

Progression of Pneumoconiosis in Coal Miners after Cessation of Dust Exposure: A Longitudinal Study Based on Periodic Chest X-ray Examinations in Hokkaido, Japan

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Abstract

Background The progression rate of pneumoconiosis in retired coal miners over ten years has not been studied in Japan.

Methods A retrospective longitudinal study was undertaken using chest X-rays of 1091 pneumoconiosis subjects in Hokkaido, Japan between 1985 and 2005.

Results The final numbers of subjects were 207 (19% of the entry) after 1 decade and 85 (8%) after 2 decades. Sixty-two percent of 207 subjects after 1 decade and 29% of 85 showed progression in 2 decades. Thirty-one percent of ILO category 1 and 55% of category 2 subjects showed progression to complicated pneumoconiosis after 1 decade, and 6% (4 of 64) of category 1 and 6% (5 of 77) of category 2 subjects progressed to complicated pneumoconiosis during 2 decades.

Conclusion The progression of pneumoconiosis was observed after the cessation of dust exposure, especially during the first 10 years.

Key words: pneumoconiosis, coal miner, ex-miner, natural history, periodic medical examination

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Introduction

Pneumoconiosis has been the representative occupational disease for several decades in Japan. Although most coal mines were officially closed in the 1990s and completely disappeared by 2002, the number of cases of pneumoconiosis has not shown any apparent decrease over the last 20 years, and more than 1,000 new cases receive compensation every year in Japan.

Since both the retirement age and the mortality age were almost the same in the late 1950's, it was difficult and unnecessary to conduct longitudinal clinico-epidemiological studies. Nowadays due to recent improvements in the infectious control of pulmonary tuberculosis and pneumonias, the life span of patients with pneumoconiosis has now reached beyond 75 years. Meanwhile the demand and the production

of coal are still increasing in the world. From the hygienic point of view, it is very important to investigate the longitudinal progression of pneumoconiosis in coal miners after cessation of dust exposure.

In order to clarify the natural course of chest X-ray findings of coal miners' pneumoconiosis, we performed a longitudinal study based on X-ray findings following the changes in subjects with pneumoconiosis that resulted from coal mining. This is the first long term study on the natural course of pneumoconiosis in coal miners in Japan. The implication of our results indicates the necessity of follow-up for a long time especially during the first 10 years even after cessation of dust exposure in retired coal miners.

Methods

The Iwamizawa Rosai Hospital (the previous name of our

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Table 1. The Profile of Subjects in Each X-P Category at the Start of this Study (1985)

	X-P Category					
	1	2	3	A	B	total
No. of subjects	363	337	49	157	185	1091
age (years)	59.9 $\pm$ 6.3	63.1 $\pm$ 8.4	63.6 $\pm$ 7.9	62.3 $\pm$ 7.9	65.0 $\pm$ 8.8	62.2 $\pm$ 8.0
Dust exposure (years)	29.7 $\pm$ 7.6	29.0 $\pm$ 7.6	27.7 $\pm$ 7.9	28.5 $\pm$ 7.9	27.2 $\pm$ 8.1	28.8 $\pm$ 7.8
Smoking (pack years)	26.3 $\pm$ 18.4	27.1 $\pm$ 17.3	30.4 $\pm$ 14.0	28.6 $\pm$ 17.0	25.5 $\pm$ 20.9	26.8 $\pm$ 18.5

mean $\pm$ SD

institution) was established in 1955 in the middle of the *Sorachi* coal mining region of Hokkaido, the northernmost part of the Japanese Archipelago. It was the greatest coal mining area in Japan, with about one hundred thousand workers at the peak. The hospital has a 54-year history of clinical studies on diagnosis and treatment, rehabilitation, early detection, and observation, and has conducted basic research mainly on coal workers' pneumoconiosis (CWP). To date, we have encountered 900 or more autopsy cases of pneumoconiosis.

Currently we are caring for more than 1,000 pneumoconiosis patients. There are about 470 cases that belong to supervision pneumoconiosis 4 in the Japanese classification system who have received compensation from workers' accident compensation insurance. There are about 600 cases that are monitored and classified as supervision pneumoconiosis 2 or 3 who have not yet received compensation. In Japan, if a case is categorized as 4C in the ILO (International Labor Organization) Classification based on the chest X-ray or has a remarkable decrease in respiratory function, that case is classified as supervision 4 in the Japanese system. If there is no remarkable respiratory reduction, category 1 is classified as supervision 2, category 2 and complicated pneumoconiosis cases except for 4C are classified as supervision 3.

Subjects

This follow-up study started in 1985. Until 2003, since the Pneumoconiosis Law System of Japan did not provide for follow-up periodical X-ray examinations of category 0 and category 1 subjects as defined by the ILO Classification, it was difficult to follow-up on these two category groups especially category 0. Because category C subjects represent the most advanced stage, they could not be evaluated to progress to a higher category of ILO Classification. Based on these, 51 category 0 and 88 category C cases were excluded from the study. Thus, 1,091 cases from category 1 to category B pneumoconiosis with complete work histories and clinical courses were followed for 10 to 20 years as the subject groups based on plain X-ray findings: 363 category

1 cases, 337 category 2 cases, 49 category 3 cases, 157 category A cases, and 185 category B cases (Table 1). All cases were male, age 62.2 ± 8.0 (mean $\pm$ SD), work history (duration of exposure to dust) of 28.8 ± 7.8 years, and smoking history (pack years) of 26.8 ± 18.5 . There were no statistically significant differences in their average age and smoking history among all the subject groups as indicated in Table 1.

The ethics committee of Hokkaido Chuo Rosai Hospital approved this study and did not require the patients' approval or informed consent for the present study for the retrospective review of their records and images.

Methods

According to the compensation system of the Pneumoconiosis Law of Japan, the cases defined as category 2 or greater can routinely undergo a medical checkup once a year for free. This was not the case for category 1 cases until 2003. After a team of pulmonary specialists in the hospital diagnosed pneumoconiosis, the Board of Pneumoconiosis of the Labor Standards Office in Hokkaido determined the final classification of the X-ray findings. Although our classification of category was similar to that of the Labor Standards Office, when the classification was different, the determination of the office was prior to ours.

Since the mean entry age for this study was already high (62.2 ± 8.0 years), there were many cases that dropped out from this study because of old age or many other kinds of diseases. The final numbers of subjects were 207 after 10 years and 85 after 20 years as indicated in Table 2.

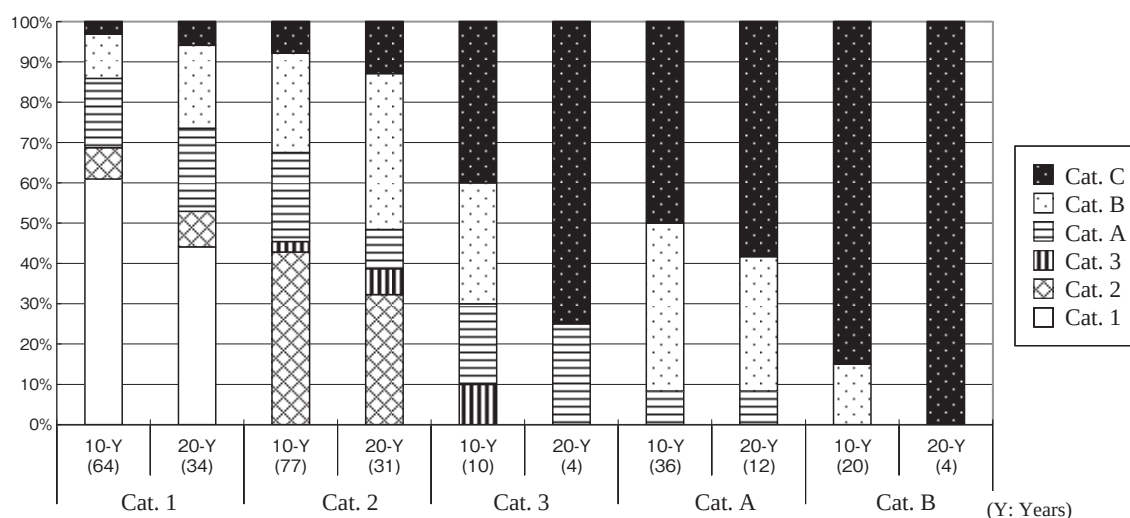
For statistical analyses, the chi-square test, student's t-test, and Mann-Whitney's U test were employed.

Results

The X-ray findings after 1 decade for 64 subjects, out of 363 primarily category 1 diagnosed, showed that there were 39 (60.9%) category 1 (unchanged) cases, 5 (7.8%) category 2 cases, 0 category 3 case, and 20 (31.3%) complicated

Table 2. The Number of the Subjects Primarily Entered in Each X-ray Category Followed Up at the Time Point of “after the First 10 Years” and “after the Second 10 Years”

	X-ray Category					
	1	2	3	A	B	total
No. of subjects						
At start	363	337	49	157	185	1091
After 10 years	64	77	10	36	20	207
After 20 years	34	31	4	12	4	85

**Figure 1.** Progression based on X-ray findings after the first and the second 10-year periods. Progression of pneumoconiosis after each 10-year period of time is shown in each category. The numbers in parenthesis are the numbers of subjects. Y: years, Cat: category

pneumoconiosis cases (Table 2, Fig. 1). In the 39 category 1 cases at 1 decade, the X-ray findings after 2 decades showed that 15 cases were category 1 (unchanged), 3 cases were category 2, 1 case was category A and 1 case was category B (19 cases had dropped out) (Fig. 1). In the 5 category 2 cases at 1 decade, 4 cases had dropped out and 1 case progressed to category A after 2 decades. Similarly, in the 11 category A cases, 5 cases retained category A and 4 cases progressed to category B (2 cases dropped out). In the 7 category B cases at 1 decade, 2 cases unchanged and 2 cases progressed to category C (3 cases dropped out). In summary, after 2 decades, the X-ray findings for 34 subjects, whose category was 1 at the beginning of this observation, showed that there were 15 (44.1%) category 1 (unchanged) cases, 3 (8.8%) category 2 cases, 0 category 3 cases, and 16 (47.1%) complicated pneumoconiosis cases as indicated in Fig. 1. Twenty-five of 64 category 1 subjects (39.1%) showed progression to advanced stages after 1 decade, and 12 of 34 category 1 (35.3%) showed progression to advanced stages after 2 decades as indicated in Fig. 1 and 2, respectively.

Forty-four out of 77 (57.1%) category 2 primarily diagnosed subjects showed progression after 1 decade. After 2 decades, in the 33 category 2 cases of the original 77 cases, 10 cases were unchanged, 1 case progressed to category A, 2 cases progressed to category B and 1 case progressed to category C (19 cases dropped out). Similarly, in the 2 category 3 cases, 1 case was unchanged and the other one case progressed to category B. In the 17 category A cases, only one case retained category A, 2 cases progressed to category B and 14 cases dropped out. In the 19 category B cases, 8 cases were unchanged and 4 cases progressed to category C (7 cases dropped out). In summary, 11 of 31 (35.5%) subjects, who were category 2 at the beginning of this observation, showed progression after 2 decades to advanced stages of pneumoconiosis based on the X-ray examinations (Fig. 1 and 2). Similarly, for primarily diagnosed category 3, category A, and category B subjects at the start of the study, 90.0%, 91.7%, and 85.0% after 1 decade, and 0%, 16.7%, and 0%, respectively, showed progression to advanced stages after 2 decades based on the X-ray findings (Fig. 1 and 2).

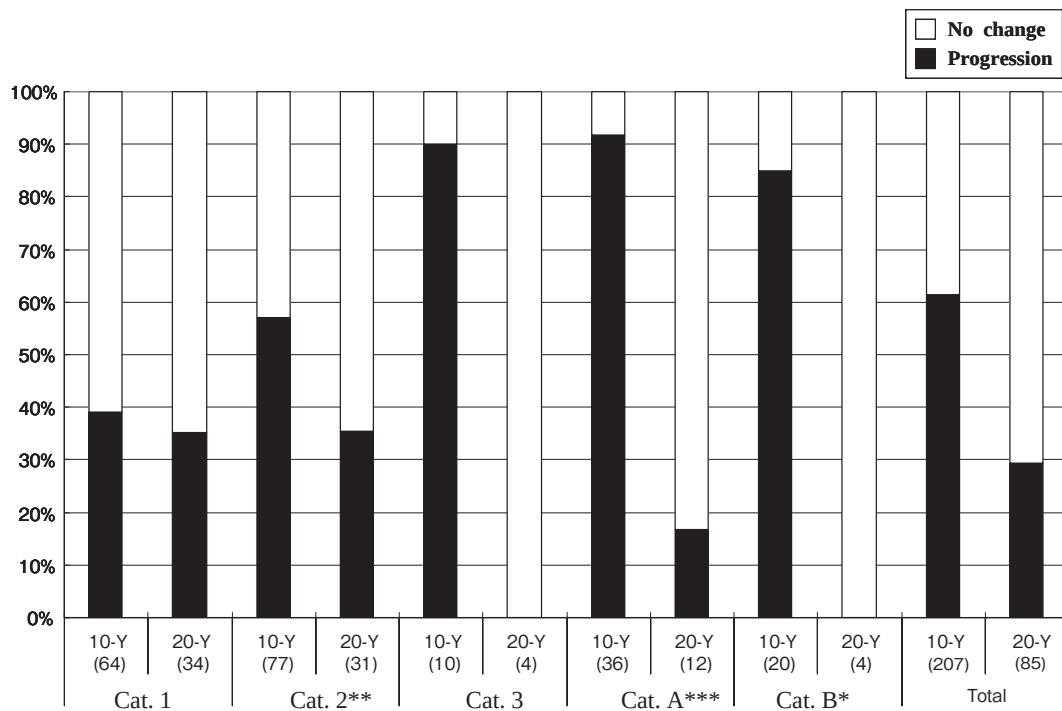


Figure 2. Proportion of the progressed cases in each category after the first and the second 10-year periods. Black columns indicate the proportion of the progressed subjects and the white column indicates the proportion of unchanged subjects in each category. The numbers in parenthesis are the numbers of subjects. Y: years, Cat: category, *: $p < 0.01$, **: $p < 0.005$, ***: $p < 0.001$

In category 2, category A, and category B, there were significantly more cases that progressed to advanced stages in 1 decade than in 2 decades. At the same time for cases with simple pneumoconiosis, it was recognized that the more the categories advanced, the more the patients progressed to a further advanced category of simple pneumoconiosis, or to complicated pneumoconiosis after 1 decade of observation. However, the same result was not observed after 2 decades as indicated in Fig. 2.

Next, we compared the progression of 1 decade with that of 2 decades within the same category. Although the difference is not statistically significant, the progression of 2 decades tended to be slower in every category compared to that of 1 decade (Fig. 3).

Since more than half of the cases could not be followed for the entire 2 decades of the observation period, the final X-ray findings of such cases were used and summarized (Fig. 3). All category groups showed a significant degree of progression and even in category 1, 50% of the cases showed progression during the prolonged observation period.

Figure 4 is the typical case with marked progression from category 1 to category C in 20 years on the chest X-ray findings. This case had an occupational history of coal mining for 42 years.

The remarkable findings were that during 1 decade from the starting point, the more advanced the category based on the chest X-ray findings of simple pneumoconiosis, the more the pneumoconiosis progressed to complicated pneu-

moconiosis. Simple pneumoconiosis such as category 1 and category 2 showed an apparent direct progression to complicated pneumoconiosis rather than progressing via category 3 (Fig. 1 and Table 3).

Finally we analyzed the age, dust exposure period, %VC, FEV₁/FVC, and smoking history among the cases that progressed and those that stayed the same. There were no significant differences between the two groups in these factors as indicated in Table 4.

Discussion

At the present, we do not have any effective way to stop or slow down the progression of pneumoconiosis itself. Thus, prevention or at least early detection is the best way to minimize the number of new cases of CWP. We have declared in this study that the progression of pneumoconiosis was observed even after cessation of dust exposure. And at least 10 years' observation after cessation of dust exposure is important. Once initial small opacities appear in the chest X-ray films, physicians should know the natural history and the clinical characteristics of the tragic, irreversible and ever-progressing nature of CWP to provide care to such workers.

Since all subjects in this follow-up study were ex-miners with pneumoconiosis after retirement age, this study is a rare opportunity to study pure ex-miners with this ultra-chronic occupational lung disease. In most studies, many workers in active service are included in the experimental

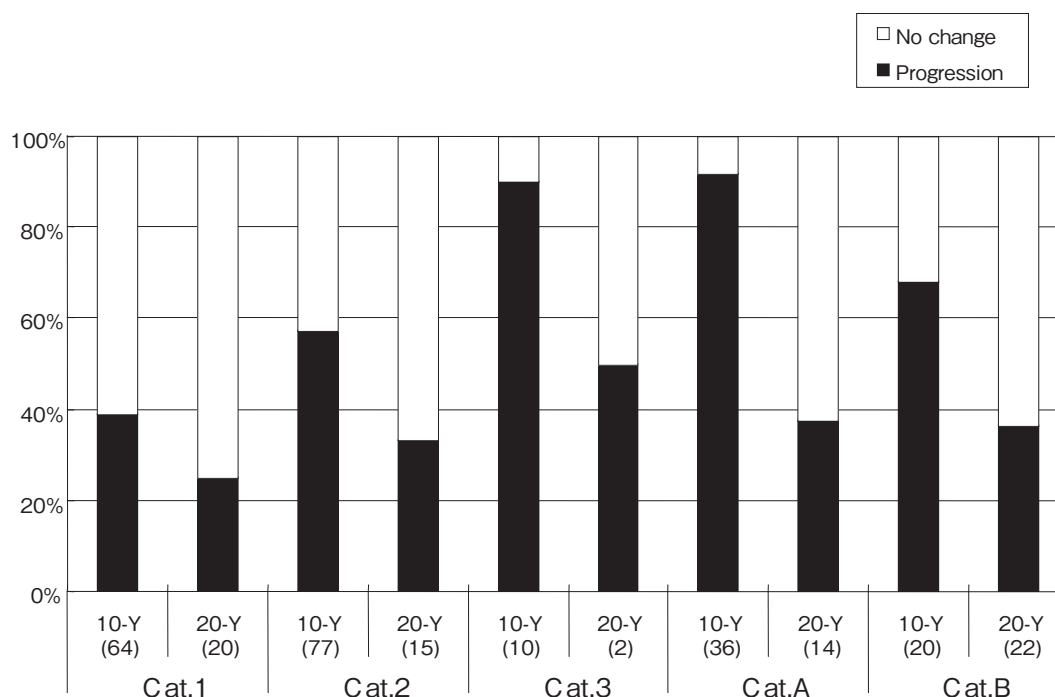


Figure 3. Proportion of the progressed cases in each category after the first and the second 10-year periods. This figure shows the proportion of the progressed cases in each category after the first and the second 10-year periods. The numbers in parenthesis on the right side in each category are the numbers of cases within each category followed up during the second 10 years. Black columns indicate the proportion of the progressed subjects and the white columns indicate the proportion of unchanged subjects in each category. Although the progression during 2 decades tended to be slower compared to that during 1 decade, the difference was not statistically significant in any category.

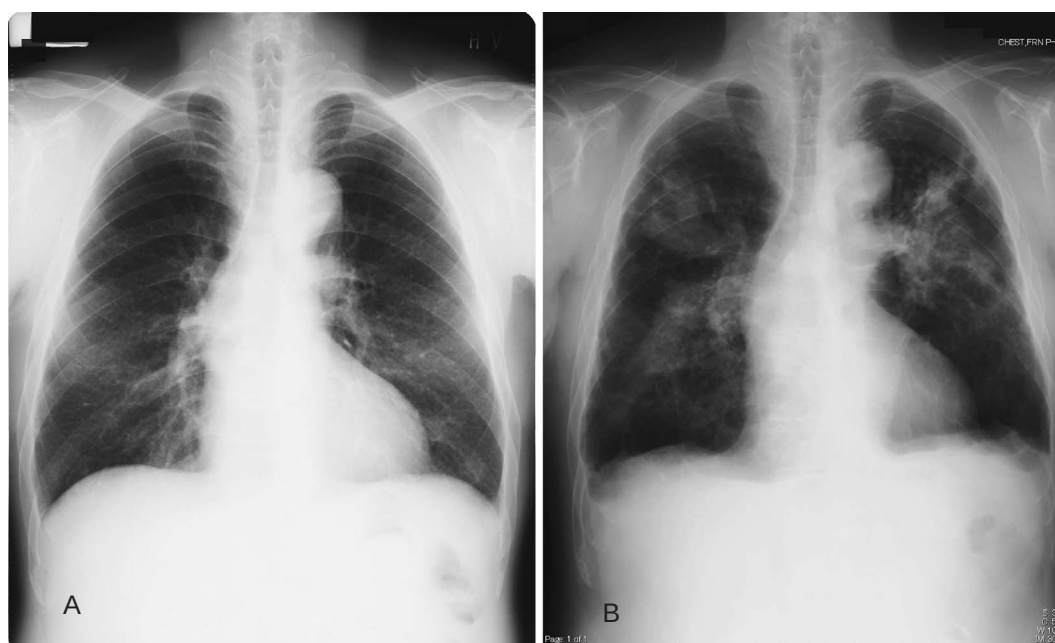


Figure 4. Typical case with marked progression on chest X-ray findings, from category 1 to category 4C. This is the case with a 42-year occupational history of coal mining. The X-ray film on the left side (A) was taken at the start of the observation. The chest X-ray film on the right side (B) was taken 20 years later, and showed the complicated form of pneumoconiosis.

Table 3. Progression Pattern of Simple Pneumoconiosis within 20 Years (Subjects Observed for Less Than 20 Years have been Included)

	X-P Category					
	1	2	3	A	B	C
No. of subjects						
Category 1		6	1	10	11	4
Category 2			2	18	20	10

Table 4. Age, Dust Exposure History, Smoking History, and Respiratory Function between Progressed and Unchanged Groups

	Unchanged	Progressed	p
No. of subjects	63	145	
Age (years old)	59.1 ± 5.4	57.4 ± 5.2	n.s.
Dust exposure (years)	30.7 ± 7.0	29.5 ± 6.6	n.s.
Smoking History (pack years)	27.2 ± 14.2	24.0 ± 0.3	n.s.
%VC	107.4 ± 16.2	106.4 ± 15.3	n.s.
FEV ₁ /FVC	70.2 ± 9.2	72.2 ± 9.8	n.s.

mean ± SD, n.s.; not significant

subject group, and the chance to study the genuine effects due to inhaled and precipitated dust on human lung tissues are usually limited to exclude the effects due to newly and/or additionally inspired dust. Most studies on the development of CWP were reported in the U.K. (1-6), and such studies on pneumoconiosis/silicosis in workers other than coal miners have also been reported in sandblasters (7, 8), in pencil slate workers (9), iron-ore miners (10), granite miners (11, 12), and so on (13-15). Without the newly additional dust exposure effects, we have declared that the progression of pneumoconiosis was observed even after retirement from coal mining.

We have also made clear that, the X-ray findings of 39.1% of category 1 cases and 57.1% of category 2 cases showed progression to a more advanced stage of pneumoconiosis after 10 years of observation (Fig. 2). Similarly, for the 36 category A cases, 33 (91.7%) cases showed progression to category B or C after 10 years (Fig. 1 and 2). However, we did not detect any clinical significant factors such as smoking habits and working periods that had a relationship to the X-ray progression among pneumoconiosis patients.

Chochrane (1) reported the rates of development of progressive massive fibrosis (PMF) from simple pneumoconiosis based on an eight-year follow-up study on 2,165 Welsh coal workers comprising a mixture of both ex-miners and active miners where 30 to 100% of the subjects showed PMF from category 3 based on the initial diagnosis, however, no PMF cases were observed from category 1. In con-

trast to their results, there were very few incidents of category 3 in the present follow-up study, and simple pneumoconiosis such as category 1 and category 2 showed an apparent direct progression to complicated pneumoconiosis rather than progressing via category 3 as indicated in Fig. 1.

Maclaren and Soutar (5) studied 7,118 coal workers for 22 years. Of these workers, 4,526 were ex-miners and the incidence of development of PMF from simple pneumoconiosis during an 11-year observation period was 19.8%. In a subgroup of 1,902 ex-miners from their study, cumulative exposure to dust, categories of initial X-ray findings, and age were probable influencing factors for the progression to complicated pneumoconiosis. They conducted a study later on the factors associated with the development of PMF in 4,772 coal miners and ex-miners. They reported a statistically significant association of age, prior category of simple pneumoconiosis, and an index of residence time of dust in the lungs with the incidence of PMF based on a case-control study in 257 cases with PMF (6). Miller et al re-examined chest radiographs in 547 Scottish colliery workers after 20 years, and they found 203 workers (38%) showed progression of at least one profusion category on the 12 point ILO Classification scale (16). Large opacities were recorded in 2.6% of their cases. They proposed that profusion of small opacities was strongly related to exposure to the quartz fraction of the dust rather than to the non-quartz fraction. In comparison to these past reports, the rate of progression of simple pneumoconiosis to advanced categories including PMF was considerably higher in the present investigation as

indicated in Fig. 1, 2, and 3. The reason for this seems to be that our cases were exposed to very high silica-containing dust in their work places (17). However, we have to consider that many cases dropped out during this observation. That is, the cases of the light category may not wish to follow-up. But, all of the subjects of this work can receive a compensation as a workmen's accident, when the patient falls into marked low-lung function, or suffers complications such as pulmonary tuberculosis and lung cancer, etc. even if his X-P category is light. Therefore, though the probability of light cases in particular having dropped out cannot be denied, we consider that such cases were not many.

Lee et al (18) suggested that progression to advanced stages was less likely to be found among those who had ended exposure to silica a long time ago. The results of the present study indicate that there were significantly more cases that progressed in 1 decade than in 2 decades, which seems to support their results.

When we focus our attention on the behavior of pneumoconiosis in category 3 cases, it was rare to observe category 3 cases accompanied with large opacities despite conducting periodic chest X-ray examination at least once a year. So, it seems more likely that scattered small opacities frequently conglomerated or grew in size rather than number, and category 1 and/or category 2 changed to form large opacities directly rather than to progress via category 3. This result was especially apparent in the case of category 1 (Fig. 1).

Since TNF- α is recognized as a central mediator of mineral-induced pulmonary fibrosis, apart from the above-mentioned phenomenological observations, individual differences in the susceptibility to CWP or in spontaneous progression from simple pneumoconiosis to PMF were investigated in relation to polymorphisms in the TNF- α promoter gene (19-24). In a previous study conducted by our group (25), the frequency of the TNF- α -308 A allele was found to be higher in patients with nodular CWP compared to those with PMF. In this study, there were only five cases with the analyzed TNF- α promoter gene. All of them had the G/G gene-type and their stages of pneumoconiosis were categorized as 1 and/or 2. These subjects progressed to complicated pneumoconiosis, which is consistent with our previous results. However, the number of subjects is too small to comment on concerning the relationship between the TNF- α gene and pneumoconiosis. Although reports on genetic factors concerning pneumoconiosis are somewhat in conflict at this time (22, 23, 25), further studies on the mechanisms of the progression of CWP are highly likely. At present, we do not have any effective way to stop or slow down the progression of these pathological changes. Analyzing the TNF- α promoter gene is only a step in the complicated mechanism of the continuous progression of pneumoconiosis. Such an unwanted progression should be stopped or should be slowed down by means of further progress in medical research.

When a worker is continually engaged in dust-prone work and opacities are apparent in chest X-ray films, regular

medical examination is required at least once every year according to the Pneumoconiosis Law in Japan. If the X-ray findings indicate a category 2 subject, measures to reduce exposure to dust must be taken. If the X-ray findings indicate a category 3, category A, or category B case, workers are required to change their occupation based on recommendation or instruction and are compensated for 30 or 60 days in order to complete the change. However, the present results show that once small opacities begin to appear in the chest X-ray films, pneumoconiosis will progress in many cases during the lifetime of the patient even if subsequent dust exposure is stopped. So their quality of life will be influenced by CWP. If possible, patients should change their occupation as soon as the early stages of development are observed at least at a level lower than category 1/0 based on the current findings of spontaneous progression based on chest X-ray findings after cessation of further dust exposure. At least, fortunately, the average age of the cases we are administering is almost equal to the average life span of Japanese males (78.5 years) in 2005. Further advances in specific research in this field are strongly expected.

In summary, our results showed that progression of pneumoconiosis was observed without the newly additional dust exposure. About 40% of category 1 and 60% of category 2 simple pneumoconiosis progressed to a more advanced stage of pneumoconiosis after 10 years of observation. Within 20 years, it seems likely that most of the complicated pneumoconiosis cases were progressed directly from category 1 and 2 rather than progressed via category 3. These results suggest the necessity of follow-up for a long time especially during the first ten-years even after cessation of dust exposure in retired coal miners.

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