period between the first exposure to asbestos and the diagnosis of this malignancy ranged from 20 to 49 years (median 43 years). Asbestos bodies were found in the lungs of all cases with definite asbestos exposure histories. Katayama *et al.* experienced 21 cases of malignant mesothelioma in National Kure Hospital from April 1975 through March 1995[27]. They counted the asbestos fibers of lung tissue among 13 cases using TEM and found that the number of asbestos fibers were 10 times more in 6 autopsied case before 1988 than in 7 cases after 1989.

Miura and his colleagues showed 12 cases (10 males, 2 females) of malignant mesothelioma from 1972 through 1985 at Yokosuka Kyousai Hospital[28]. The latent period between the first exposure to asbestos and the diagnosis was 37.6 years on average. They further observed a total of 36 cases during the next 13 years (1986 to 1998)[29].

Murai *et al.* counted asbestos bodies in the lungs of 27 malignant mesothelioma (23 pleura, 4 peritoneal) cases and estimated high level exposure in 12 cases (44.4%), moderate level in two cases (7.4%) and low level in 13 cases (48.2%) according their own criteria[30]. The type and size of asbestos fibers in the lungs of 12 high level exposure was analyzed by SEM. Amosite was found predominantly in 11 pleural mesothelioma, and crocidolite in one peritoneal mesothelioma. Most fibers were longer than 5 μm and thicker than 0.1 μm.

Sakai *et al.* examined asbestos fibers and non-asbestos fibers in the lungs of 16 malignant pleural mesothelioma (12 males, 4 females) and 16 non-asbestos-related diseases[31]. These cases were diagnosed between 1983 and 1990. Of the 16 patients, 13 lived in Aichi prefecture. In both cases and controls, chrysotile and amphibole asbestos were found, but the amount of those asbestos and non-asbestos fibers such as aluminum silicates was significantly found in cases than controls.

Kishizuchi *et al.* analyzed the asbestos fibers deposited in lung tissue of 18 autopsy cases with malignant mesothelioma along with 16 autopsy cases with pleural plaques using TEM[32]. They found crocidolite in all cases with mesothelioma and 15 cases with pleural plaques, the number of asbestos fibers was greater in cases with mesothelioma than in pleural plaques, and the fiber length was not different between the two groups. Both two groups were collected from the hospitals in Hiroshima prefecture including Kure city.

Epidemiological Studies

A hospital based case-control study on 116 male patients with lung cancer in Yokosuka Kyousai Hospital was conducted[33]. One control whose cause of death was other than cancer, pneumoconiosis, accidents or suicide, was selected for each case matched for sex and age in the same hospital. Information including occupational and smoking history was obtained by interviews with their relatives for 96 cases and 86 controls. The relative risk of lung cancer for asbestos exposure was 2.41 ($p<0.05$) after controlling for age and smoking. The age controlled relative risk of smoking without asbestos exposure was 3.38, while that of smoking with asbestos exposure was 8.28 ($p<0.05$), which suggested a synergistic relationship between smoking and asbestos exposure.

A population-based case-control study on lung cancer was carried out in Sennan district of Osaka prefecture[34, 35]. There were 79 deaths aged less than 80 years old from lung cancer on death certificates between 1985 and 1988 in the two cities where a lot of asbestos factories had been located. As for controls, one per twenty inhabitants whose year of birth was between 1912 and 1949 in these two cities was randomly selected from the Registry files. Self-administered questionnaires were sent to 2304 controls, and 1175 were collected. Four controls were selected from those respondents to each case, matched for sex and date of birth. Information about occupational asbestos exposure, smoking history, and the frequency of taking green vegetables was obtained for 63 (79.7%) cases. Matched pair analysis for 63 cases and 252 controls using conditional logistic model, showed that the risk ratio of smoking was 9.06 (95%CI: 1.95–42.07) and working history in asbestos factories was 4.53 (95%CI: 1.67–12.31).

Cohort studies on asbestos exposed workers are limited in Japan (Table 3). Some of them did not actually follow up each subject. Between 1972 and 1974, a health survey was conducted on asbestos workers in Sennan district. During 1975 to 1981, 6 workers died from lung cancer. Its SMR was 4.6 for both sexes based on the sex-age specific mortality of Osaka population[44, 45]. For 10 years' follow-up (1975–1984), 32 were dead, and eight (5 males, 3 females) died from respiratory cancers (7 lung cancer, and one pleural mesothelioma suspected) among total 32 deaths. SMR for respiratory cancer was 3.88 (95%CI: 1.68–7.65)[38]. Airborne asbestos fibers in the working environment in 4 factories in

Table 3. Cohort studies on asbestos-exposed workers in Japan

Study	(year)	Observation period	Type of asbestos exposure	No. of subjects	All causes		Lung cancer			Reference
					No.	SMR	No.	SMR	(95%CI)	
Hosoda Y, et al.	(1982)	1960–78	maintenance of steam locomotive	32,556	NA	NA	27	#0.76–1.57		36
		1970–79	maintenance of steam locomotive	15,260	557	0.58	27	0.82 (0.54-1.19)		
Miyazaki R, et al.	(1983)		asbestos textile, friction	1,210	NA	NA	9	*4.81 (2.20-9.14)		37
Morinaga K, et al.	(1991)	1975–84	mainly asbestos textile	789	32	1.15	8	3.88 (1.68-7.65)		38
	(1994 updated)	1975–89			96	1.09	12	2.52 (1.30-4.39)		39
Morinaga K, et al.	(1990)	1964–83	asbestos textile	208	15	1.10	3	6.81 (1.40-19.9)		40
Morinaga K, et al.	(1993)	1971–90	asbestosis patients	M 269	131	3.11	43	15.47 (11.2-20.8)		41
Sun J, et al.	(1997)	1973–93	construction	17,667	942	0.92	71	1.27 (099-1.60)		42
Kurumatani N, et al.	(1999)	1947–96	shipbuilding (lagging, boiler repair)	249	114	1.22	10	2.20 (1.05-4.04)		43

NA: Not Available. # Risk ratio.

Table 4. Airborne asbestos fibers in the working environment of 4 asbestos textile mills in Sennan district, Osaka (Feb, 1957)

Mill	No. of workers	No. of asbestosis	Mixing	Carding	Roving	Spining	Weaving
N	28	7	3,025 f/cc 52 mg/m^3	2,845 f/cc 55 mg/m^3	215 f/cc	144 f/cc	398 f/cc
S	41	8	2,685 f/cc 44 mg/m^3	1,330 f/cc 26 mg/m^3	715 f/cc	498 f/cc	1,250 f/cc
Mo	12	2	4,023 f/cc 68 mg/m^3	2,535 f/cc 41 mg/m^3	836 f/cc	445 f/cc	–
Mi	110	10	2,380 f/cc 47 mg/m^3	716 f/cc 16 mg/m^3	183 f/cc	115 f/cc	372 f/cc

Measurement method: Impinger (50 liter/min), membrane filter (300 liter/min) by Osaka Labor Standard Office.

Sennan district were measured using both impinger and membrane filter method in 1957 (Table 4). Asbestos fiber concentration exceeded 1,000 fiber/cc in the mixing process in 3 mills. The Ministry of Labor issued the Ordinance on the Prevention of Hazards due to Specified Chemical Substances on September 30, 1972, and began to superintend for improving working environments and controlling asbestos exposure level less than 2 fiber/cc (static sampling) since 1976 regulated by Working Environment Measurement Law and its Enforcement. The environmental data of the most of asbestos textile factories measured between 1975 and 1978 showed less than 3 fiber/cc, but some small-scale asbestos textile mills exceeded 50 fiber/cc in the mixing process.

Another cohort study on workers in an asbestos factory located in northeastern part of Osaka prefecture was carried out[40, 46]. A total of 208 workers (73 males, 135 females) between 1964 and 1981 were followed up. This factory was reopened in 1963 and closed in the autumn of 1981. Among them, 43 workers had also been working in this mill before 1963. During 20 years' observation since 1964, three asbestosis (2 males, 1 female), three lung cancer (2 males, 1 female) and one peritoneal mesothelioma (male) were found to be dead. SMR for all causes was 1.10, and for lung cancer was 6.81 (95%CI: 1.40–19.9). All deaths from these asbestos-related cancers had more than 18 years' exposure duration, and their latency was 32 years on average. One worker who died from peritoneal mesothelioma had been working in another asbestos mill where crocidolite had been used.

Miyazaki reported nine cases of lung cancer among 1,210 asbestos workers (946 retired and 264 active) in an asbestos factory in Nara prefecture[42]. This factory had been manufacturing asbestos textile, friction materials and board between 1955 and 1982. Eight were smokers and one was never smoker. The latent period between the initial exposure and the occurrence of lung cancer was 33 years on average ranging from 23 to 43 years. In this factory, Canadian

chrysotile was mainly used, but a small amount of crocidolite had been also used. During the same observation period, one case of peritoneal mesothelioma was found to be dead[47]. In this factory some working environments were measured 3 times by impinger method since 1952, that showed over 400 mg/m^3 in carding, spinning, weaving and friction board departments[48]. Working environments improved in 1960s and 1970s. In 1979, asbestos dust concentration measured by membrane filter method showed 0.40 fiber/cc in unpacking, 0.41 carding, 0.65 spinning, 0.63 weaving, and 0.43 friction board departments.

Three retrospective cohort studies were carried out on asbestos exposed workers other than textile workers.

Hosoda *et al.* examined the lung cancer risk of railroad workers who had engaged in the maintenance and repair of steam locomotives[36]. Follow-up for the retired workers was not done and excess risk of lung cancer was not shown.

A mortality study of the construction workers was done by Sun *et al.*[42, 49]. The cohort consisted of 17,667 male members of the Construction Workers' Health Insurance Society of Mie Prefecture at least one year's membership during April 2, 1973 to April 1, 1993. Actual follow-up was conducted for 17,427 (98.6%) and the remaining 240 members were considered lost to follow-up. The risk of lung cancer was 1.27 (95% CI: 0.99–1.60) based on the age-specific mortality rate of Mie population.

Kurumatani *et al.* conducted a historical cohort study on the workers in refitting shipyard in Yokosuka[43]. This cohort consisted of 90 laggers and 159 boiler repairers in a single US. Navy shipyard. Between 1947 and 1996, 114 were dead. Among them, 10 died from lung cancer and one from pleural mesothelioma. SMR for lung cancer was 2.20 (95%CI: 1.05–4.04). These 11 cases were all ever smokers. According to the interview to the living subjects, white asbestos had been mainly used, and brown one was sometimes used, and never blue one.

A total of 269 male and 180 female outpatients with asbestosis at National Kinki-chuo Hospital during 1971 to 1985 were followed up till the end of 1990[41]. High risk for all causes, lung cancer, and non-malignant respiratory diseases were observed. Only one death from lung cancer was found among nonsmokers. The risk of lung cancer for nonsmoking asbestos workers was 11.3 and 48.3 for smoking asbestos workers. Expected deaths of lung cancer for nonsmokers and ever-smokers were calculated separately using the age mortality death rate for nonsmokers and ever-smokers obtained from a large-scale cohort study in Japan[50]. A synergistic effect between smoking and asbestos exposure was observed in producing lung cancer.

Discussion

Only two case-control studies on asbestos exposure and lung cancer had been carried out in Japan[33–35]. Both studies showed that smoking had a higher risk of lung cancer than asbestos exposure. But in both case-control studies, no quantitative assessment of asbestos exposure was done, and in the heavy exposed cohort such as asbestosis, asbestos exposure had about 2 times of lung cancer risk than smoking[41]. Unfortunately, clinicians who diagnose lung cancer are apt to ignore occupational etiology. Even chest physician, most of them in Japan do not recognize health hazard of asbestos exposure well. There are two case series studies, which demonstrated a significant content of asbestos fibers or bodies in the lungs of silicosis patients with or without lung cancer[51, 52].

In the prevention and prediction of lung cancer, a synergistic effect between the two factors is important. In Japan, smoking rate of the general population is 53.5% for males and 13.7 for females in 2000. A questionnaire survey on 885 (794 males, 91 females) asbestos workers (except textile workers) in Osaka prefecture conducted in 1983 showed that 67% was current smoker, 13% ex-smoker for males, and 23% current smoker, and 4% ex-smokers for females[53]. As for male asbestos workers, current smoking rate was a little low in all age groups compared with 72.3% of the general male population in 1983, but for female workers, it was higher than general female rate (15.3%). The males' smoking rate in the Japanese general population reached the peak (83.7%) in 1966, and has been decreasing afterwards, but even now more than half are smokers. So, lung cancer deaths will be continuing to increase in Japan, which is probably caused by smoking and in parts by asbestos exposure.

Mesothelioma is closely related to exposure to asbestos, and this mortality may be an index of past asbestos exposure[54, 55]. Some authors wonder why the incidence of mesothelioma in Japan is far low compared with that in the developed Western counties or high asbestos consumption per capita[56, 57]. In France, the mortality rate of mesothelioma was less than 0.5 million/year during 1965 to 1978 as well as in Japan[19, 58]. French imports of asbestos was increasing 10 years behind United Kingdom, reaching their peak in 1975[54, 59, 60]. As shown in Fig. 1, Japanese imports grew up since 1960, compared with the fact that the import into the United Kingdom steadily increased since 1950, and already in 1940, more than 900,000 tons of asbestos including crocidolite had been imported. Before World War II, the most asbestos exposed groups might be those in shipbuilding,

especially Navy dockyards such as Kure and Yokosuka. A series of mesothelioma had been reported since 1980s. Kishimoto *et al.* presented 8 cases of pleural mesothelioma with definite asbestos exposure in Kure, who was diagnosed between 1984 and 1986. Seven cases were exposed to asbestos in the dockyards during World War II[25]. Natori *et al.* examined asbestos bodies in the lungs of 72 shipyard workers in Yokosuka and their occupational histories including asbestos exposure autopsied between 1986 and 1992[61]. Fifty cases (69.4%) had been exposed to asbestos before 1950. The latent period between the first exposure to asbestos and the occurrence of malignant mesothelioma is 40 to 50 years. So, the number of deaths from mesothelioma in 1980s reflects the past asbestos exposure mainly in 1940s. An extreme increase of asbestos imports was observed between 1960 and 1974. In 1960, 77,056 tons of asbestos was imported, but in 1974, 4.6 times of asbestos (352, 316 tons) was imported. This slope from 1960 to 1974 is far steeper than French one compared with the plateau in United Kingdom and Sweden[54, 59, 60, 62]. The recent trend of the rapid increase in mortality of pleural mesothelioma corresponds with this extreme rise of use of asbestos, considering 30–50 years' incubation period of mesothelioma. Misdiagnosis or overdiagnosis surely exists between 1979 and 1999. But along with the development of immunohistochemical staining technique, the diagnosis of malignant mesothelioma has becoming more accurate than before[63]. So, diagnostic trend cannot account for a large part of the recent increase[54].

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