A SUGGESTION CONCERNING MEDICAL PREVENTION AND CONTROL OF CHRONIC PULMONARY BERYLLIOSIS

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Introduction

Beryllium is one of the indispensable metals to the modern industries on account of its properties as a metal and a compound and the demand has been rapidly increasing for the last several years in Japan also.

Among the health hazards caused by beryllium and its compounds, there are acute hazards centering around skin, mucosae and respiratory organs and chronic hazards known for the formation of pulmonary berylliosis and subcutaneous granulomata.

Until recently, almost all cases of the hazards in Japan were acute, as shown in the data of Table 2 dealing with the records during the past 17 years of the employees at a certain beryllium refinery. During the same period, owing to the improvement of beryllium exposure environment and the efforts made in health control, the frequency of the occurrence of the hazards drastically decreased, and the tendency was observed in the recent several years that the conditions of these acute cases became clearly slighter than the previous cases.

The fact showed without doubt that the measures taken against beryllium hazards until recently had been quite effective for proventing the occurrence of acute hazards at least, and the same fact seemed also to serve as a specific clue toward preventing future chronic hazards.

In spite of the marked decrement in the occurrences of acute hazards, however, in the last few years 5 cases of chronic pulmonary berylliousis were reported to occur at a few factories around the country, and, furthermore, their conditions involved some problems that would shake up even the accept industrial hygienic views on the prevention of beryllium hazards.

Learning from these new conditions, we are endeavoring to clarify causes for the occurrence of chronic beryllium hazards not as a mere interest in some cases studies of pulmonary berylliosis, but because this is a problem directly related to the health of many people who handle beryllium. On the other hand, these new conditions must be regarded as being extremely significant in finding out the maximum allowable concentration of beryllium in the environment and the desirable manners of the prevention and control of chronic beryllium hazards.

1. Examination of Cases of Chronic Pulmonary Berylliosis in Japan

Cases of pulmonary berylliosis what have been reported so far are five and some details are shown in Tables 2 and 3. Patients consist of 3 males and 2 females and their ages range from 21 to 43. The kind of beryllium they were exposed to is in nearly all cases beryllium oxide. Situations where they were exposed include: (1) chemical analysis of beryllium oxide; (2) moving in and out of a refinery and manual work of insorting plastic frames of beryllia ceramic heat sink; (3) isostatic molding using beryllium oxide; (4) beryllia body molding and (5) firing of beryllium oxide, ceramic inspection and moving in and out of a refinery. The ralated work periods are from 13 months to 11 years and 2 months, but the actual exposure hours are far below such periods in every case. The initiations for discovery were such subjective symptoms as short breath, coughing, expectoration, etc. and chest X-ray examination. One person (Case 4) was discovered about one year after she left a beryllium related work with a routine chest rentgenogram without having any symptom. The bases for diagnosis for all cases roughly satisfy the prescribed items of diagnosis (table 3).

An environmental factor common to these five cases is that the exposed beryllium concentration behind them is considered as very low, and it is also extraodinary that all cases are closely related to beryllium oxide.

Case 2, 31 years old female, had never been engaged in a specific beryllium work, but engaged in a clerical work in a separate room for 480 days during which she moved in and out of a beryllium workshop for about one hour a day. Later she left the company to get married and for about 8 years after that as a side-job she did the manual work of inserting beryllia ceramic (heat sink, small disc of 20 mm in diameter and 1.5 mm in thickness) into plastic frame. Then, a beryllium pollution survey was made by reproducing the beryllium concentration and the manual plastic frame

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insertion work of the work environment where the patient was involved. The assumed inhalation amount which the patient was presumed to have inhaled was calculated as 897 μg. Supposing that the patient would have stayed for 8 hours a day in a beryllium exposed environment of 2 $\mu g/m^3$ (maximum allowable beryllium concentration), the period would be a little less than 10 months.

The other four cases do not differ largely from the above case in the circumstances leading to the outbreak of beryllium hazards. This is a most noteworthy fact in the conditions affecting the outbreaks of the preceding beryllium exposed cases and this particular case.

A similar fact has been pointed out in the recent cases found in North America. It has been reported that in the cases of younger workers engaged in aircraft, gyroscope and nuclear power industries discovered since 1972 the outbreak occurred in every case at a beryllium exposed environment of less than 2 $\mu g/m^3$. This is interesting in comparison with our cases.

Two types of results are observed in the chest X-ray examinations covering the present cases: (A) sudden occurrence of diffuse, nodular shadow covering almost all of the lung and (B) comparatively gradual progress of chest X-ray findings, reticular or abnormal linear marking, minute nodular opacities, pulmonary emphysema image, etc. The latter result should be particularly noted in distinguish from pneumoconiosis and other non-tubercular lung diseases.

All of these cases are provided with internal medical treatment including adrenocortical hormone drugs and are placed under the control of medical doctors.

2. Prevention and Control of Chronic Beryllium Hazards

1) Beryllium concentration in the environment and environment control

The occurrence of the acute beryllium hazard markedly decreases if general environmental improvements are successful to an extent, such as improvement in the environment exposed to beryllium of comparatively high concentration, avoidance of contact with soluble beryllium compounds, etc. There is sufficient possibility, however, that chronic pulmonary berylliosis, as mentioned above, can break out at an environment of less than 2 $\mu g/m^3$, the maximum allowable concentration, and further its condition presents the question of relevance of allergic factors. That is, beryllium concentration to be desired in the environment should principally be at a level of suppressing the manifestation of allergy due to beryllium. Industrial hygienic approach to this problem has a grave significance of its being relevant not only to beryllium but being common to all of the numerous sensitive substances widely used in industries.

Concerning an environmental beryllium concentration which does not constitute an organic sensitivity by exposure, the auther previously examined the changes to positivity in a patch test using 1 % Na_2BeF_4 under various relevant environments as shown in Figure 6, and pointed out that this reaction did not turn positive under a beryllium exposed environment of 0.1 - 0.03 $\mu g/m^3$. As long as organic sensitivity due to beryllium is not established, this condentration has an important significance in preventing at least the occurrence of chronic pulmonary berylliosis which is caused by an allergy. On the other hand, it will be a most difficult task to maintain the environmental concentration constantly at this level in an actual complex production site. Therefore, an environmental technological breakthrough to approach this target and a transformation in thinking on a thoroughgoing beryllium control are being demanded of the entire beryllium industry as urgent and serious propositions.

2) Desirable direction of beryllium health control

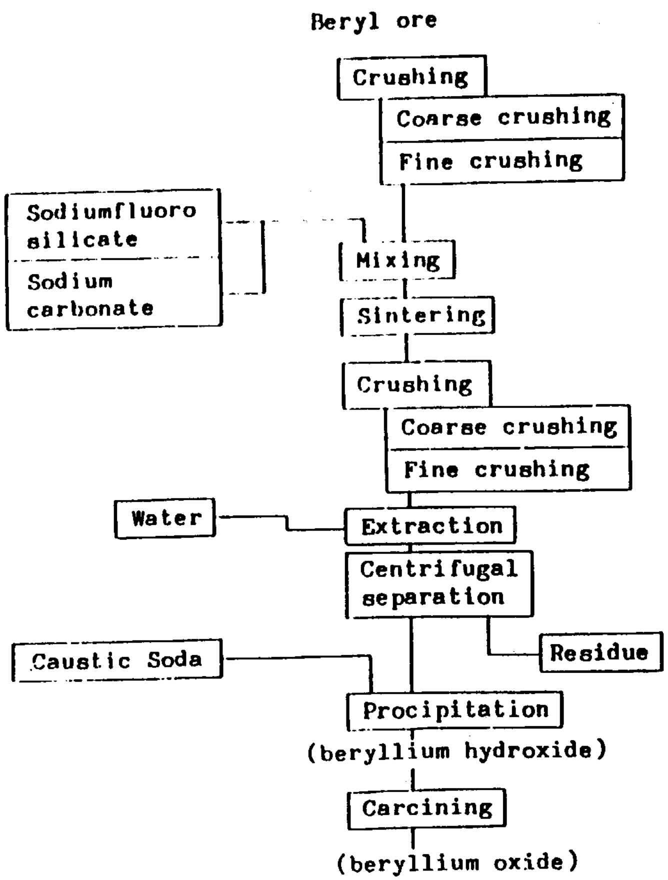
As stated already, the conditions of chronic pulmonary berylliosis are divided into those having sudden remarkable chest X-ray findings with or without serious symtoms and those with a comparatively gradual development similar to pneumoconiosis. For the former cases, the immediate relief from work and the necessary medical treatments can be given, but for the latter it is dificult to find proper way of how to deal.

Next, it is important to resolve the problem of former employees who were exposed to beryllium. Since it is not rare that this hazard breaks out several or over 10 years after the initial exposure, one of the essential tasks for the prevention and control is to follow up the developments after leaving the company. To make the health diagnosis for such former employees smoothly and effectively, a useful method will be to obligate them to receive periodical health examination even after their retirement by the expence of company or government.

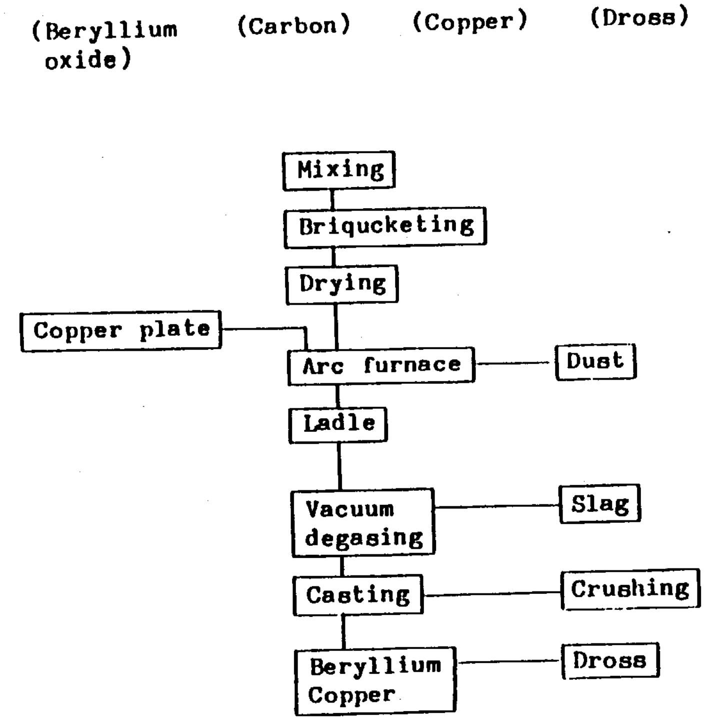
I have expressed a few comments on the cases of chronic pulmonary berylliosis in Japan and the prospective direction of its prevention and control. At the present stage where pulmonary berylliosis itself involves a number of medically unknown factors, even if we may end up making trials and errors, I believe that we should try our best efforts to protect the health of workers.

Fig. 1. Manufacturing flow sheet

A) Beryllium oxide, commerial grade



B) Beryllium copper alloy



(1) $3\,BeO\,Al_2O_3\,6\,SiO_2 + 2\,Na_2SiF_6 + Na_2CO_3$

$\qquad 3Na_2BeF_4 + 8\,SiO_2 + Al_2O_3 + CO_2$

(2) $Na_2BeF_4 + 2NaOH \qquad Be(OH_2 + 4NaF$

(3) $Be(OH)_2 \qquad BeO + H_2O$

(4) $BeO + C + Cu \qquad Be - Cu + CO$

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(3) Be (OH)$_2$ BeO + H_2O

(4) Be O + C + Cu Be - Cu + CO

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C) Beryllia products

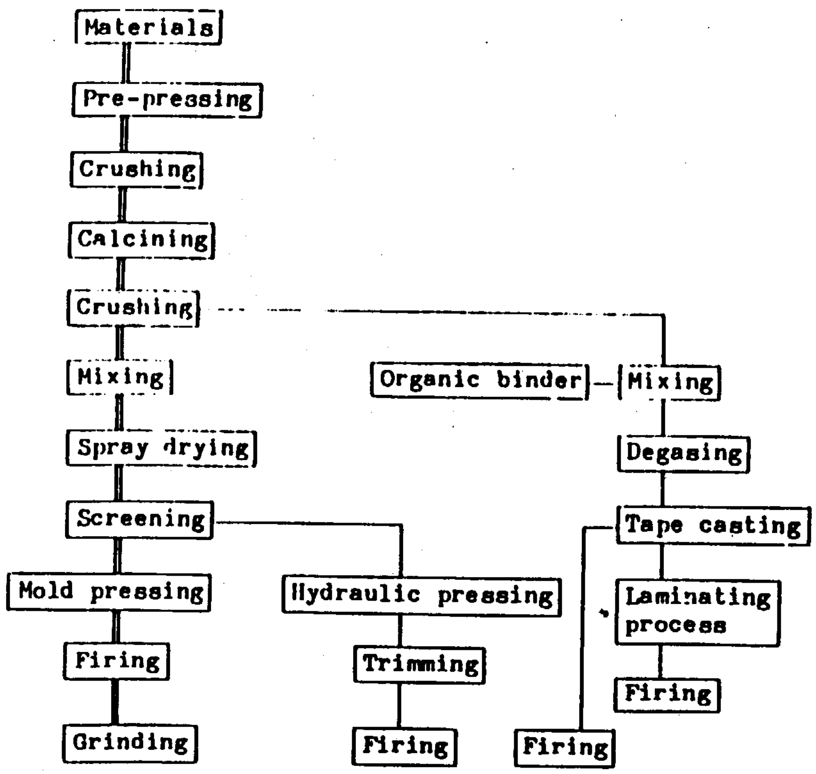

TABLE 1 Frequency of the occurrence of Be hazards in a certain Be factory from 1958 to 1973

Years / No. of employees / Disease	'58	'59	'60	'61	'62	'63	'64	'65	'66	'67	'68	'69	'70	'71	'72	'73	Total
No. of employees	28	46	78	100	147	242	247	284	291	302	325	326	370	443	370	383	4030
acute Be pnemonitis	6 (158)	2 (4.3)	7 (9.0)	2 (1.8)	3 (2.0)	2 (0.8)	1 (0.4)	1 (0.1)	1 (0.4)	0	1 (0.4)	0	0	0	1	0	27 (067)
tracheo-bronchitis	11 (2.9)	2 (1.1)	10 (128)	0	3 (2.1)	1 (0.4)	0	1 (0.1)	3 (2.2)	7 (2.3)	5 (1.5)	5 (1.5)	0	0	0	0	45 (1.12)
contact dermatitis	21 (553)	5 (110)	9 (242)	25 (228)	26 (177)	24 (9.9)	15 (6.1)	5 (1.4)	4 (1.4)	23 (7.6)	2 (0.6)	5 (1.4)	8 (2.1)	7 (1.2)	5 (1.4)	2 (0.5)	195 (484)
conjunctivitis	5 (132)	1 (2.2)	10 (128)	12 (109)	8 (5.4)	6 (2.5)	4 (1.0)	0	4 (1.4)	1 (0.3)	0	0	0	0	0	0	51 (127)
others	5 (132)	2 (4.3)	5 (6.4)	0	2 (0.8)	1 (0.4)	0	1 (0.4)	6 (2.1)	1 (0.3)	0	0	0	0	0	0	26 (061)
chronic pulmonary beryllioisis	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2 (0.5)	2 (005)

( ) ... %

The 345 cases of Be hazards consisted of 27 cases of acute pneumonitis (0.67%), 45 tracheo-bronchitis (0.67%), 45 tracheo-bronchitis (1.12%), 195 contact dermatitis (4.85), 51 conjunctivitis (1.27%), 26 others (0.64%) and 2 chronic pulmonary berylliosis. The frequency of the acute cases was very high during the period of 1958 to 1967, but began to fall rapidly , therafter, owing to the improvement of Be exposure environment and the efforts made in health control.

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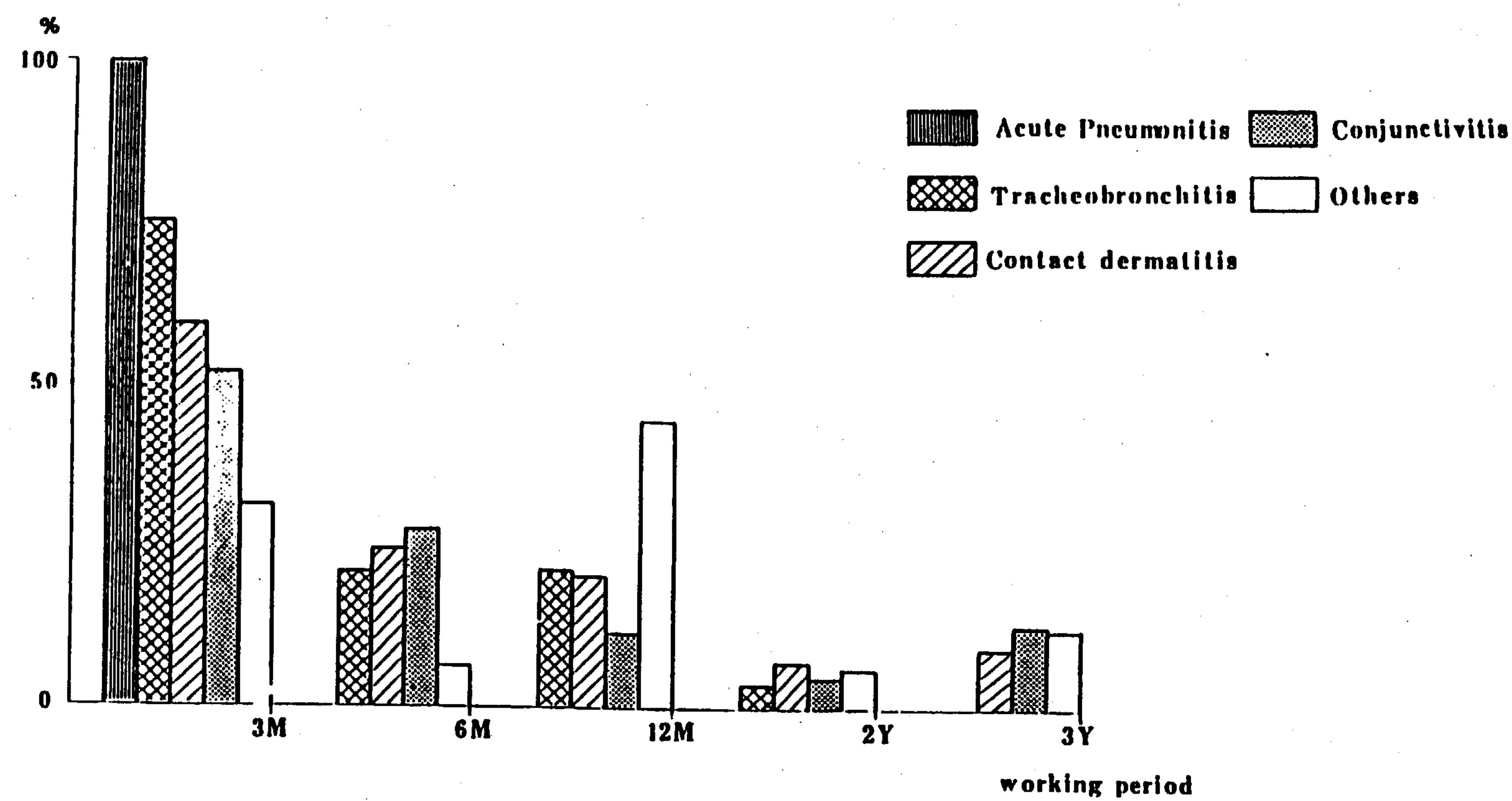
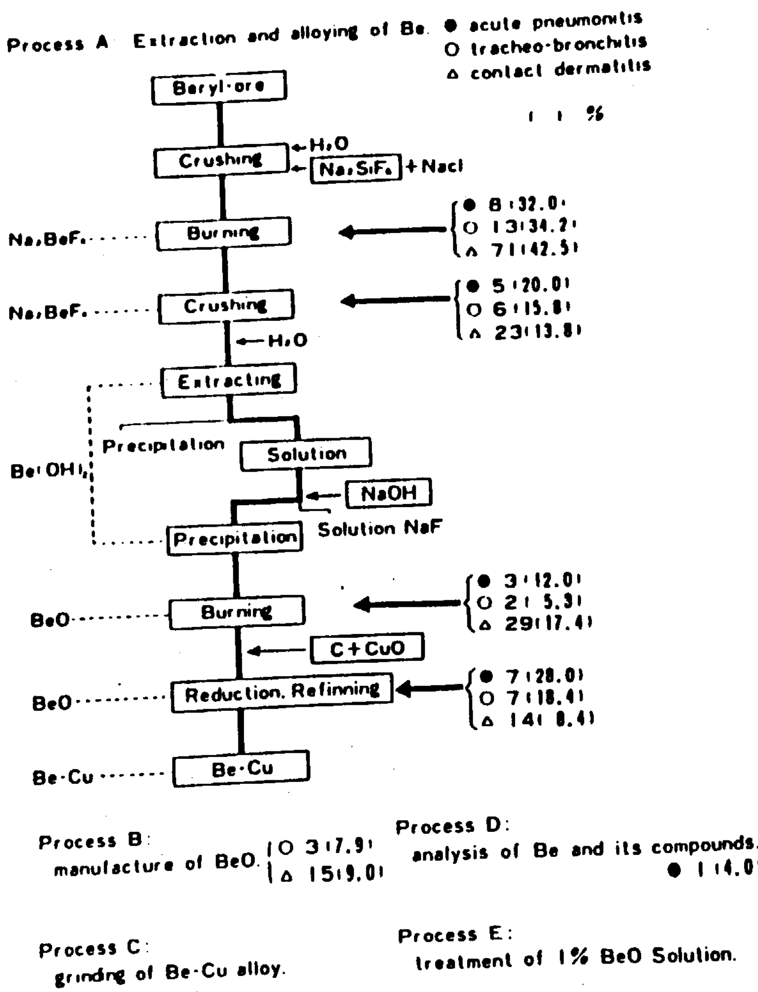
Fig. 2. Interval between employment and the onset of the Be hazards.



These cases occurred during earlier period after employment. Special attention should be paid to the finding that all cases of acute pneumonitis occurred within only three months after new employment.

Fig. 3. Correlation between the Be hazards and process of the Be workplace.



Acute Be hazards frequently occurred in the burning and crushing of Na_2BeF_4, the burning and reduction of BeO. All cases recovered clinically within 7~53 days.

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Process C
grinding of Be·Cu alloy

Process E.
treatment of 1% BeO ... on

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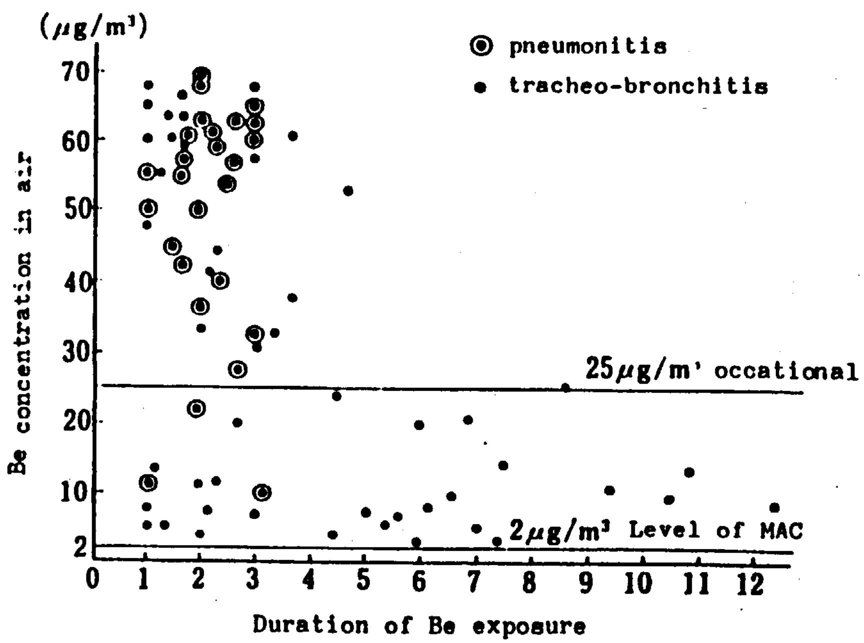
Fig. 4. Correlation between the occurrence of acute pneumonitis and the Be concentration in the air.



Most cases of acute pneumonitis occurred in the environmental condition of Be concentration over 25 $\mu g/m^3$.

Otherwise, the cases of tracheo-bronchitis such a tendency of more cases did not show in more concentrated Be environment.

Table 2. Cases of chronic pulmonary berylliosis in Japan

Case	Industry	Discovery	Sex	Age	Kind of work, Be exposure condition	Kind of exposed Be	Working period	Chance of Discovery	Initial Symptoms	Note
1	Ceramic	1964, Fall	Male	Years old 42	Chemical analysis of BeO (Several times a month)	BeO powder	Years months 5.6	Subjective complaints	Short breathness cough, sputum	
2	Ceramic	1970,8	Female	31	BeO ceramics assemblying, Be refining plant(1hr. a day)	BeO shapes gas, dust	9.8	Subjective complaints	Short breathness, cough, malasia (loss of body weight)	Assumed inhalation doses of Be 988 μg +a
3	Electrical	1971,12	Male	33	Isostatic pressing of BeO (2~7 days a month)	BeO powder	1.5	Subjective complaints	General fatigue	—
4	Ceramic	1972,4	Female	21	BeO molding (2 hrs a week)	BeO powder	1.1	Periodical health examination	None	—
5	Ceramic	1972,11	Male	43	BeO firing (5 month), moving in and out of BeO refining plant (1 hr a day), BeO ceramics inspection	BeO gas, fume, dust	1.2	Subjective complaints	Short breathness, cough	Assumed inhalation doses of Be 1872 μg +a

Patients consist of 3 males and 2 females and their ages range from 21 to 43. The kind of Be they were exposed to is in nearly all cases Beryllium oxide. A environmental factor common to these five cases is that the exposed Be concentration behind them is considered as very small.

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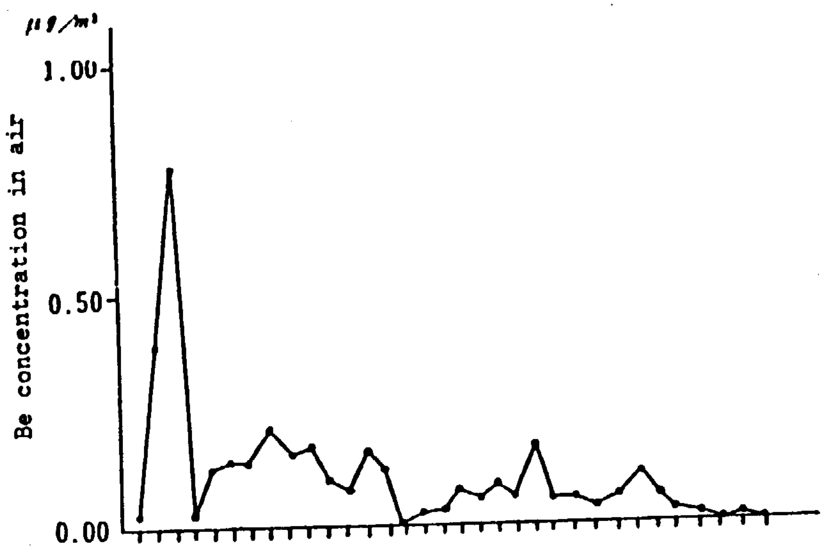
Table 3. Criteria for making the diagnosis of chronic pulmonay berylliosis in Japan.

Findings \ No. of Case	1	2	3	4	5
a. Establishment of significant beryllium exposure based on annual environmental survey.	O	O	O	O	O
b. Chest X-ray films with radiologic evidence of diffuse fibro-nodular shabows.	O	O	O	O	△
c. Pulmonary interstitial granulomatosis.	O	O	O	O	O
d. Positive reaction of 1% Na_2BeF_4 patch test	O	O	O	O	O
e. Presence of beryllium in the blood, urine or lung tissue.	O	×	O	O	O
f. Apperance of pulmonary disfunction.	O	O	O	O	O
g. Change to negative reaction of Mantoux's reaction.	O	O	O	O	O
h. Presence or Worsing of respiratory complaints.	O	O	O	×	O

All cases satisfied the criteria necessary for the diagnosis of chronic pulmonary berylliosis.

In case 2, Be was not found in urine, and in case 4, resperatory complaints was not observed.

Fig. 5. Change of the Be concentration that case No. 5 was exposed in his workplace.



Duration of Be exposure (1964 1973)

In case No. 5 the patient was engaged in firing of BeO, ceramic inspection and moving in and out of a refinery plant. The Be concentration to which he was exposed was the lower than 2 $\mu g/m^3$.

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Table 4. Result of the patch test on the skin using the various Be compounds.

Groupe	Healthy Be Worker		Be Non-exposed Worker	
Tested Numbers	80 (Male)		40 (Male)	
Patch Test	positive	negative	positive	negative
1% Na_2BeF_4	80(100)	0	1 (2.5)	39(97.5)
0.1% Na_2BeF_4	62(77.5)	18(22.5)	0	40(100)
1% BeF_2	72(90.0)	8(10.0)	8(20.0)	32(80.0)
0.1% BeF_2	68(85.0)	12(15.0)	3(7.5)	37(92.5)
1% BeO	2(2.7)	78(95.5)	0	40(100)
0.1% BeO	0	80(100)	0	40(100)
1% NaF	1(1.2)	79(98.8)	0	40(100)
1% HF	0	80(100)	0	40(100)
Hydrophilic Ointment	0	80(100)	0	40(100)

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Each material in hydrophili ointment was pasted and fixed over a circular areas, 2 cm in diameter on the center of the upper arm. Readings were made 48 hours later for the local redding and eruption.

1% Na_2BeF_4 gives the higher positivity in the healthy Be worker, and the lower in controle.

Table 5. Patch test positivity using 1% Na_2BeF_4 in the Be non-exposed workers.

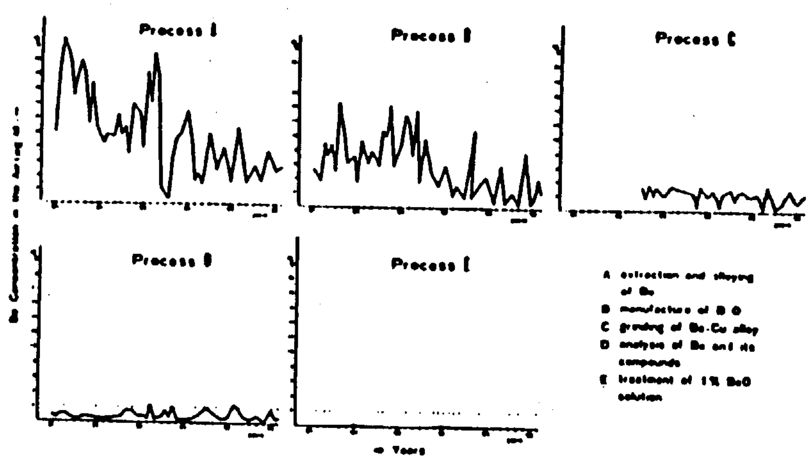
Age		10~	20~	30~	40~	Total
Male	Tested Numbers	161	158	23	13	355
	Patch Test Positive	4 (2.5)	8 (5.1)	1	0	13 (3.7)
Female	Tested Numbers	46	10	4	5	65
	Patch test Positive	0	1	1	1	3 (4.6)

( ) ···%

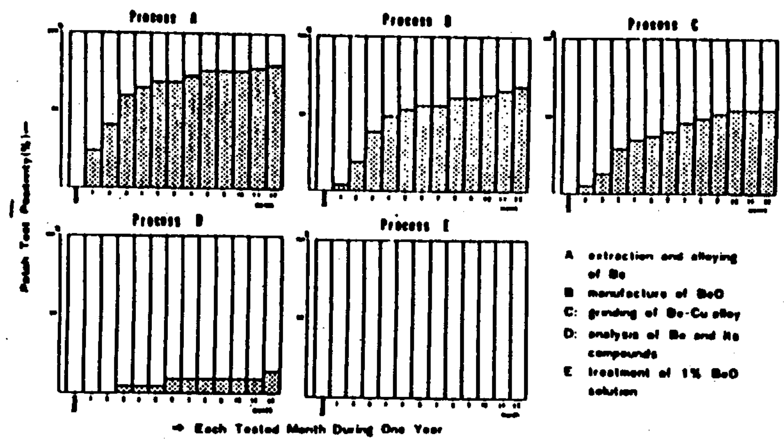
The natural hypersentitivy to Be of these workers was 3.7% in male and 4.6% in femal. From the results of table 4 and 5 it was decided that 1% Na_2BeF_4 is to be used for the patch test in the following suveys.

Fig. 6. Correlation between the Be concentration in each work process and the positivity of patch test of healthy Be workers.

A) Beryllium air concentration in each working process

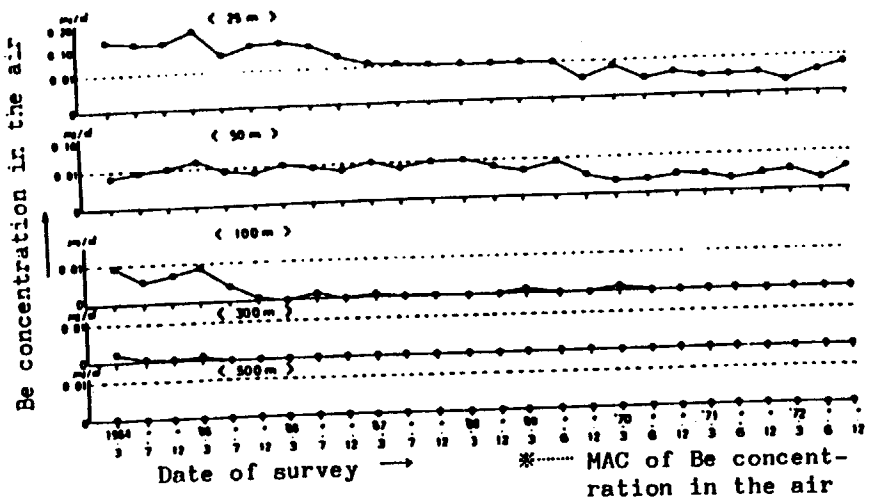


B) Patch test positivity for healthy Be workers in each working process during one year.



For 172 workers who had been shown to be patch-test-negative in the start of employment, a monthly test was carried out during one year with special reference to the Be concentration in the five work processes. These data shows that the positive rate was increased in proportion to the Be concentration in each working place. On the other hand, the positive rate in process E (Be concentration was $0.10 \sim 0.03 \mu g/m^3$) was all negative even after one year. These findings indicate the important facts that for healthy Be workers a Be concentration below $0.1 \mu g/m^3$ in the air hardly induced the hypersensitivity.

Fig. 7. Change of the Be concentration in the air around the Be plant.



The Be concentration in the air around the Be plant is gradualy decreased during the past 17 years.

The concentration of the distant place of more than 100 m of from the Be plant is constantly zero level, since 1970.

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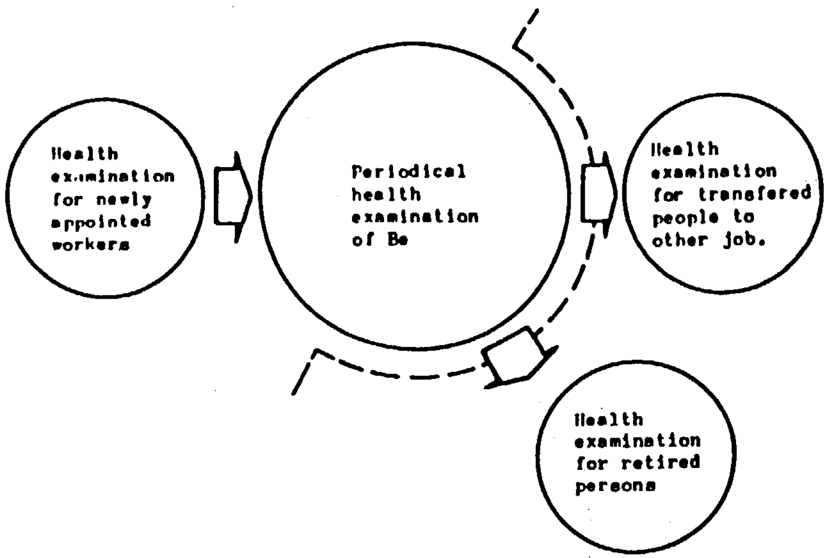
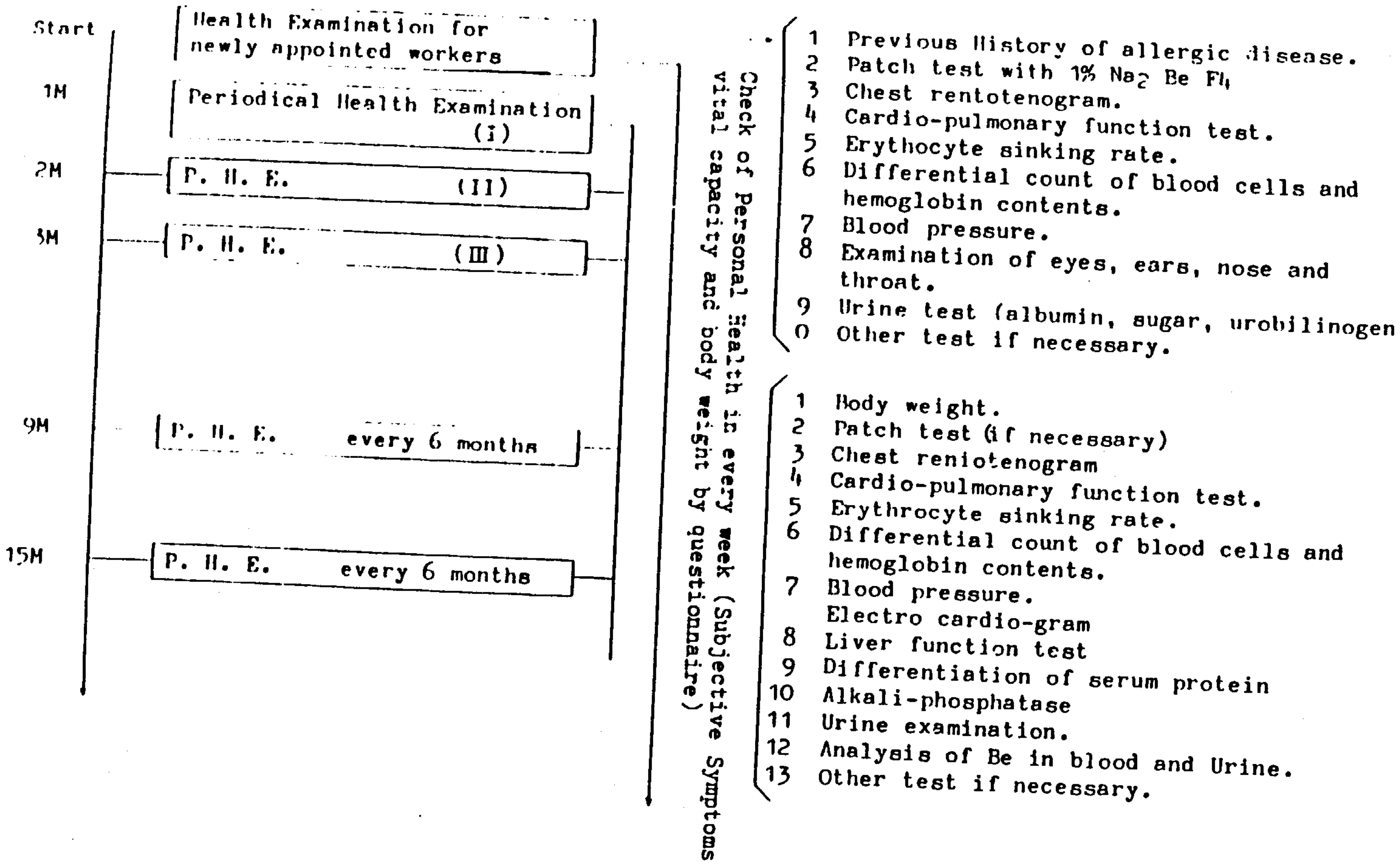
Fig. 9. Medical care to the Be workers.



Medical care to the Be workers consists of the examination at the time of new employment, pediodical health examination (check of personal health condition in every week and health examination in every 3 or 6 months after employment) examination for the workers who were transfered to the jobs of no Be exposure and retired persons.

Fig. 10. Health examination system to the Be workers.



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