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A COHORT STUDY ON MORTALITY FROM CANCER AND OTHER CAUSES AMONG WORKERS AT A METAL REFINERY

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Summary. *A non-concurrent prospective study was made on deaths from cancer and other causes occurring among 2,675 male workers at a metal refinery from 1949 to 1971. The expected number of deaths computed by applying age- and cause-specific death rates of Japanese males to these workers was compared with the observed number of deaths. Among 839 copper smelters, significantly increased mortalities were noted for lung cancer (SMR = 1,189) and colon cancer, but not for cancer of the stomach, liver (primary) and biliary passages, pancreas and skin or for leukemia, tuberculosis, cerebrovascular diseases, heart diseases and liver cirrhosis. A dose-response relationship was demonstrated between the mortality from lung cancer and the degree of exposure. A very high excess mortality from lung cancer (SMR = 2,500) was seen among copper smelters who were considered to have been most heavily exposed to arsenic or workers who had engaged in sintering and blast furnace operations for 15 years of more before 1949. The latent period of lung cancer was 37.6 years on average, and not related to level of exposure. Twenty-six of 29 deaths from lung cancer among copper smelters occurred after they had left the refinery. Other production workers and clerical workers showed no significant excess mortality from any kind of cancer.*

As reported, a case-control study made by using mortality cards demonstrated hidden cases of occupational lung cancer among copper smelters at a metal refinery in Ooita prefecture (Kuratsune *et al.*, 1974). This necessitated a more extensive investigation of the current and former employees of the refinery for their mortality experience of cancer and other diseases. A so-called non-concurrent prospective (Lilienfeld *et al.*, 1967) or retrospective cohort (MacMahon and Pugh, 1970) study was undertaken, the results of which are reported in this paper.

MATERIAL AND METHODS

Nominal rolls of the following four groups of workers were provided by the refinery: (1) copper smelters who retired before December 31, 1948; (2) workers employed up to December 31, 1948 and who retired after January 1, 1949; (3) workers who were employed and who retired after January 1, 1949; and (4) workers still employed on August 1, 1971. Name, sex, date of birth, date of employment, date of retirement, history of work (work section and job), *Honseki* (place of permanent family residence), present residence, cause of retirement, vital status (alive or dead) on December 31, 1971 and date of death were listed for each worker on these rolls. Deaths which occurred among these workers during the 23-year period from January 1, 1949 to December 31, 1971 were analyzed in this study.

The survey for vital status was made in the following way. The refinery questioned the village, town or city office at the *Honseki* of each of the workers about his vital status since vital records of the Japanese are kept there, irrespective of place of residence. When the death of a worker was noted, the Ooita Labor Standards Office collected a copy of his death certificate from the District Legal Affairs Bureau at his *Honseki*, since the certificates are legally preserved there for 27 years after death. Thus, practically all the deaths during the above study period could be traced.

From death certificates thus collected, we assigned an underlying cause of death to each death according to the 8th Revision of the International Classification of Diseases, Injuries and Causes of Death (WHO, 1967). In contrast to our previous study (Kuratsune *et al.*, 1974), the validity of diagnosis was not examined by making any particular investigation.

Although the nominal rolls listed 4,797 persons in all, female workers, male workers whose *Honseki* was outside Ooita prefecture, those who had died before or on December 31, 1948, those who had been employed less than 1 year before December 31, 1971 and those listed in duplicate, were excluded from the analysis. The above exclusion of workers having their *Honseki* outside Ooita prefecture was simply due to the fact that their mortality information was not provided by the Labor Standards Office by the time of this analysis. Furthermore, persons whose *Honseki*, date of birth, date of employment or vital status was unknown were excluded. Thus, the remaining 2,675 workers including 839 copper smelters were used for the current analysis and their vital and employment status on December 31, 1971 is shown in Table 1.

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TABLE I

VITAL AND EMPLOYMENT STATUS OF STUDY POPULATION ON DECEMBER 31, 1971

Known to be alive		2,350 (682) [1]
Still employed	1,261 (324)	
Ex-workers	1,089 (358)	
Known to be deceased		325 (157)
Total study population		2,675 (839)

[1] Figures in parentheses are number of copper smelters.

As shown in Table II, the workers were divided into five cohorts according to their jobs, considering both the work sections to which they belonged and the work they were engaged in. Cohort 1 included the workers (copper smelters) who had belonged to the copper smelting section for at least 1 year. Some of these workers had engaged in lead smelting but were included in this cohort. Those who had worked in the section for less than 1 year and were transferred to other sections were included in one of the following cohorts: 2, 3 or 4. Cohort 2 consisted of the workers belonging to the ferro-nickel smelting section, while cohort 3 comprised those belonging to the maintenance or transportation section and cohort 4 those belonging to the section of copper or lead electrolysis or of sulfuric acid production. Some of these workers had belonged to more than one section. They were assigned to cohorts according to the section to which they had belonged for the longest period of time. Cohort 5 consisted of those engaged exclusively in clerical work, irrespective of the work sections to which they belonged.

For more detailed analysis, cohort 1 was further subdivided into several cohorts by degree of exposure (Table V). First, it was divided into 3 cohorts, namely cohorts 11, 12 and 13, according to length of employment. It was also divided into 3 cohorts designated as cohorts 21, 22 and 23 by level of exposure. This subdivision, however, was approximate due to the lack of quantitative information in regard to exposure to arsenic and other related compounds released by the smelting processes. Therefore, after consulting the technical managers and physicians of the refinery, the subdivision was made according to work engaged on for the longest period of time, as described at the bottom of Table V. Furthermore, cohort 1 was divided into 3 cohorts designated as cohorts 31, 32, and 33 according to time of exposure (time when exposure occurred) and to length of employment as copper smelters.

TABLE II

COHORTS BY JOB, NUMBER OF WORKERS, DEATHS AND TOTAL PERSON-YEARS AT RISK

Cohort		Number of workers	Number of deaths	Total person-years at risk
1	Copper smelting	839	157	15,521.5
2	Ferro-nickel smelting	268	6	3,599.5
3	Maintenance or transportation	821	108	15,396.0
4	Copper or lead electrolysis or production of sulfuric acid	389	22	5,858.0
5	Clerical work	358	32	6,068.0
Total		2,675	325	46,443.0

For each cohort, populations at risk were calculated by the ordinary person-years method (Doll and Hill, 1956), computing age-specific mid-year population in each of the calendar years from 1949 to 1971.

In order to examine possible excess risks of mortality from cancer and other causes of death in the cohorts, the observed number of deaths from a specific cause was tabulated for each cohort over the calendar years and compared with the corresponding expected number of deaths which was computed by applying age- and cause-specific death rates by calendar year for male Japanese to the populations at risk of each of the cohorts and by accumulating overall age groups and the calendar years. In this calculation, the sex- and age-specific death rates for malignant neoplasms and other diseases for all Japanese males in 1950, 1955, 1960, 1965 and 1970, appearing in the Vital Statistics, 1971 (1973) and in the Death Statistics of Malignant Neoplasms (1973) were used. For convenience, death rates *e.g.* for 1955 were applied to the populations at risk not only for 1955 but also for the 2 preceding and 2 following years, namely 1953, 1954, 1956 and 1957. This lineal interpolation of death rates was based upon the fact that it yielded a good approximation even for lung cancer death which was increasing most rapidly.

Although the ICD was revised three times, giving the 6th, 7th and 8th Revisions during the period from 1950 to 1970, the categorization of the specific diseases studied was practically the same except for "malignant neoplasm of respiratory system" and "malignant neoplasm of trachea, bronchus, and lung." Thus, the expected number of deaths calculated from the above mortality rates was considered to be comparable with the observed number of deaths tabulated according to the 8th Revision of ICD. For respiratory cancer, however, "malignant neoplasm of respiratory system specified as secondary" was included in "malignant neoplasm of respiratory system" in the 6th and 7th Revisions of ICD but not in the 8th Revision, and "malignant

neoplasm of pleura " was included in " malignant neoplasm of trachea, bronchus, and lung " in the 6th and 7th Revisions of ICD but not in the 8th. Therefore, the expected number of deaths from " malignant neoplasm of respiratory system " or from " malignant neoplasm of trachea, bronchus and lung " was not completely comparable to the corresponding observed number of deaths classified by the 8th Revision of ICD. However, the discrepancy must be very small because deaths from " malignant neoplasm of respiratory system, specified as secondary " or from " malignant neoplasm of pleura " were rare in Japan.

The standardized mortality ratio (SMR) was calculated by observed and expected number of deaths and their differences were examined by the Chi-square test when the expected number of deaths was over 10 or by Poisson distribution when the number was 10 or less.

RESULTS

Mortality experience of cohorts doing different jobs

Among copper smelters (cohort 1), significantly increased SMRs were observed for total malignant neoplasms, malignant neoplasm of large intestine, except rectum (abbreviated as colon cancer), malignant neoplasm of respiratory system, and malignant neoplasm of trachea, bronchus, and lung (hereafter abbreviated as lung cancer), as shown in Table III and IV. The increase was most marked for lung cancer, the ratio of observed to expected deaths being as high as 12:1, followed by the ratio of approximately 3:1 for colon cancer. No such increased mortality was observed for malignant neoplasms, of stomach, liver (primary) and biliary passages and pancreas. Besides one primary malignant neoplasm of liver, 10 deaths from unspecified malignant neoplasm of liver were seen. These 11

TABLE III

OBSERVED AND EXPECTED NUMBER OF DEATHS FROM SELECTED CAUSES, WITH STANDARDIZED MORTALITY RATIOS (SMR) [1] AMONG COHORTS BY JOB, 1949-1971

Cause of death	Detailed list No. [2]		Cohort 1 (copper smelting)	Cohort 2 (ferro-nickel smelting)	Cohort 3 (transport or maintenance)	Cohort 4 (copper or lead electrolysis, sulfuric acid production)	Cohort 5 (clerical)
Tuberculosis	010-019	Obs.	13	1	11	3	6
		Exp.	15.95	1.81	13.98	4.01	4.59
		SMR	82	55	79	75	131
Malignant neoplasm	140-209	Obs.	55	1	24	3	4
		Exp.	28.82	1.86	20.80	3.99	7 15
		SMR	191 ** [3]	54	115	75	56
Cerebrovascular diseases	430-438	Obs.	26	0	12	0	5
		Exp.	34.18	1.56	23.91	3.89	9.26
		SMR	76	—	50 *	—*	54
Heart diseases	393-398, 410-414, 420-429	Obs.	7	1	3	3	4
		Exp.	14.90	1.01	11.08	2.18	4.33
		SMR	47	99	27 *	138	92
Ulcer of stomach and duodenum	531-533	Obs.	8	0	1	0	0
		Exp.	4.15	0.27	3.03	0.62	1.12
		SMR	193	—	33	—	—
Cirrhosis of liver	571	Obs.	2	1	7	3	1
		Exp.	3.42	0.33	2.64	0.62	0 90
		SMR	58	303	265 *	484 *	111
Accidents	E800-E949	Obs.	9	1	18	2	0
		Exp.	11.30	2.32	10.70	3.81	4.14
		SMR	80	43	168 *	52	—*
All other causes	Residual	Obs.	37	1	32	8	12
		Exp.	39.20	3.89	31.60	7.70	13.38
		SMR	94	26	101	104	90
Total causes	000-E999	Obs.	157	6	108	22	32
		Exp.	151.92	13.05	117.74	26.82	44.87
		SMR	103	46	92	82	71

[1] SMR = (observed/expected) × 100. — [2] 8th Revision of International Classification of Diseases, Injuries and Causes of Death. — [3] * significant at 5% level; ** significant at 1% level.

OBSERVE WITH

Malignant neoplasm

Stomach

Large intestine (exce rectum)

Liver (primary, seco and unspecified) a biliary passages

Liver (primary) and passages

Pancreas

Respiratory system

Trachea, bronchus a lung

All other malignant neoplasms

Total malignant neo

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TABLE IV

OBSERVED AND EXPECTED NUMBER OF DEATHS FROM SELECTED MALIGNANT NEOPLASM, WITH STANDARDIZED MORTALITY RATIOS (SMR) [1] AMONG COHORTS BY JOB, 1949-1971

Malignant neoplasm	Detailed list No. [2]		Cohort 1 (copper smelting)	Cohort 2 (ferro-nickel smelting)	Cohort 3 (transport or maintenance)	Cohort 4 (copper or lead electrolysis, sulfuric acid production)	Cohort 5 (clerical)
Stomach	151	Obs.	10	0	12	1	0
		Exp.	14.71	0.87	10.46	1.94	3.61
		SMR	68	—	115	52	— [3]
Large intestine (except rectum)	153	Obs.	3	0	1	0	0
		Exp.	0.59	0.05	0.45	0.10	0.16
		SMR	508 * [3]	—	222	—	—
Liver (primary, secondary and unspecified) and biliary passages	155, 156, 197.7, 197.8	Obs.	11	1	5	2	1
		Exp.	3.26	0.20	2.34	0.44	0.79
		SMR	337 **	500	214	455	127
Liver (primary) and biliary passages	155, 156	Obs.	1	0	0	1	0
		Exp.	0.72	0.04	0.52	0.10	0.17
		SMR	139	—	—	1,000	—
Pancreas	157	Obs.	2	0	0	0	0
		Exp.	0.91	0.06	0.67	0.13	0.21
		SMR	220	—	—	—	—
Respiratory system	160-163	Obs.	29	0	2	0	2
		Exp.	3.18	0.18	2.27	0.39	0.75
		SMR	912 **	—	88	—	267
Trachea, bronchus and lung	162	Obs.	29	0	2	0	1
		Exp.	2.44	0.13	1.74	0.29	0.57
		SMR	1,189 **	—	115	—	175
All other malignant neoplasms	Residual	Obs.	0	0	4	0	1
		Exp.	6.17	0.50	4.61	0.99	1.63
		SMR	— **	—	87	—	61
Total malignant neoplasms	140-209	Obs.	55	1	24	3	4
		Exp.	28.82	1.86	20.80	3.99	7.15
		SMR	191 **	54	115	75	56

[1] SMR = (observed/expected) × 100. — [2] 8th Revision of International Classification of Diseases, Injuries and Causes of Death. — [3] * significant at 5% level; ** significant at 1% level.

deaths were significantly more than the expected number of deaths, 3.26, calculated from the mortality from malignant neoplasm of liver (primary, secondary and unspecified) and biliary passages ($p<0.01$). No deaths from skin cancer or leukemia were noted. No excess mortality from tuberculosis, cerebrovascular diseases, heart diseases, ulcer of stomach and duodenum, cirrhosis of liver, accidents and total causes of death was observed. Similarly, deaths from hypertensive diseases, pneumonia and bronchitis, nephritis and nephrosis, *diabetes mellitus* and suicide were not elevated as compared with the corresponding expected number of deaths.

In cohort 2 consisting of ferro-nickel smelters, mortality from all causes was considerably lower than the expected rate with no significantly increased mortality for any causes of death examined.

In cohort 3 consisting of the workers engaged in maintenance or transportation, significantly increased mortalities were noted only for cirrhosis of liver and for accidents, while significantly lower mortalities for cerebrovascular diseases and heart diseases were observed.

An increased mortality from cirrhosis of liver and a decreased mortality from cerebrovascular diseases were noted in cohort 4 consisting of workers engaged in copper or lead electrolysis or in production of sulfuric acid.

Cohort 5 consisting of clerical workers experienced a similar mortality to the general population except for malignant neoplasm of the stomach and accidents, both of which were significantly lower.

Mortality from lung cancer among copper smelters by length of employment

As described, a distinct excess SMR was observed for lung cancer among copper smelters. A possible association of such excess mortality with length of employment was then sought. Significant excess SMRs were observed in all of the cohorts and a definite positive gradient was seen between SMRs and length of employment, as shown in Table V.

TABLE V

OBSERVED AND EXPECTED NUMBER OF DEATHS FROM MALIGNANT NEOPLASM OF TRACHEA, BRONCHUS AND LUNG, WITH STANDARDIZED MORTALITY RATIOS (SMR) AMONG COHORTS OF COPPER SMELTERS BY LENGTH OF EMPLOYMENT, LEVEL OF EXPOSURE, LENGTH OF EMPLOYMENT AND TIME OF EXPOSURE, 1949-1971

	Length of employment			Level of exposure			Length of employment and time of exposure		
	Cohort 11 (over 20 years)	Cohort 12 (10-19 years)	Cohort 13 (1-9 years)	Cohort 21 (heavy [1])	Cohort 22 (medium [2])	Cohort 23 (light [3])	Cohort 31 (15 years or more, with 15th year completed before December 31, 1948)	Cohort 32 (15 years or more, with 15th year completed during 1949-1971)	Cohort 33 (1-14 years, irrespective of time of exposure)
Obs.	20	5	4	15	10	4	17	5	3
Exp.	1.05	0.68	0.71	1.01	0.80	0.63	0.83	0.47	1.14
SMR	1,905 ** [4]	735 **	563 **	1,485 **	1,250 **	635 **	2,048 **	1,064 **	614 **

[1] Sintering by "Pot" or "Greenawalt" method, crushing of sinters, blast furnace operation. — [2] Operation of converter, production of by-products (mainly arsenic trioxide), operation of lead blast furnace, operation of lead electric furnace and reverberatory furnace for lead slimes. — [3] Transport, sampling and general maintenance at the copper smelting section, flash furnace operation including ore blending and control operation. — [4] ** significant at 1% level.

Mortality from lung cancer among copper smelters by level of exposure

A significantly increased mortality was noted in all of the cohorts examined and again a distinct positive gradient could be seen between mortality and level of exposure, ratios of observed to expected mortality as high as approximately 15, 13 and 6 being noted in the heavy, medium and light exposure groups, respectively (Table V).

Mortality from lung cancer among copper smelters by length of employment and time of exposure

Significantly increased mortality ratios were seen in all of the cohorts 31, 32 and 33 as shown in Table V. SMR of cohort 31 was considerably higher than that of cohort 32, indicating that those exposed for 15 years or more before 1949 experienced a much higher mortality risk than those exposed for a similar duration but with the 15th year completed between 1949 and 1971. Cohort 33 consisting of copper smelters exposed for less than 15 years irrespective of time of exposure also showed a significantly increased mortality as mentioned but the increase was much less marked as compared with cohorts 31 and 32. Furthermore, an interesting fact was observed, namely that 28 of 29 copper smelters who died from lung cancer had been engaged in the smelting work before 1949.

Mortality from lung cancer among copper smelters by length of employment, time of exposure and level of exposure

As shown in Table VI, the markedly increased mortality from lung cancer among smelters employed for 15 years or more before 1949 (cohort 31) was closely associated with their jobs, the mortality risk ratios being 25, 18 and 14 in those heavily exposed, moderately exposed and lightly exposed, as classified by job, respectively. However, the smelters who were employed for 15 years or more with the 15th year completed during 1949-1971 (cohort 32) did not show any definite mortality gradient associated with their jobs.

Table VI also shows that the smelters most heavily exposed to arsenic and other related compounds experienced a strikingly different mortality from lung cancer depending on time of exposure in spite of their approximately equal duration of exposure. Similar differences in mortality experience were also noted among those moderately exposed and those lightly exposed, but they were less marked.

Mortality from colon cancer among copper smelters by degree of exposure

As mentioned, a significant excess mortality was also observed for colon cancer among copper smelters. A possible association of such excess mortality with length of employment, level of exposure and time of exposure was examined but no

TABLE VI

OBSERVED AND EXPECTED NUMBER OF DEATHS FROM MALIGNANT NEOPLASM OF TRACHEA, BRONCHUS AND LUNG, WITH STANDARDIZED MORTALITY RATIOS (SMR) AMONG COPPER SMELTERS BY LENGTH OF EMPLOYMENT, TIME OF EXPOSURE AND LEVEL OF EXPOSURE, 1949-1971

		Heavy exposure	Medium exposure	Light exposure
Cohort 31 (over 15 years, before 1949)	Obs.	10	4	3
	Exp.	0.40	0.22	0.21
	SMR	2,500 **	1,818 **	1,429 **
Cohort 32 (over 15 years, 1949-1971)	Obs.	1	3	1
	Exp.	0.18	0.17	0.13
	SMR	556	1,765 **	769

** significant at 1% level.

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Latent period of lung cancer seen among copper smelters

As shown in Table IV, 29 deaths from lung cancer had occurred among copper smelters during the study period. The distribution of age at death was 2, 9, 13 and 5 cases for the age-classes 40-49, 50-59, 60-69 and 70-79 years, respectively. The youngest age was 42 and the oldest 76, with an average of 61.7 years. It was also noted that these deaths had occurred in 26 workers after they had left the refinery. The latent period (designated as period between time of first employment as copper smelter and time of death) ranged from 13 to 50 years, 37.6 years on average. The distribution was 1, 2, 15, 8 and 3 cases for 10-19, 20-29, 30-39, 40-49 and 50-59 years of latent period, respectively. It also ranged from 31 to 50 years with an average of 37.9 years in 15 copper smelters with heavy exposure (cohort 21). The corresponding figures were 13 to 47 years with an average of 34.1 years in 10 coppers smelters with medium exposure (cohort 22) and 35 to 50 years with an average of 45.3 years in 4 copper smelters with light exposure (cohort 23). Thus, no definite gradient could be seen in the length of latent period in association with levels of exposure.

Cohorts 21, 22 and 23 differed in age on employment, being 24.7, 25.3 and 19.0 years of age on average, respectively. Therefore, an additional similar analysis was made by adjusting for age on employment. Nine deaths in the workers undergoing heavy exposure who were employed as copper smelters in their twenties were compared for the length of latent period with the corresponding 7 deaths occurring in those with moderate exposure. The latent periods of the former group ranged from 34 to 40 years with an average of 36.8 years, while the corresponding figures of the latter group were 25 to 47 years, with an average of 37.6 years. Thus, again, no significant difference attributable to level of exposure could be seen in the length of latent period.

DISCUSSION

Our previous case-control study with mortality records from 1967 to 1969 revealed an excess mortality from lung cancer among copper smelters in the refinery. Our present study confirmed this fact by extending observations backwards to 1949 and forwards up to 1971. It demonstrated not only a definitely increased mortality from lung cancer (SMR = 1,189) among copper smelters but also a clear dose-response relationship. Our study therefore well supports the observations by Lee and Fraumeni (1969) and Ott *et al.*, (1974) who reported an excess mortality from respiratory cancer among copper smelters and workers exposed to arsenicals by similar cohort analysis to ours.

The refinery is known to have started its copper smelting operations in 1916. The operations consisted of sintering by the "Pot" method, followed by processings with blast furnaces and "Mabuki" hearths which are old Japanese traditional converters. As shown in Figure 1, the "Pot" method was discarded in 1945, replaced by the "Greenawalt" method which had been introduced in 1936. This new sintering method was also discontinued in 1953. The blast furnaces were used until quite recently and replaced by a modern type of flash smelting furnace, while the "Mabuki" hearths were replaced by converters in 1930. Figure 1 also shows that a drastic decline in copper production as well as in the amount of arsenic contained in the processed ores occurred after the end of World War II. It is also known that a fairly large amount of "Kinkaseki" ore from Taiwan which is particularly rich in arsenic was used before World War II. Therefore, it is reasonable to consider that the pre-war exposure was far worse than the recent one. These historical facts seem to be well associated with our findings. Although our study does not specify the causal agent or agents, we consider that arsenic compounds and sulfur dioxide to which copper smelters must have been heavily exposed are probably responsible for the excess mortality observed. Other carcinogens such as polycyclic aromatic hydrocarbons might also be involved because the sintering and smelting processes formerly used must have released a fairly large amount of these compounds.

Since smoking is generally accepted as one of the most dominant causes of lung cancer and our previous case-control study showed that 10 out of 11 copper smelters who died of lung cancer had been smokers, a causative role of smoking cannot be overlooked for the increased mortality from lung cancer among copper smelters. It does not seem probable, however, that such an increased risk can be explained exclusively by this factor. This is because their smoking habits cannot be considered to be unusual compared with those of other workers. According to Segi *et al.* (1965) and Segi and Kurihara (1972), the mortality from lung cancer among males in Ooita prefecture where the refinery is located was very close to the national average. Therefore, the excess mortality from lung cancer seen among the copper smelters cannot be attributed to any local peculiarity in cancer mortality either.

Besides lung cancer, a significant excess mortality was noted for malignant neoplasm of liver (primary, secondary and unspecified) and biliary passages

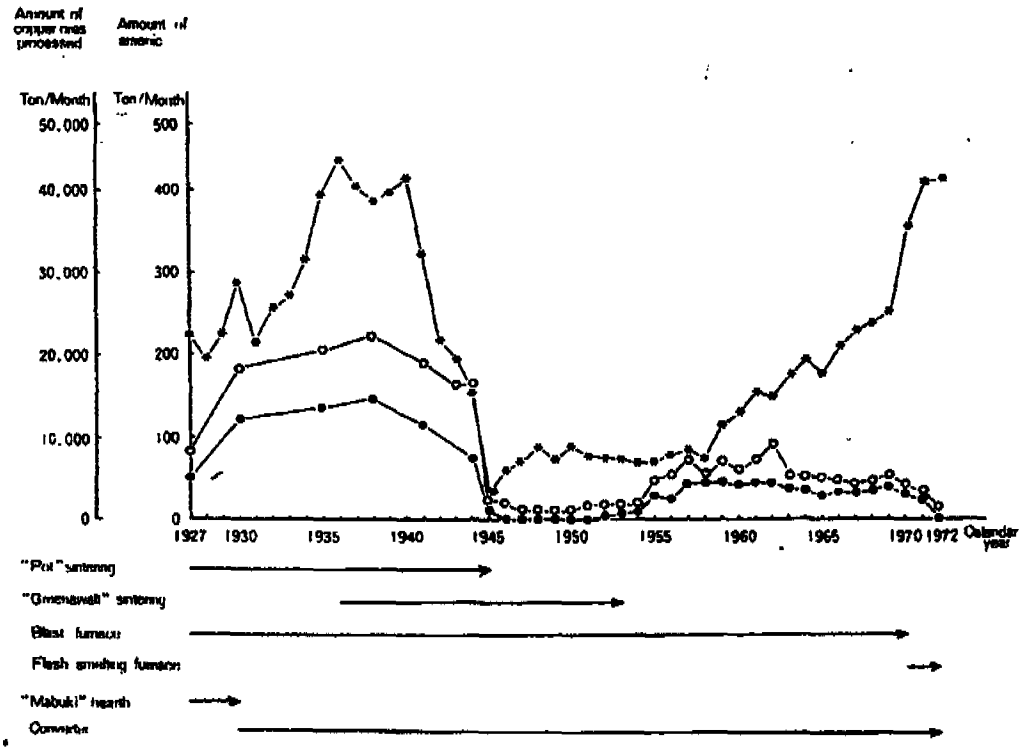

FIGURE 1

Long-term trends of the annual amount of copper ores processed (*——*), the amounts of arsenic in these (o——o) and in "Kinkaseki" ore (●——●), and of the smelting operations in the refinery, during 1927-1972. This figure was provided by the Ministry of Labor.

among the copper smelters. Since the majority of these deaths were unspecified malignant neoplasms of liver without adequate diagnostic validity, any further reference can hardly be made with confidence. It seems highly desirable that similar epidemiologic studies with particular attention to this site of cancer should be made at other copper refineries.

It seems noteworthy that no deaths from skin cancer could be seen among all the workers examined. Since arsenic is known to cause skin cancer in man and some of the workers in the refinery suffered from dermatitis and pigmentation due to a heavy exposure to arsenic compounds particularly arsenic trioxide, some excess mortality from skin cancer was expected. Our negative result might be due to the well-known favorable prognosis of this type of cancer.

Our previous study indicated the necessity of establishing a thorough life-long health care system for copper smelters. The present study reconfirmed it because as already described, 26 of 29 lung cancer deaths seen among copper smelters had occurred after they left the refinery. This may be partially due to the considerably long latent period. Another important aspect of latent period is its possible association with level of exposure. It was expected that the latent period of lung cancer seen among copper smelters would be in inverse proportion to level of exposure, in view of the observations by Lee and Fraumeni (1969) and of the results from the extensive animal experiments conducted by Druckrey (1967), but this could not be demonstrated in our study. Our results were practically the same as those obtained by Ott *et al.*, (1974).

Finally, the fact that as many as 971 workers were excluded from the present analysis due to the fact that their *Honseki* was outside Ooita prefecture, must be considered. If they had had any unusual, either high or low, experience in incidence or mortality from cancer, their elimination must have seriously distorted the results. However, it is hard to imagine that the *Honseki* is firmly connected with cancer risk, because it is decided primarily for registrative purposes. Even if it is in some way related to cancer, it is still difficult to see how it

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could explain the observed increase in mortality from the specific types of cancer among the very specific workers and the observed dose-response relationships.

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UNE ÉTUDE DE LA MORTALITÉ PAR CANCER ET DES AUTRES CAUSES DE DÉCÈS CHEZ LES EMPLOYÉS D'UNE FONDERIE

Les auteurs ont effectué une étude prospective non chronologico-concordante des décès par cancer et des autres causes de décès chez 2675 hommes ayant travaillé dans une fonderie entre 1949 et 1971. Le nombre théorique de décès, déterminé d'après les taux de mortalité par âge et par cause calculés pour les Japonais, a été comparé au nombre de décès observé. Dans une cohorte de 839 fondeurs de cuivre, on a constaté une augmentation significative de la mortalité par cancers du poumon (taux comparatif de mortalité (SMR) = 1189) et du côlon, mais pas par cancers de l'estomac, du foie (primitif) et des voies biliaires, du pancréas et de la peau, ni par leucémie, tuberculose, maladies cérébrovasculaires, cardiopathies ou cirrhose du foie. On a mis en évidence un rapport dose-réponse entre la mortalité par cancers du poumon et le degré d'exposition. Une très nette surmortalité par cancers du poumon (SMR = 2500) a été observée parmi les fondeurs de cuivre qui étaient considérés comme les plus fortement exposés à l'arsenic ou les ouvriers qui avaient été employés au frittage ou aux hauts fourneaux pendant au moins 15 ans avant 1949. La période de latence du cancer pulmonaire est en moyenne de 37,6 ans et n'est pas liée au degré d'exposition. Sur les 29 décès par cancer du poumon constatés parmi les fondeurs de cuivre, 26 se sont produits après leur départ de l'usine. Pour d'autres employés travaillant à la production ou dans les bureaux, la surmortalité par les divers types de cancer n'est pas significative.

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