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〒 602-0912　京都市上京区烏丸通り下長者町上がる龍前町 605
TEL ： 075 － 411 － 0111　　FAX ： 075 － 411 － 0401
３．参 加 費： 10,000 円（懇親会費を含む）
４．事務局
〒 461-0047　滋賀県志賀郡志賀町大字輪邇中 298
国立療養所比良病院
第７回日本職業アレルギー学会事務局　事務局長　藤 村 直 樹
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日　　時：平成 11 年７月 15 日（木）（18 ： 00 ～ 20 ： 00）
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8．交通機関

ＪＲ新幹線「京都駅」下車後

（1）タクシーにて約15分

（2）地下鉄烏丸線国際会館行きにて「丸太町駅」下車後、徒歩約５分

なお、当日は祇園祭の宵山、宵々山にあたりますので、地下鉄ご利用のほうが確実と考えられます。また、宿泊が混み合っておりますので、早めの御手配をお薦め申し上げます。

9．日本医師会産業医単位申請中。

・地下鉄

丸太町駅２番出口徒歩８分

今出川駅６番出口徒歩８分

・お　車

JR京都駅より約15分／阪急烏丸駅より約10分

名神東インターより、三条通り経由30分

名神南インターより、１号線東寺経由30分

Occupational contact dermatitis

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Abstract

Two hundred and two patients were diagnosed as having occupational contact dermatitis based on their occupational histories, onset situations, clinical features and the results of skin testing. Two hundred and two patients composed of 62 males and 142 females. Age distribution showed a peak in the 20s age group. Atopic predisposition was detected in 95 (47.1%) cases. The jobs of all the subjects were distributed in different occupations : 12 cases in primary industries, 43 cases in secondary industries and 147 in tertiary industries. Occupations and number of cases in tertiary industries were as following; 79 cases of beauticians/barbers, 18 nurses, 17 cooks, 11 dentist/dental assistant, and 22 others. The causative agents were determined by skin testing in 153 out of the 202 cases.

Keywords : occupation, contact dermatitis, skin testing,
chemical allergy, prediction, prevention

Introduction

The conditions of occupational dermatoses in Japan before the 1970's were summarized by Nomura.[1] in 1974. The skin disorders accounted for 25-30% of all the reported occupational diseases. In 1992, an epidemiological investigation of occupational dermatoses was performed by the Japan Occupational Dermatoses Research Group (JODRG) of the German-Japanese Society of Dermatology (GJSD)[2]. According to this study, contact dermatitis, distributing widely in all kinds of occupations, was the most common skin trouble in the 450 cases of occupational dermatoses collected by the members of JODRG. It consisted of 86.2% of all the dermatoses, in which patch testing was performed on 58.5% of cases with contact dermatitis. The skin test technique has

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become an effective measure in detecting causative agents, by which the relevancy between the disorders and the occupational exposures could be easily established. Several large-sample studies showed that the prognosis of occupational contact dermatitis was controversial for those who changed their jobs or stopped working[2-5]. Although many studies of occupational contact dermatitis were published recently in Japan[1, 6-10], there were not so many reports available on the protection measures and prognosis of occupational contact dermatitis.

We experienced 202 cases with occupational contact dermatitis in the past 8 years. We studied their clinical aspects, causative agents, protection measures and prognosis under the different protection measures.

Subjects and methods

Subjects

Two hundred and two patients with occupational contact dermatitis who visited our clinic in a 8-year period from January 1997 to December 1996 were enrolled in this study. They were diagnosed as having occupational contact dermatitis based on their occupational histories, onset situations, clinical features and results of skin testing. The following data were recorded in the case-recording files: occupation, age, sex, atopic diathesis, involved area, skin test results, protection measures, prognosis and job proceeding.

Test materials

Materials and chemicals relevant to patients' jobs, allergens relevant to the individual's exposure, and twenty-five Japanese standard allergens recommended by the Japanese Society for Contact Dermatitis (JSCD) were tested[11].

Skin testing

Closed patch testing

Using Finn Chambers (EPITEST Ltd Oy, Hyrylä, Finland) on Scanpor (NORGESPIASTER, A/S Norway) tape[12], 48 hour-closed patch testing was performed on the upper back of the subjects. Unknown materials / chemicals were tested by a 48 hour-closed patch testing after confirming by an open testing that they were not irritant. Suspected materials such as cutting fluids and detergents were diluted to usage concentration. Relevant allergens were diluted to optimum concentrations by petrolatum or distilled water. Readings were made at 1 and 24 hours after removal according to the recommendations of the International Contact Dermatitis Research Group (ICDRG)[13]. Just after the first reading, the patched areas were irradiated with 6J/cm^2 of UVA to observe for possible photosensitivity.

Scratch testing

The tested areas on arms were scratched with a PRICK-LANCETTER 1 mm spiss (Ewo Care AB, Bredaryd, Sweden).

Suspected materials such as meat, fish and vegetables were put on and rubbed gently into the scratched areas. Latex extract solutions were made by incubating rubber gloves or the latex sheet in sterile distilled water[14, 15]. The readings were first made at 20 minutes and again at 24 hours after applying the test chemicals. When the control material was negative, a wheal with a flare larger than 10mm × 10mm at the 20 minute reading was judged as an urticarial reaction. Erythema, edema and papules with or without vesicles at the 24 hour reading were judged as an allergic reaction. When the control (petrolatum or distilled water) was positive, the judgment was made in comparison with their reactions.

Open testing

This test was conducted by applying test chemicals or products for 20 minutes without occlusion. As a rule, open testing is done with suspected materials at the concentrations used in workplaces. The readings were performed in the same manner as that of the scratch test.

Protection measures and prognosis of the subjects

We could investigate the protecting measures and prognosis of the 66 patients who visited our clinic during a 2-year period from January, 1995 and December, 1996.

After a final diagnosis was established, all of the cases were given topical treatments and medical advice according to the results of skin testing. The patients visited our clinic to receive regular consultations. All the 66 subjects had been followed up from 6 months to 2.5 years. To compare the effects of various countermeasures, we classified the patients into three groups based on the protection measures. Group I included those who quit their jobs or changed their duty, and the causative chemicals or materials were eliminated from their work places. Group II included those who were protected by gloves. Group III included those who were protected by a film-forming lotion or other methods. The evaluation of prognosis was made as follows; Cured: lesions disappeared completely, Improved: conditions changed for the better, Relapsed: lesions recurred after disappearing once as a result of treatment, and Undetermined: those who dropped out. The effective rates of the three groups were calculated on the level of the improved and the cured.

Results

Background of subjects

The females in this study accounted for two thirds of the total (Fig.1). Patients in their 20' s were dominant in the age distribution (Table 1, Fig.2). Ninety five cases (47%) had atopic diathesis (Fig. 3). The subjects' occupations were classified into seven groups based on the similarity of their jobs. The patients comprised of 12 agriculture-related workers in the primary industries, 43 factory workers in the

secondary industries, and 147 subjects in the tertiary industries (Fig.4). The tertiary industries included 79 hairdressers and barbers, 18 nurses, 17 cooks, 11 dentists and dental technicians, and 22 others (Table 2, Fig.5).

Areas involved

The most frequently involved area was the hands and forearms (149cases : 72.3%). Thirty three (16.3%) were injured on their face. Twenty three subjects (11.4%) were injured on both hands and feet and/or their trunks (Table 3).

Types of dermatitis

One hundred and sixty three cases (80.7%) were diagnosed with allergic contact dermatitis (ACD), 26 cases with irritant contact dermatitis (ICD), 7 cases

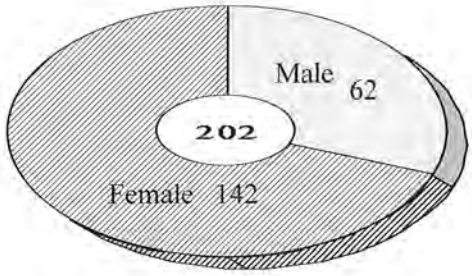

Fig.1 Subjects

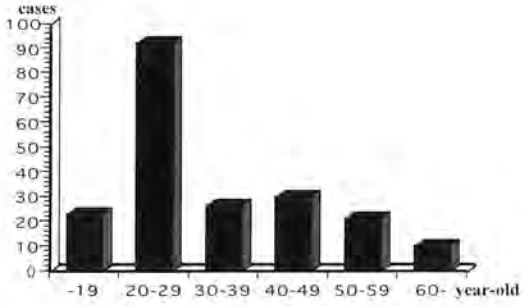

Fig.2 Age distribution

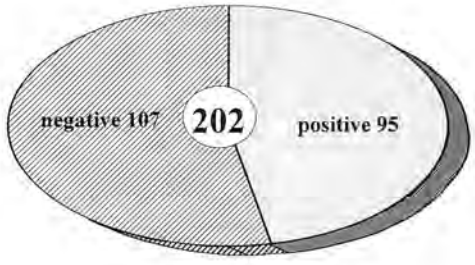

Fig.3 Atopic predisposition

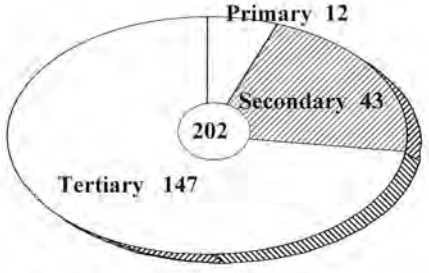

Fig.4 Classification of the industries

Table 1. Age distribution

−19year-old	:	23cases
20−29year-old	:	92cases
30−39year-old	:	26cases
40−49year-old	:	30cases
50−59year-old	:	21cases
60year-old	:	10cases

Table 2. Occupations and cases in the tertiary industries

Beauticians·barbers	:	79cases
Nurses	:	18cases
Cooks	:	17cases
Dentists·dental assistants	:	11cases
Others	:	22cases
Total	:	147cases

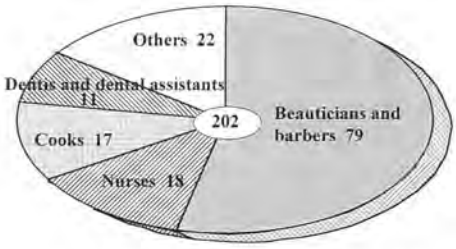

Fig.5 Occupations and cases in the tertiary industries

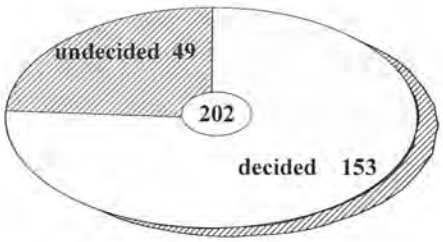

Fig.6 Decision of causative agents

Table 3. Involved areas of dermatitis

Sites	Cases	Rates
hands only or hands and forearms	146	72.3%
face, hands and forearms, face only	33	16.3%
hands and feet or trunk	23	11.4%

with contact urticaria (CU), and 3 cases with CU accompanied by ACD.

Causative agents

Table 4 shows the causative products and chemicals of the subjects. The causative agents were determined in 153 (75.7%) out of 202 cases (Fig.6).

Countermeasures and prognosis of the subjects

We could investigate the protecting measures and prognosis.oft 66 patients who visited our clinic during a 2-year period from January, 1995 and December, 1996.

Group I was composed of 21 cases (31.8%). Most of them were protected completely by eliminating causative chemicals from their workplaces. Group II was composed of 31 (47.0%), more than half of them using plastic gloves. Group III was composed of 14 (21.2%), most of them using a film-forming lotion. Since subjects' occupations and causative materiels or chemicals were different, the protection methods were different. In hairdressers, nurses and dental technicians, twenty-four subjects used gloves. In some cases of factory workers, elimination of causative chemicals was practicable. While in some other cases, they had to change their jobs. In some moderate cases the film-forming lotion was used. Cooks did not use the gloves (Table 5). The effective rate of using protection for the improved and the cured in group I was 81.0%, in group II 83.9% and in group III 71.4% (Table 6).

Job proceeding and recurrence

Except for 5 who quit their jobs and 3 who changed their duties, 50 (86.2%) of 58 subjects could proceed their jobs.

Table 4. Causative products and chemicals in each occupation

Occupation	Causative products and chemidals
Agricultural and related Workers:	
Farmer	chrysanthemum, primrose, croton, vinyl gloves, boots, fig, primin, Parsol A, rubber gloves
Florist	chrysanthemum, spinach, fig, spinach
Gardener	viburnum awabuki, ginkgo, urushiol
Vegetable company worker	spinach, tomato, orange, fig, banana(CU); spinach(AR)
Factory workers:	
Cement worker	cement(IR), cobalt, rubber gloves, rubber boots
Plumber	glue(CU)
Interior decorator	formaldehyde, Kathon CG
Metal worker	machine oil, nickel, cobalt, chromium
Welder	machine oil
Electrician	chromate, cobalt, rubber gloves; protective cream(IR),
Dye worker	pigment, dyes, p-t-butylphenol formaldehyde resin(PTBP-FR), lacquer, glue
Rubber grinder (home worker)	N-isopropyl-N'-phenyl-p-phenylenediamine(IPPD)
Pottery worker	mercury, formaldehyde, melamine resin
Cosmetic factory worker	soap, 1,3-butylene glycol(1,3-BG)
Epoxy resin handler	epoxy resin
Baker	wheat flour, bread crumbs
Fireworks	black powder
Lacker work	urushi
Hairdressers:	hair dye(open), permanent wave solution(open), shampoo, latex gloves, p-phenylenediamine, p-aminoazobenzene, ammonium thioglycolate(open), p-tolulenediamine, p-aminophenol, Sudan Ⅲ
Dental technicians:	dental materials(primer, adhesive, etchant), disinfectants, anesthetic, mercury, cobalt, latex gloves(CU or AR)
Cooks:	raw lobster, onion, squid, banana, vinegar, acetic acid, soy sause(CU); detergent
Nurses:	Isodine, chlorphexidine gluconate, benzalkonium
Others:	Chloride (IR), rubber gloves thiuram mix, TMTD, TETD, TMTM, $HgCl_2$, Vinyl gloves(IR)
Waitress	lettuce, cucumber, latex(CU), thiuram mix, TMTD, TETD, ZDMC, ZDEC
Printed paper saleswoman	packing paper, cotton gloves, rubber gloves
Printer of computer basis	green ink(IR)
Laboratory technician	Isodine, aldehyde reagent, Samson solution
Tailor	cloth(IR)
Tea ceremony teacher	chrysanthemum

There were five subjects with recurrence of dermatitis. The relapses were due to the following reasons: one hairdresser complained of difficulty when doing delicate work while wearing protective gloves; one interior decoration worker still exposed himself to formaldehyde while working, and three other cases failed to avoid causative agents.

Discussion

The subjects engaged in 26 different occupations. This wide distribution of the

Table 5. The methods for protection in each occupation

Protective measures	Cases	Agric worker	Factry worker	Hairdresser	Dental technician	Cook	Nurse	Others
I : Duty-changing	3		2					1
Job-quitting	5		1	3				1
Cause-removing	13	3	5		3	1	1	
II : Gloves:								
plastic	19		1	11	4		1	2
plastic with long cuffs	4			4				
latex	4	2		1			1	
low latex	1	1						
material unknown	3		1	2				
III : Film-forming lotion	9		3	1		2	1	2
Others	5	1	2			1		1
Total	66	7	15	22	7	4	4	7

Table 6. Prognosis of the three groupus

Groups	Cases	Cured	Improved	Relapsed	Undetermined	Effective ratio
I	21	2	15	1	3	81.0%
II	31	1	25	1	4	83.9%
III	14	0	10	3	1	71.4%
Total	66	3	50	5	8	81.3%

occupations was in accordance with a previous report[9]. The cases of the tertiary industries accounted for 72.8% (142/202) of the total. The hairdressers were observable for their large proportions as reported in other studies[2, 8-9]. Nagoya is an industrial city in Japan. There are a large number of workers employed in the secondary industries. Large companies usually have their own hospitals. Therefore, the companies'hospitals are usually the first places to visit for patients in the secondary industries who suffer from occupational contact dermatitis. The Department of Environmental Dermatology of a university hospital is usually the first choice for the patients with occupational contact dermatitis from the tertiary industries to come to. Therefore, the patients with occupational contact dermatitis in the tertiary industries became the main proportion in this study.

In this study, the age distribution of the subjects showed a peak in patients in their 20's. This suggested that the onset of dermatitis begins within a short period after the initial exposure to occupational chemicals.

Our study confirmed the usefulness of skin testing in determining the causative agents of occupational contact dermatitis. In this study, the causative agents were determined by skin testing in 153 (75.7%) out of 202 cases. Rietschel[10] also recently commented that patch testing is invaluable for the investigation of most forms of

occupational contact dermatitis.

One hundred and forty six cases involved only hands or hands and forearms. All the cases that involved hands reached 179 cases (88.6%). This reflects the fact that direct contact with causative materials while working is the major way of exposure.

In a general-population study of 2800 subjects in the Netherlands, about 70% of contact dermatitis individuals had irritant and about 30% had allergic dermatitis[17]. In our study, the proportion of ACD was 80.7% and ICD was 12.9%. Since this study was clinic-based in a university hospital where all the subjects were patch tested, allergic reactions were well investigated. Irritant dermatitis, especially cumulated irritant contact dermatitis, usually has a light clinical symptom, and a quick remission. Therefore, patients with allergic dermatitis are more common than those with irritant dermatitis in the clinic.

According to the effective rates of protection methods, group I (cause-removing) and group II (gloves) showed ideal results for prognosis. A study by Rosen et al[5] showed that the overall improvement rate was in excess of 70%. Their study also demonstrated that the prognosis greatly improved by changing their work duties or leaving the industries. Although the protection methods through cause-removing or duty-changing including job-quitting showed a better effect on preventing patients from the recurrence, these measures could not be adapted to most of the patients. Glove-protection should be recommended in workplaces. Holness et al.[18] reported that workers with a greater knowledge of the causes of their dermatitis had a better prognosis. Education is an important step to improving the prognosis of occupational contact dermatitis.

As mentioned above, skin testings are useful for detecting the causative materials and /or chemicals. We have to consider that there will be false negative or false positive reactions in skin testings. The reasons of the false negative results are as follows : 1) conditions needed to develop dermatitis such as perspiration, friction and pressure were not revived, 2) concentrations of the test materials were too low to develop positive reaction, 3) application time was not long enough or reading time was too early, 4) vehicles of the test materials were not suitable, 5) it needed UV energy to develop positive reactions. The reasons of the false positive results are 1) stuffiness with perspiration, 2) too high concentration, 3) over pressure, 4) causes of the past dermatitis. Therefore, we cannot decide the causative materials and /or chemicals only from the skin test positive results. We have to confirm the patients' actual contact with the positive products or chemicals. If they have not had contact with the positive products or chemicals, the skin test results indicate the patients' past dermatitis due to above products or chemicals. Otherwise, the positive results are cross reactions to real causative agents. On the other hand, even when they present negative results, we can not decide that the products or chemicals are not causes without much

thought. We have to consider the skin testings were conducted correctly. Process required for decision of the causative materials and/or chemicals is as followings ;1) interview of patient's history and situation of development (process of their eruptions, affected areas and exposure period, 2) speculation of the causative materials and /or chemicals from the histories of the patients, 3) decision of the most suitable skin test method, 4) correct explanation of the skin test results, and 5) confirmation of the relevance between skin eruptions and skin test results.

After the decision of their causes, having a regular medical examination, appropriate treatment and education are necessary for reducing the number of persistence.

In summary, skin testings are effective measures in confirming a relevance between the disorders and the occupational exposures through determining causative agents. However, proficient technique and enough knowledge are necessary to utilize the skin testings correctly.

Proper protection with gloves was as effective as removing causative agents from the workplaces. Optimum protections based on the determination of causative agents were important to improving the prognosis of occupational contact dermatitis.

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Special Lecture

Occupational Dilemmas in Latex Allergy

Ian R. WHITE

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Although the majority of cases of latex protein hypersensitivity have been reported among health care workers (the prevalence of latex allergy in hospital employees varies from 3/12%) and their patients, hypersensitivity is a problem in other occupational groups where latex gloves are worn for employee protection. Examples of these occurrences can be taken from the pharmaceutical, electronic and cosmetic industries were up to 6% of employees may be affected.

The exact prevalence of latex protein allergy in general populations have not been clarified. However, in the non-atopic general population it may be $<1\%$, in Finland the minimum prevalence is 33/100,000 inhabitants. In the USA, ant-latex IgE antibodies (≥ 1.5IU/ml) have been found in 2% of blood donors. A current study in London suggests that 2.5% of a local population are allergic to latex proteins as determined by skin prick testing. Questionnaire based assessments of the problem within industries have been advocated0.

Because of the current problem in industries other than health care, itis necessary for occupational health physicians practicing in these industries to be as aware of the problem of latex protein hypersensitivity as their colleagues working in health care. It is essential that information on the protein content of gloves is requested from suppliers in the absence of such information being carried on product labels. Additionally, the physician should be familiar with routes of sensitization and differences in assay methods for protein content. It is the total extractable protein (TEP) rather than the allergenic protein content which is generally available. Non-sterile gloves with a TEP of $<20\,\mu g/g$ of glove are readily available0 There is no justification for the continued supply and use of starch powdered gloves. In situations in which starch powdered latex gloves are worn> 3500 starch particles per cubic meter of air have been detected and the aeroallergen may be 100 times higher than where non-powdered gloves are used.

In many occupations, gloves made of natural rubber latex are ideal for skin protection. The cost per unit of a glove with low TEP and starch free may be higher than alternatives. For the primary

prevention of latex protein allergy it is important that short term financial considerations do not compromise health. In the UK, containment of latex protein allergy has been obtained by accepting this. The economic effects of employee morbidity caused by latex protein allergy can be enormous and dependent on industry. Litigation has been a factor in increasing awareness of the importance of primary prevention. Although the term "hypoallergenic" is to be discouraged it is incumbent on the employer to provide the safest practicable environment for the employee. Dissemination of protein carried on starch particles can contaminate wide areas of a work place.

In secondary prevention, some latex protein allergic individuals may be able to were gloves with vary low protein content. Others will require gloves made from synthetic polymers such as neoprene. These do not, as yet, have the same 'feel' as gloves made from natural latex but neoprene gloves can now provide the degree of protection against biological agents.

Clinical course of 10 cases of chronic beryllium disease in ceramic workers in Japan.

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Chronic beryllium disease is immunological granulomatous disorder involving multiple organs,caused by beryllium metal or its salt mainly BeO. Be is widely used in many modern industries because of its lightness, tensile strength, heatresistance and electronical, radiological characteristics, such as nonmagneticity and X-ray transmission.

Therefore, exposure is related to some occupations such as Be metal and alloy workers, ceramic manufacturing, workers, and electronic,space and atomic industry engineering.

As CBD is caused by T lymphocyte sensitization for Be, disease developes after start of exposure as late as one month to some years,and manifest some immunological signs,and reactions to Be. Tuberculin test is often negative, and Be patch skin test shows positive although it is contraindicated because of the risk to trigger the onset of CBD or its exacerbation. Bronchoalveolar lavage fluid:BALF finding shows highly increased and activated T lymphocytes with increased CD4/CD8 ratio. Lymphocytes from patient with CBD react significantly with incubation with $BeSO_4$.BALF cells response more than peripheral blood lymphocytes.

Diagnosis is established by the presence of noncaseating giant cell granuloma with tissue Be.Exposure history is not always demonstrated because of indirect exposure.

First case of CBD in ceramic workers in Japan was reported by one of the authors in 1976[1],with a prediagnosis clinical features as follows.

Nov.1967: Worked as a molder and exposed to BeO once a month.
April.1971: No abnormal finding on chest X ray.
Nov.1971: Malaise,fatigue developed followed with dyspnea.

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Dense mottlings were found on chest X-ray throughout the both lungs.
Anti-tuberculosis therapy by a tentative diagnosis of milliary TB was started but resulted in failure to respond.

Feb.1972: Dyspnea deteriorated and required oxygen therapy.

May.1972: Corticosteroids therapy started for suspecting sever sarcoidosis, or CBD. resulted in marked improvement.

Jun.1972: Be patch test with 1% Na_2BeSO_4 showed strong positive.

Feb.1973: Open lung biopsy was performed that showedepitheloid cell granuloma 0.186ppm Be in the lung tissue negative ZiehlNeelsen stain for TB bacillus

these findings confirmed the diagnosis of CBD.

Referabce

After the first case,three symptomatic cases and six asymptomatic cases with diffuse abnormal shadow on chest X-ray were detected and diagnosed as having CBD (table2). There was no difference between symptomatic and asymptomatic groups, concerning age at on set or duration for Be exposure (table 2,3). However, the prognosis were obviously worse in symptomatic group (table4, 1-4). Repeated spontaneous pneumothorax was notable as a clinical feature (figure 6). And all of these progressive cases had histories of administration of oral corticosteroids (figure 1-7).

Three asymptomatic cases detected by routine chest X-ray examination showed spontaneous remission of the disease[2]. These cases had no history of administration of oral corticosteroids.

After the regal regulation to keep the Be concentration in the work place below $2\mu g/m^3$ only one exceptional case occurred in a scrap metal worker(table1).

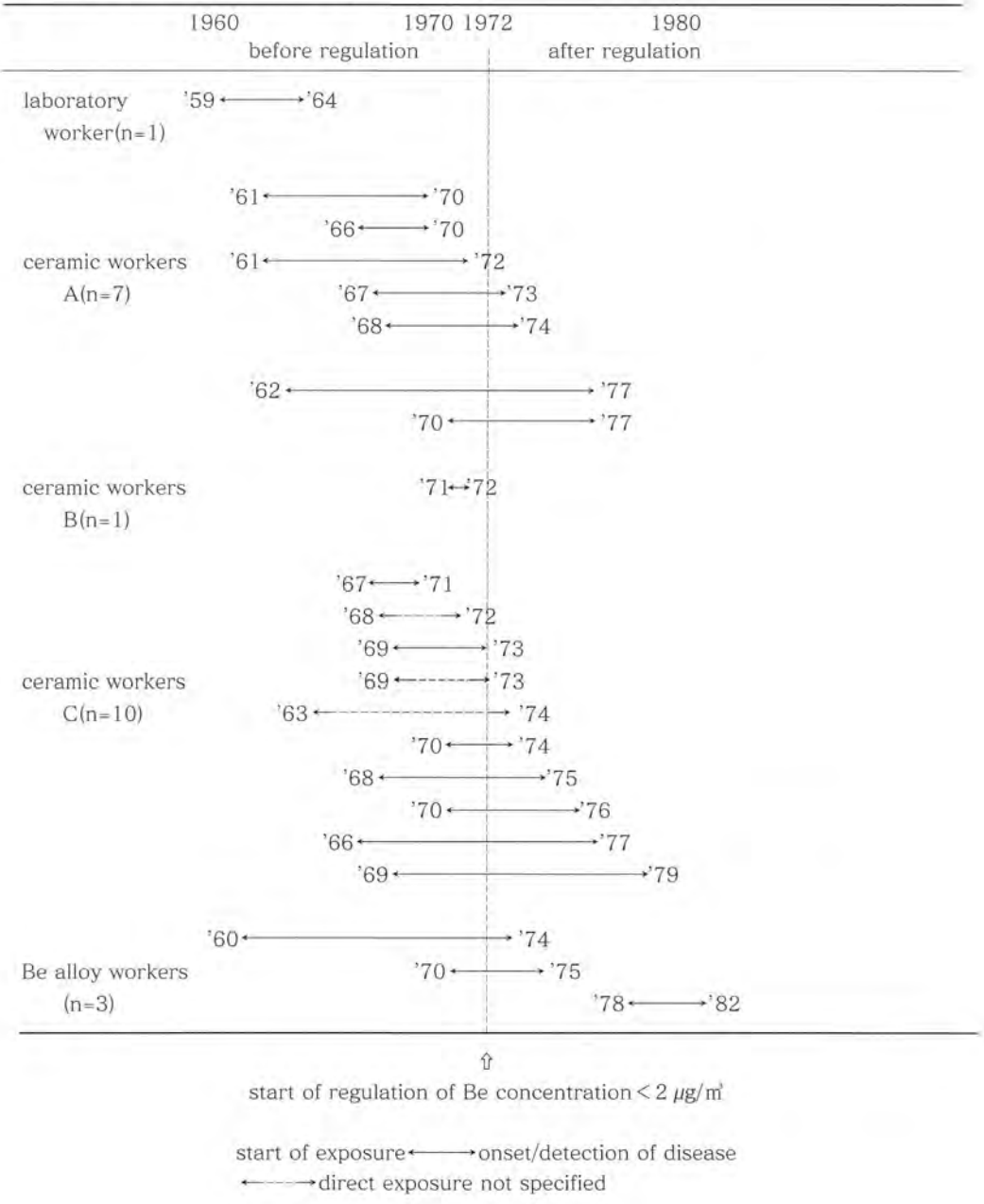
summary

1. Chronic beryllium disease(CBD) is an occupational ling disorder with very slow progression caused by exposure to BeO.
2. The regal regulation to keep the Be concentration in the work place below $2\mu g/m^3$ was considered highly effective in preventing the occurrence of CBD.
3. Be is widely used in modern industry,and the risk of CBD increases with industrization in areas where the handling of Be is not strictly controlled. If doctors fail to accurately recognize a disease condition as CBD, it may be misdiagnosed as sarcoidosis with poor prognosis, even with lung biopsy.

References

1) Izumi T, Kobara Y, Inui S, Tokunaga R, Orita Y, Kitano M, Williams JW : The first seven cases of chronic beryllium disease in ceramic factory workers in Japan. Ann NY Acad Sci 278 : 636, 1976
2) Nishikawa S, Hirata T, Kitaichi M, Izumi T : Three year prospective study of Mantoux reactions in factory workers exposed to beryllium oxide. 8th Inter-national Conf on Sar and granulomat dis. edit Jones Williams W and Davis BH, 722. Alpha Omega Publ, Cardiff. 1980

Table 1.22 cases of CBD in Japan



Clinical course of 10 cases of chronic beryllium disease in ceramic workers in Japan.

table 2.10 cases of CBD caused by exposure to BeO in a ceramic factory

name sex age	onset/detection of disease	duration after exposure to Be	symptoms
B. S. M 31	Nov.1971	4y 0m	malaise, fatigue and exertional dyspnea
M. N. F 47	Feb.1972	3y 6m	weightloss, exertional dyspnea and cough
T. U. F 38	Dec.1973	5y11m	malaise, cough and dyspnea
C. Y. F 28	Feb.1974	0y 8m	fatigue, exertional dyspnea and cough
N. M. M 35	May 1974	4y 9m	routine chest X-ray examination
S. F. M 25	Apr.1975	7y 1m	routine chest X-ray examination
Y. S. M 28	Apr.1975	5y 2m	routine chest X-ray examination
K. K. F 24	Apr.1976	6y 1m	routine chest X-ray examination
N. I. F 40	Apr.1977	10y 5m	routine chest X-ray examination
K. S. F 35	Apr.1977	8y 0m	routine chest X-ray examination

table 3.Clinical and laboratory profiles at time of detection of the disease.

mode of detection	symptoms	routine chest X-ray examination	total
No	4	6	10
M/F	1/3	3/3	4/6
age at onset	28-47	24-40	24-47
from start of Be exposure to onset of CBD	3y6m-10y	4y9m-10y5m	3y6m-10y5m
method of diagnosis			
open lung biopsy	4	2	6
TBLB		1	1
positive LST to Be		3	3

Table 4. Clinical course of 10 cases with CBD

Four cases detected by symptoms.
Three female cases died: (figure 2-4)
Two women died of chronic respiratory failure,9 years and 13 years after detection
One male case who is still alive 27 years after the onset, shows definite progression of the disease, and requires inhaled corticosteroids therapy for asthmatic symptoms (figure 1).
All cases had histories of administration of oral corticosteroids.

Six cases detected by routine chest X-ray examination.
Three cases,two females and one male,showed spontaneous remission of the disease.
Three cases, two males and one female, showed definite progression of the disease (figure 5-7). One male case developed repeated spontaneous pneumothorax (figure 6).
All of three progressive cases had histories of administration of oral corticosteroids.

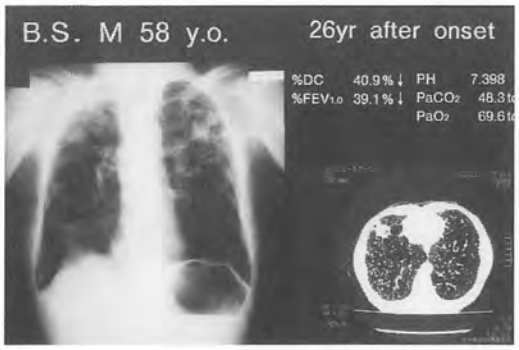


figure 1:First case of CBD in ceramic workers in Japan.

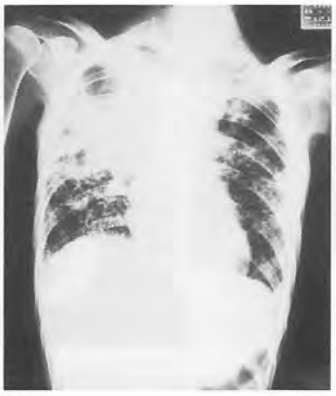


figure 2:Fatal case of CBD, M. N. female, 9 years after detection of the disease.

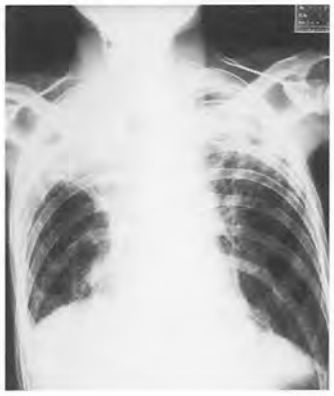


figure 3:Fatal case of CBD,T.U.female, 16 years after detection of the disease.

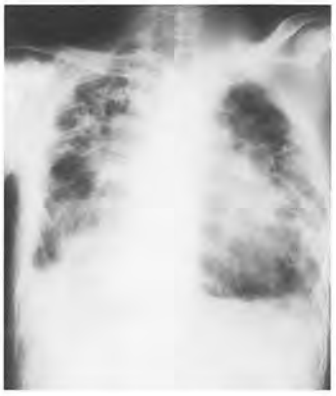


figure 4:Fatal case of CBD,C.Y.female, 13 years after detection of the disease.

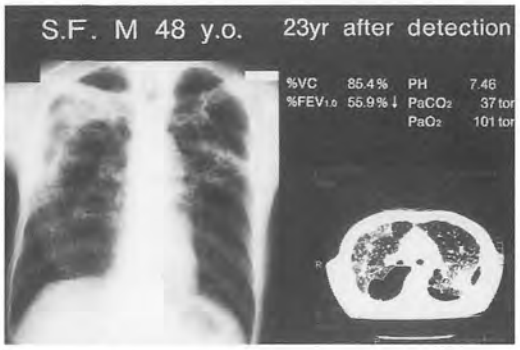


figure 5:Progressive case of CBD detected by routine X-ray examination

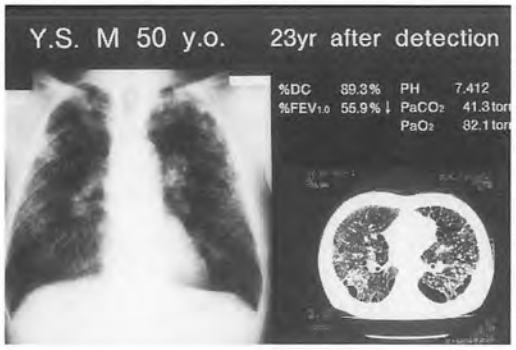


figure 6:Progressive case of CBD detected by routine X-ray examination

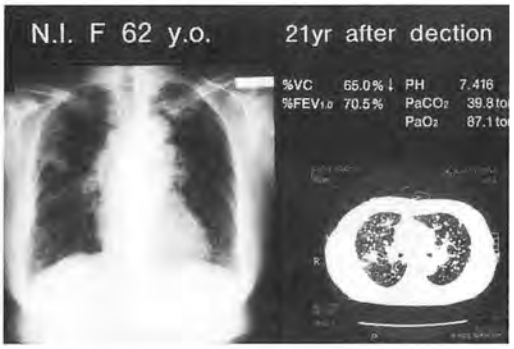


figure 7:Progressive case of CBD detected by routine X-ray examination

林業従事者におけるスギ花粉症
第2報－スギ花粉症の発症と素因について－

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要　旨

毎年，多量のスギ花粉に曝露されていると考えられる林業従事者と曝露量の少ない名古屋市内某事業所勤務者を対象としてスギ花粉症の遺伝的素因について聞き取り調査を行い，さらに血清総IgE値，スギ花粉特異IgE抗体価を測定し，スギ花粉症の発症要因について調べた．2親等以内にスギ花粉症患者のいる人を素因陽性とすると，林業者，都市勤務者いずれも素因陽性と陰性では血清総IgE値，スギ花粉特異IgE抗体価に有意差はみられなかった．

スギ花粉症を発症している人の割合を素因陽性と陰性で比較すると，林業者では有意差はみられなかったが，都市勤務者では素因陽性のスギ花粉症発現率が陰性より有意に高かった．さらに素因陽性でスギ花粉症患者の血清抗体値についてみると総IgE値，スギ花粉特異IgE抗体価のいずれも林業者の方が都市勤務者より有意に高い値を示した．

この調査によりスギ花粉症は素因を有する者が多量のスギ花粉に曝露されることによってのみ発症するという単純な機構ではなく，その他の要因も関与していることが示唆された．

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緒　言

前報[1]において，我々は毎年多量のスギ花粉に曝露されていると考えられる林業従事者とそれより花粉曝露量の少ない名古屋市内の某事業所に勤務する成人男性を対象としてスギ花粉症の発現率と血清スギ花粉特異IgE抗体陽性率を比較した．その結果,両者の間に発現率，抗体陽性率ともに有意な相違は認められず，長期的に見た場合，スギ花粉症の感作や発症は単に花粉の曝露量だけによって規定されているのではないことが窺われた．今回，我々はアレルギー性疾患発症に極めて重要な因子である遺伝的素因の関与について林業従事者と市内某事業所勤務者を対象に家族歴の聞き取り調査を行い，スギ花粉症の発現率，血清総IgE値，スギ花粉特異IgE抗体価について検討し興味ある結果を得たので報告する．

対象と方法

1）対象

林業従事者（以下林業者）は愛知県内の主として新城地方の山林で働いており，林業組合に所属している男性59名で，年齢は20～75歳

（平均46.7±12.1歳），林業従事歴は平均22.0±13.3年であった．名古屋市内事業所勤務者（以下都市勤務者）は名古屋市内の某事業所に勤務する男性職員57名で，年齢は25～59歳（平均45.6±8.8歳），林業従事歴のある者はいなかった．

採血は林業者が1995年8月及び1996年3月，都市勤務者は1996年の6月にそれぞれ行った．血液採取できたのは林業者59名，都市勤務者48名であった．測定項目は血清総IgE値，スギ花粉特異IgE抗体価である．

2）測定方法

スギ・ヒノキ花粉数は愛知県新城保健所と名古屋市内某事業所屋上にて測定した．花粉測定器具はロータリー型花粉捕集器を使用し，1㎠当たりのスギ・ヒノキ花粉数をカウントした．測定期間は1990年から1996年までの2月から4月までである．

血清総IgE値はELISA法で測定し，単位はIU/mℓで，スギ花粉特異IgE抗体価は間接ELISA法で測定し，単位はFU（fluorescence unit）で表現した[2]．

3）スギ花粉症素因調査

聞き取り調査により，2親等以内（親，兄弟，姉妹，子供，祖父母，孫）に毎年春先にくしゃみ，水様性鼻漏，鼻閉，目の掻痒感などの自覚症状を有し，医療機関でスギ花粉症と診断された人がいる者を素因陽性者とした．

成　績

1）平均年齢

林業者の平均年齢は46.7±12.0歳，都市勤務者は45.6±8.8歳で有意差はみられなかった（U検定）．

2）一人当りの2親等数

林業者の一人当りの2親等数は4.8±2.0人，都市勤務者のそれは4.7±1.8人で有意差はみられなかった（t検定）．

3）素因陽性者数

林業者59名中，素因陽性は24名（40.7%），都市勤務者は57名中21名（36.8%）と両群で有意差はみられなかった（χ^2検定）．

4）スギ・ヒノキ花粉数

林業者が主に働いている愛知県新城地方と都市勤務者の勤める名古屋市内某事業所屋上で測定した1990年から1996年までのスギ・ヒノキ花粉数を示す（Fig.1）．いずれのシーズンも新城地方は名古屋市内の1.5～5倍多く飛散している．

5）血清総IgE値

林業者で素因陽性24名の血清総IgE値は275.4±398.6IU/mℓ，素因陰性35名のそれは235.5±379.6IU/mℓで有意差は認められなかった（t検定）．都市勤務者では素因陽性18名の総IgE値は241.4±248.9IU/mℓ，陰性30名のそれは233.1±340.1IU/mℓで同じく有意差はみられなかった（t検定，Fig.2）．

6）血清スギ花粉特異IgE抗体価

林業者で素因陽性24名のスギ花粉特異IgE抗体価は357.8±554.6FU，素因陰性35名のそれは333.8±426.4FUで有意差はみられなかった（t検定）．都市勤務者では素因陽性18名のスギ花粉特異IgE抗体価は338.6±411.9FU，陰性30名のそれは191.8±386.0FUで有意差はみられなかった（t検定，Fig.3）．林業者の採血は業務の都合上1995年8月（13名）と1996年3月（46名）に分けて行った．総IgE値は8月採血者が474.8±591.5IU/mℓ，3月採血者が189.0±286.0IU/mℓで有意差は認められず（U検定），スギ花粉特異IgE抗体価もそれぞれ491.5±598.6FU，301.8±437.1FUと有意差はみられなかった（t検定）．

7）血清スギ花粉特異IgE抗体陽性率

血清スギ花粉特異IgE抗体価が100FU以上を陽性[3]とすると，林業者で素因陽性24名のうちスギ花粉特異IgE抗体陽性者は9名

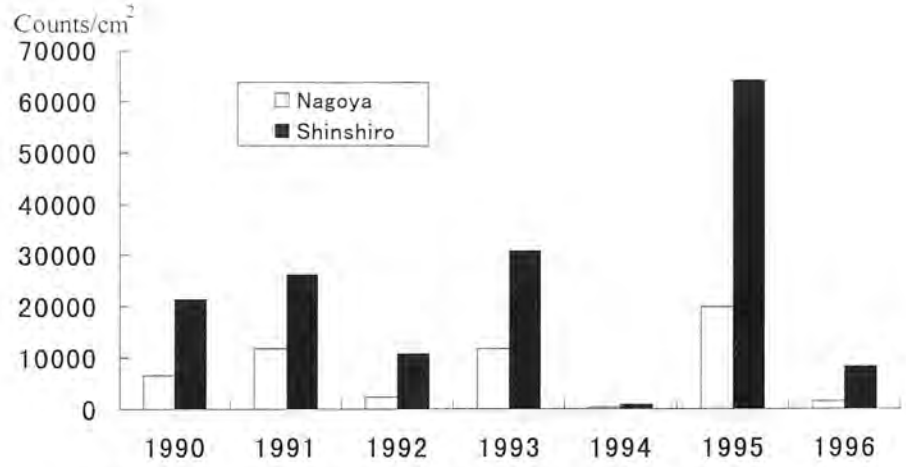

Fig.1 Pollen Counts of Airborne Japanese Cedar (*Cryptomeria japonica*) and Japanese Cypress (*Chamaecyparis obtusa*) in Nagoya (City) and Shinshiro (Woodland)

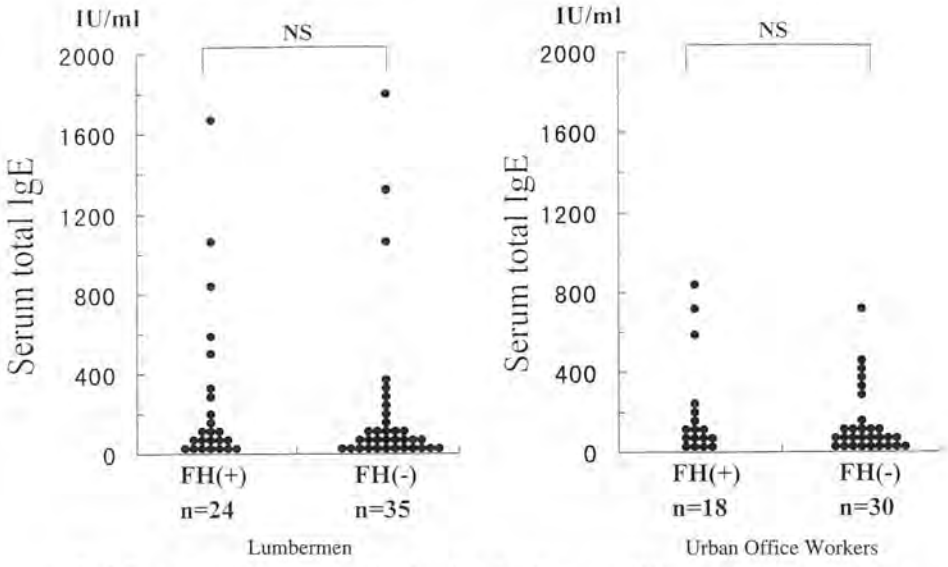

Fig.2 Comparisons of Serum Total IgE Levels in Lumbermen and Urban Office Workers with or without the positive Family History (FH) of Japanese Cedar Pollinosis.

(37.5%)，素因陰性では35名中16名（45.7%）で有意差はみられなかった（χ^2検定）．都市勤務者ではそれぞれ18名中9名（50.0%），30名中9名（30.0%）で同じく有意差はみられなかった（χ^2検定）．

8）スギ花粉症発現率

林業者で素因陽性24名のうちスギ花粉症患者は5名（20.8%），陰性では35名中7名（20.0%）で有意差はみられなかった（χ^2検定）．しかし，都市勤務者においては素因陽性21名中スギ花粉症患者は8名（38.1%）で陰性36名中3名（8.3%）に比較して素因陽性が有意に高い割合を示した（χ^2検定，$P<0.01$）．

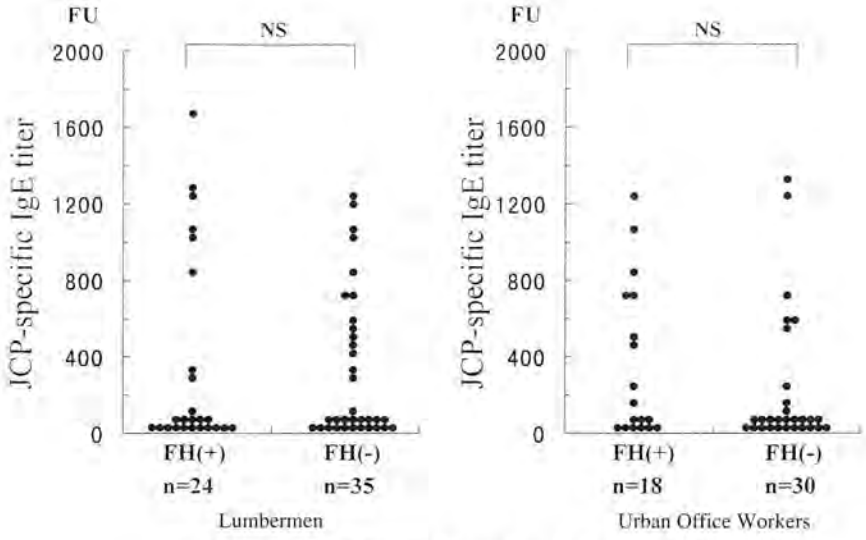

Fig.3 Comparisons of Values of Serum Specific IgE to Japanese Cedar Pollen between Lumbermen and Urban Office Workers with or without the positive Family History (FH) of Japanese Cedar Pollinosis

9）林業者と都市勤務者における素因陽性スギ花粉症患者の血清総IgE値，スギ花粉特異IgE抗体価の比較．

素因陽性でスギ花粉症患者の林業者5名および都市勤務者7名の血清総IgE値，スギ花粉特異IgE抗体価を比較した．

血清総IgE値は林業者では728.6±638.2IU/mℓ，都市勤務者では135.4±87.7IU/mℓで林業者の方が有意に高い値を示した（U検定，$P<0.05$）．スギ花粉特異IgE　抗体価は林業者が1,248.8±243.4FU，都市勤務者は713.6±365.1FUで同じく林業者の方が有意に高い値を示した（t検定，$P<0.05$）（Fig.4）

考　察

近年，スギ花粉症が増加した最も大きな原因の一つとして抗原であるスギ花粉の増多が指摘されている．しかし，単にスギ花粉飛散量が増えたことだけがスギ花粉症増加の主因であると仮定すると，長年にわたり毎年多量のスギ花粉に曝露されている林業従事者においては林業にたずさわっていない都市生活者に比し高頻度にスギ花粉症患者がみられるはずである．

Fig.1に見られるように林業者が働いているスギ・ヒノキ山林に近い新城地方とスギ・ヒノキ林から遠く離れた名古屋市内のスギ・ヒノキ花粉数を比較すると，ここ5年間でも新城地方が約1.5～5倍多く飛散している．スギ・ヒノキ林の中で働く林業者はそれよりさらに多量のスギ花粉に曝露されていることになる．しかし，緒言でも述べたように，これら林業者と都市勤務者の間でスギ花粉症発現率及びスギ花粉特異IgE抗体陽性率に有意差が認められなかった[1]ことは，スギ花粉症の感作や発症は単に抗原曝露量のみで規定されているのではないことが推察された．

一方，スギ花粉症はアレルギー性疾患であることから遺伝的素因が関与していることが十分に考えられる．現にスギ花粉症患者においては多発家系[4,5]が存在することや遺伝子マーカーであるHLA-DQW3との正の相関が報告[1]されている．高岡[7]のナシ栽培者，石崎[8]のイチゴ

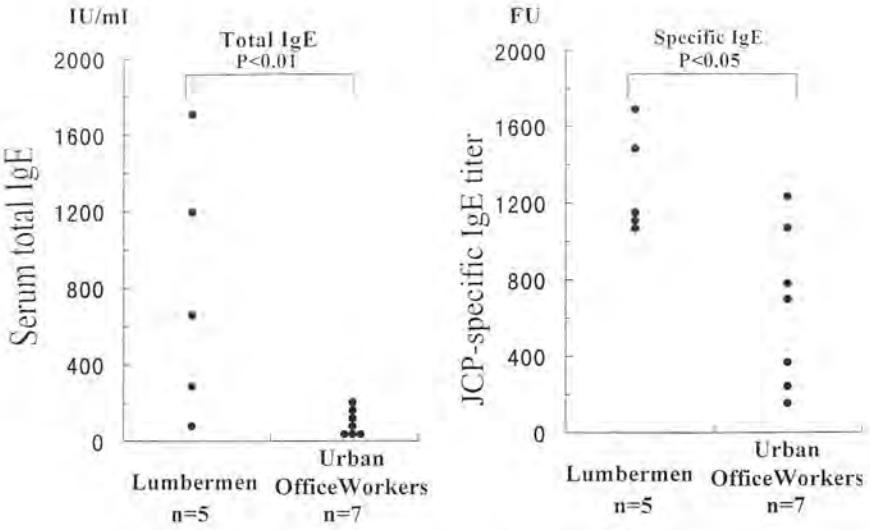

Fig.4 Comparisons of Serum Total IgE Levels and Values of Specific IgE to Japanese Cedar Pollen between Lumbermen and Urban Office Workers in Japanese Cedar Pollinosis (JCP) with the positive Family History of JCP.

栽培農業従事者の調査でもアレルギー素質群において自覚症状を有する者が有意に多く，職業性アレルギーの発生要因としてアレルギー素因は重要であると考えられる[9,10]．このような報告からすると平均22年という長い期間，高濃度のスギ花粉に曝露されている林業者の素因陽性者においては特にスギ花粉症の発症者が多いことが想定される．我々はこれらのことを確認するため林業者と都市勤務者について聞き取り調査を行い，スギ花粉症についての素因とスギ花粉症の発現率，および血清総IgE値，スギ花粉特異IgE抗体価ついて検討してみた．素因の設定としては3親等以内とする報告もあるが[11]，3親等では範囲が広すぎて情報が不正確となりやすいなどの問題から，今回の調査では比較的聞き取りが容易である2親等以内とした．また，アレルギー素因については調査対象が多量のスギ花粉に曝露されている林業者であることからスギ花粉症という単独の疾患に限定して調べた．その結果，林業者の素因陽性者と陰性者では血清総IgE値，スギ花粉特異IgE抗体価，抗体陽性率およびスギ花粉症発現率に差がみられず，逆に曝露量の少ない都市勤務者の素因陽性者にスギ花粉症の発現率が陰性者より有意に高いことが認められた．この成績は，種々の職業性アレルギーに関する報告[7-10]や我々の予想に反するものであった．

このような相反する結果となった原因を追求する目的で，素因陽性のスギ花粉症患者に限って血清総IgE値とスギ花粉特異IgE抗体価を林業者と都市勤務者の間で比較検討してみたところ，いずれも林業者の方が有意に高い値を示した．これは素因陽性のスギ花粉症患者の血清抗体値は，スギ花粉曝露量の影響を受けていると思われるが，素因陽性者が症状を発現するには多量の抗原に曝露され血清高IgE抗体価となるだけでなく，状況によっては低濃度曝露，低IgE抗体価でも発症することを示しており，素因と花粉量の他にもスギ花粉症の発症には何らかの要因が関係しているものと考えられた．

遠藤[12]らは都市環境が鼻アレルギーの発症に影響を及ぼす因子として大気汚染，生活様式，

生活環境，都市気候などを挙げている．このうち大気汚染を例にとってみると，今回我々が調査した両対象となる名古屋市と新城市（新城市は大気汚染調査が行われていないので隣接の豊川市の測定結果を採用した）の大気環境はNO_2，SO_2，浮遊粒子状物質などの大気汚染物質が名古屋市内の方で約1.5～2倍高い値を示している[3]．また，名古屋市内でも重工業地帯である南区のスギ花粉症患者と林業を主産業として発達した新城市の患者の重症度を比べたところ，南区の方が花粉飛散量が少ないにもかかわらず，重症例が多いという報告もある[4]．今回の対象において両地域の大気状況の相違も花粉症の症状発現に関与する重要な因子の一つとして考えられる．しかし，アレルギー疾患の発症には様々な要因が複合的に関与しており，大気環境だけを，スギ花粉症の発症を促進する因子であると断定するの早計であろう．

今回の我々の調査成績からは，スギ花粉症は素因を有する者が多量のスギ花粉曝露によって発症するという単純な機構ではなく，その他に大気汚染を含む何らかの要因が関与していることを示唆したものと考える．それらの原因をさらに詳しく追求するためには，両群それぞれのスギ花粉症患者の発症時期，ダニやその他の重複抗原の検索，住居や生活環境あるいは生活様式の調査，また，喘息，アトピー性皮膚炎等他のアレルギー性疾患を含めたアレルギー素因の調査，家族歴も3親等以内に広げるなどさらなる追加検討が必要と思われた．

結　語

毎年，多量のスギ花粉に曝露されている林業従事者と曝露量の少ない都市勤務者を対象として，アレルギー発症要因の一つである遺伝的素因の面からスギ花粉症発症について検討してみた．その結果，スギ花粉症は素因を有する者が多量のスギ花粉に曝露されることによってのみ発症するという単純な機構ではなく，その他に大気汚染を含めた何らかの要因が関与していることが示唆された．

稿を終えるにあたり，本研究に対して多大な協力を賜りました名古屋市衛生研究所の小川保先生，愛知県林業センターの中山　学先生に深く感謝致します．

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Japanese cedar pollinosis in lumbermen Ⅱ:
Serum level of IgE antibody
and hereditary factor

To determine the influence of antigen exposure and hereditary factors on appearance of Japanese cedar (*Cryptomeria japonica*) pollinosis (JCP) attack, we assessed the presence of the positive family history (FH) of Japanese cedar pollinosis and measured serum levels of specific IgE to JCP and total IgE antibodies by means of an enzyme linked immunosorbent assay (ELISA) of lumbermen exposed to high counts of Japanese cedar pollen and urban office workers exposed to low counts of Japanese cedar pollen.

No significant differences of the serum levels of specific IgE to JCP and total IgE antibodies between the individuals with and without the positive FH of JCP either in lumbermen or urban office workers were found. In urban office workers, the incidence of JCP with the positive FH was significantly higher than that without the positive FH, but not in lumbermen. In the patients with JCP with the positive FH, the serum levels of specific IgE to JCP and total IgE antibodies in urban office workers were significantly lower than those in lumbermen.

Key words:lumberman, family history,
Japanese cedar pollen, pollinosis, IgE

干エビ製造従業者にみられた職業性喘息

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はじめに

近年、産業の発達に伴い職種も多様化し、職場で扱われる物質も多種類となり、職場でこれら物質の微細粉塵に感作されて発症する職業性アレルギー疾患が注目され、種々の職業性喘息が報告されるに至っている。

筆者は約37年間実地医家として地域医療に携わっているうちに、真珠養殖従業者に発症したホヤ喘息の発見を契機として、職業性喘息に関心を持つようになり、これまで20種類を見出し報告した。

今回、干エビ製造従業者にエビに起因すると考えられる職業性喘息を見出し、若干のアレルギー学的検索と治療を行ったので報告する。

症例1

患者：55歳　女性

職業：干エビ製造業従業者

家族歴：特記すべき疾患なし

既往歴：特記すべき疾患なし

現病歴：平成2年3月より干エビ製造作業を行ってから約3年後より鼻水、咳嗽などの感冒様症状を訴えるようになり、対症療法を行っていた。さらに約1年3ヶ月後の平成6年7月3日に作業中に呼吸困難発作を起こして当院受診した。

作業内容を聞いてみたところ、生エビを煮たあと、従来は天日にて乾燥していたのであるが、機械化されて乾燥機にかけて乾燥し、脱殻も機械で行うようになり、その後を手作業にてエビを篩にかけて粉塵を下ろしたり、選別や袋詰作業を行っていて、その時多量の粉塵が発生するということであった。

職業と喘息発作との関係では、休業すると喘息症状は寛解し、就業すると喘息発作が起こると訴えた。

来院時現症：咳嗽、喘鳴を訴え、胸部に乾性ラ音を聴取した以外、理学的に身体各部に異常所見は認められなかった。

一般検査成績：表1に示したごとく、末梢血好酸球9.5％増加し、免疫グロブリン血清IgE値が2126IU/mℓと上昇を示した以外には胸部X線像に異常なく、心電図正常範囲、血清蛋白分画、肝機能検査、血清電解質などはいずれも正常値であった。

アレルギー学的検査成績

1　皮内反応

本症例における皮内反応は表2に示したごとく、エビ、カニ、ハウスダストエキス1,000倍希釈液で陽性を示したが、他のアレルゲンエキスはすべて陰性であった。

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2　エビエキスによる閾値検査

エビエキスによる皮内反応陽性閾値検査を行ったところ表3に示すごとく10万倍を示した。

3　IgE RAST

表4に示すごとく、エビでクラス3、カニとコナヒヨウダニでクラス1を示した以外にはイワシ、ハウスダスト、真菌類はクラス0であった。

職場におけるピークフロー値の変動

患者にピークフローメーターを職場に持って行かせて、就業前後を測定させたところ、就業20分でピークフロー値30％の減少を認めたので、本喘息は即時型の職業性喘息と診断された。

特異的減感作療養の治療成績

以上の検査成績により本喘息がエビ粉に起因する職業性喘息と判明したのであるが、抗原回避のための対策は零細企業のため実施出来ず、職場の配置転換や転職も困難であり、患者も現職場での作業継続を希望するので、エビエキスによる特異的減感作療法を実施した。

図1に示すように、エビエキスにて型のごとく実施したところ、当初は対症剤、インタール吸入を併用していたが、開始後4週間より軽快し始め、10週後には対症剤、インタールを中止しても喘息発作は起こらなくなり、現在維持療法を行って作業継続しているところである。

症例2

患者：52歳　女性

職業：干エビ製造業従業者

家族歴：特記すべき疾患なし

表1　一般血液検査成績（症例1）

末梢血液検査		血清電解質	
赤血球数	446×10⁴/μℓ	Na	138mEq/ℓ
血色素量	12.4g/dℓ	K	4.5mEq/ℓ
白血球数	6800/μℓ	Cl	104mEq/ℓ
ヘマトクリット	44.8%	Ca	9.6mEq/ℓ
白血球百分率（%）		血清蛋白分画（%）	
好中球	62.5	アルブミン	62.6
好酸球	9.5	α1-グロブリン	2.6
好塩基球	0.7	α2-グロブリン	10.3
単球	8.2	β-グロブリン	6.4
リンパ球	29.1	γ-グロブリン	20.1
生化学検査		免疫グロブリン	
血清総蛋白	7.2g/dℓ	IgG	1824mg/dℓ
総ビリルビン	0.4mg/dℓ	IgM	94mg/dℓ
総コレステロール	164mg/dℓ	IgA	206mg/dℓ
GOT	24U/ℓ	IgE	2126IU/mℓ
GPT	21U/ℓ	その他	
ALP	3.3K-A-U	RA	(−)
LDH	346U/ℓ	CRP	(−)
γ-GPT	27U/ℓ	ASO	142N/mℓ
TTT	2.1M-U	赤沈	8mm/hr
ZTT	8.6K-U	心電図	異常なし
		胸部X線像	異常なし

表2　皮内反応（症例1）

抗　　原	希釈倍数	発　赤	膨　疹
エ　　ビ	1,000×	25×24	11×10
カ　　ニ	1,000×	21×20	9×8
イ　ワ　シ	1,000×	9×7	4×3
ハウスダスト	1,000×	20×18	9×9
アルテルナリア	1,000×	14×12	7×7
ペニシリウム	10,000×	10×8	6×6
クラドスポリウム	10,000×	9×7	3×3
アスペルギルス	10,000×	11×10	5×5
カ　ン　ジ　ダ	10,000×	16×15	8×7

表3　エビエキスによる閾値検査

希釈倍数	発　赤	膨　疹
10,000×	22×21	10×10
100,000×	20×19	9×9
1,000,000×	16×14	7×6

表4　IgE RAST

抗　　原	スコア
エ　　ビ	3
カ　　ニ	1
ハウスダスト1	0
ハウスダスト2	0
コナヒョウダニ	1
ヤケヒョウダニ	0
カンジダ	0
ペニシリウム	0
クラドスポリウム	0
アスペルギルス	0
アルテルナリア	0

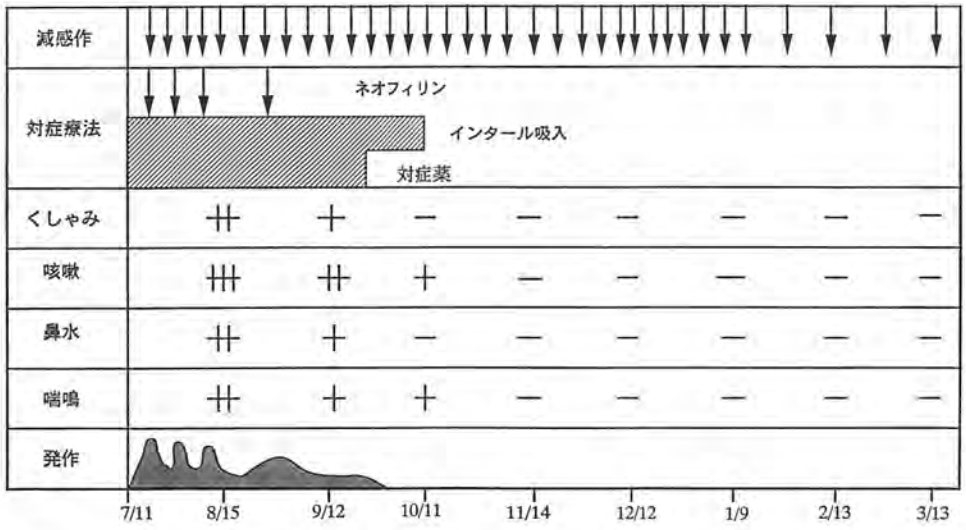

図1　エビエキスによる特異的減感作療法の経過（症例1）

既往歴：特記すべき疾患なし

主訴：喘鳴を伴う発作性呼吸困難

現病歴：平成4年6月より干エビ製造作業を行ってから約1年後より鼻水、咳嗽などの感冒様症状を訴えるようになり、さらに1年後の10月21日に作業中に呼吸困難発作を起こして当院受診した。本症例は症例1とは他の作業場で働いていたが、作業内容は全く同じで、作業と喘息発作との関係も認められた。

来院時現症：咳嗽、喘鳴を訴え、胸部に乾性ラ音を聴取した以外、理学的に身体各部に異常所見は認められなかった。

一般検査成績：表5に示したごとく、末梢血好酸球12.6％と増加し、免疫グロブリン血清IgE値が3164IU/mlと上昇を示した以外には胸部X線像に異常なく、心電図正常範囲、血清蛋白分画、肝機能検査、血清電解質などはいずれも正常値であった。

アレルギー学的検査成績

1　皮内反応

本症例における皮内反応は表6に示したごとく、エビ、カニ、ハウスダストエキス1,000倍希釈液で陽性を示したが、他のアレルゲンエキスではすべて陰性であった。

2　エビエキスによる閾値検査

エビエキスによる皮内反応陽性閾値検査を行ったところ表7に示すごとく100万倍を示した。

3　IgE RAST

表8に示すごとく、エビでクラス4、カニでクラス3、ヤケヒョウダニでクラス2、コナヒヨウダニとハウスダスト1でクラス1を示した以外はすべてクラス0であった。

職場におけるピークフロー値の変動

患者にピークフローメーターを職場に持って行かせて、就業前後を測定させたところ、就業20分でピークフロー値35％の減少を認めたので、本喘息は即時型の職業性喘息と診断された。

特異的減感作療法の治療成績

以上の検査成績により本喘息もエビ粉に起因する職業性喘息と判明したのであるが、第1症例と同様抗原回避の対策が困難であったので、エビエキスによる特異的減感作療法を実施し

た。

図2に示すように、型のごとく実施したところ、当初は対症剤、インタール吸入を併用していたが、開始後6週より軽快し始め、12週で対症例、インタールを中止しても喘息発作は起こらなくなり、現在維持療法を行って作業継続しているところである。

考　察

近年、一定の職業に従事することによって発症する職業性アレルギー疾患が注目され、とくに気管支喘息については職業との関連を重視したアレルゲンの検索が広く行われるようになり、その結果、種々の職業性喘息が報告されるに至っている。その中で水産業に関するものは、広島のカキの打ち子に発症するホヤ喘息[1)～3)]が有名であるが、筆者もかって真珠養殖作業員に発生したホヤ喘息[5)]、水産業加工従業者のイワシ粉に起因する職業性喘息[6)]を報告した。

本喘息は2例とも水産加工の干エビ製造従業者で、作業中に喘息症状が誘発されたので職業性喘息と考えアレルギー学的検索を行ったところ、エビ粉の吸入により感作されて発症した職業性喘息と診断されたのであるが、2例ともエビによる喘息の経口的発症はみられなかった。なおアレルギー反応では2例ともエビエキスの他にカニエキスにも抗原性示したが、この理由としては、漁網に入っているエビの他に小ガニが混在していて、それを一緒に熱風乾燥、脱穀するので、エビ粉の中にカニ粉が混在するために、カニ粉にも感作されたものと考えられた。

表5　一般血液検査成績（症例2）

血液検査		血清電解質	
赤血球数	473×10⁴/μℓ	Na	136mEq/ℓ
血色素量	12.8g/dℓ	K	4.7mEq/ℓ
白血球数	6400/μℓ	Cl	106mEq/ℓ
ヘマトクリット	46.2%	Ca	9.2mEq/ℓ
白血球百分率（%）		血清蛋白分画（%）	
好中球	60.4	アルブミン	64.5
好酸球	12.6	α1-グロブリン	2.7
好塩基球	0.6	α2-グロブリン	8.3
単球	8.1	β-グロブリン	6.3
リンパ球	28.3	γ-グロブリン	18.2
生化学検査		免疫グロブリン	
血清総蛋白	7.6g/dℓ	IgG	1868mg/dℓ
総ビリルビン	0.5mg/dℓ	IgM	92mg/dℓ
総コレステロール	176mg/dℓ	IgA	225mg/dℓ
GOT	19U/ℓ	IgE	3164IU/mℓ
GPT	18U/ℓ	その他	
ALP	3.4K-A-U	RA	(−)
LDH	324U/ℓ	CRP	(−)
γ-GPT	31U/ℓ	ASO	126u/mℓ
TTT	2.8M-U	赤沈	7mm/hr
ZTT	8.7K-U	心電図	異常なし
		胸部X線像	異常なし

表6　皮内反応（症例2）

抗　原	希釈倍数	発　赤	膨　疹
エ　ビ	1,000×	30×29	14×13
カ　ニ	1,000×	23×22	11×10
イ　ワ　シ	1,000×	8×7	4×4
ハウスダスト	1,000×	22×21	10×10
アルテルナリア	1,000×	13×13	7×7
ペニシリウム	10,000×	10×9	6×6
クラドスポリウム	10,000×	8×7	4×4
アスペルギルス	10,000×	12×12	6×6
カ　ン　ジ　ダ	10,000×	15×15	7×7

表7　エビエキスによる閾値検査

希釈倍数	発　赤	膨　疹
10,000×	26×24	12×12
100,000×	22×21	11×9
1,000,000×	20×19	9×9
10,000,000×	14×14	7×6

表8　IgE RAST

抗　原	スコア
エ　ビ	4
カ　ニ	3
ハウスダスト1	1
ハウスダスト2	0
コナヒョウダニ	1
ヤケヒョウダニ	2
カンジダ	0
ペニシリウム	0
クラドスポリウム	0
アスペルギルス	0
アルテルナリア	0

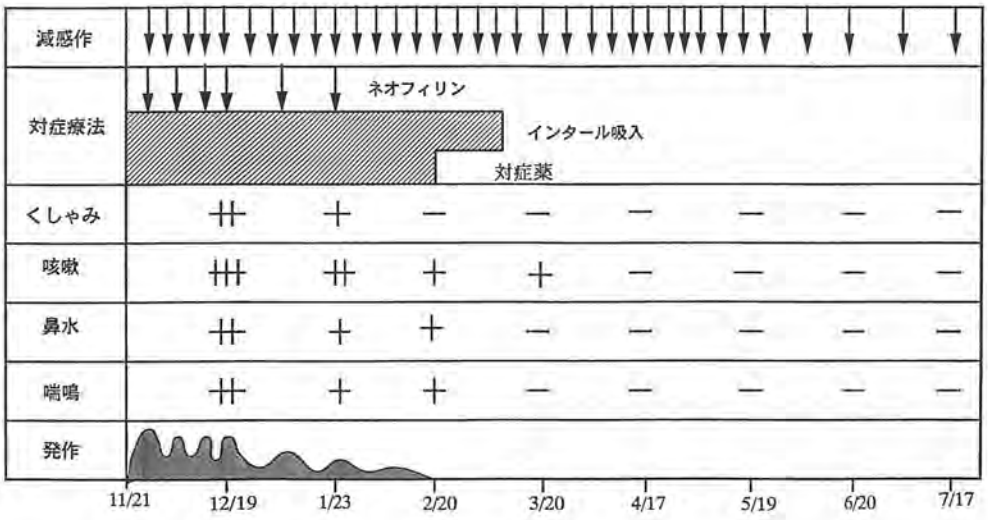

図1　エビエキスによる特異的減感作療法の経過（症例2）

本喘息患者は2例とも抗原からの回避が困難であったし、作業継続を希望するのでエビエキスによる特異的減感作療法を実施したところ奏功した。

職業性喘息は発症に複雑な諸因子の介入が少なく、アレルギーの型としては1型の外因性喘息が多いために、特異的減感作療法が奏功したものと考えられる。

これまで報告された職業性喘息の魚介類の中には、エビを抗原としたものは見あたらないようなので、興味ある症例と考え報告した。

おわりに

職業性喘息は中小ないし零細企業、家庭内労働という産業医や衛生管理者のいない状況下で発生することが多いと言われているが、この度筆者の経験した職業性喘息は従業者が20人程度の小企業であった。したがって、抗原の除去回避のための措置や、作業環境の整備などの予防対策は困難であった。職業性喘息は予防が第一であるのに、零細な作業場まで管理が及ばないようである。

現在社会における技術革新や産業構造の変化に伴い、職場には日々新たな抗原物質が導入され、新種の職業性喘息の発生も予想されるので、この疾患に対する発見と解明への努力、さらに予防の対策と治療が要求されるところである。

本論文の要旨は第6回日本職業アレルギー学会において発表した。

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Occupational asthma causes by inhalation of dried shrimp powder in a marine products factory.

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Takamoto clinic

Two patients engaged in a marine products factory who suffered from asthma with dried shrimp as antigen were found by some allergological investigations and treatment in this report.

The other one was a 55 year old female and the was a 52 year old female. They developed asthma about a few years after they engaged in the factory. Both patients were inhaling a lot of power of dried shrimp while working. On allergological tests, their serum level of IgE were indicated to have raisen and IgE RAST to shrimp and crab were found to be positive. The intracutaneous allergic reactions were demonstrated to be positive in respect of shrimp powder extract. Therefore it was assumed that their attack of asthma could be caused by inhalation of shrimp powder. They reacted very well to the specific desentization treatment.

Two cases are reported here as it assumed that patients who were engaged in a marine products factory had been sentitized with shrimp.

Pigeon breeder's lung in a heavy smoker

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ABSTRACT

The patient, a 47 year-old woman, was admitted due to marked hypoxemia and diffuse ground glass appearance in chest roentgenography. Laboratory data showed inflammatory change and lung biopsy specimen showed marked alveolitis. She recovered from clinical symptoms such as fever, coldness, cough and dyspnea with no therapy. When she returned home, these symptoms recurred immediately. Her husband began keeping pigeons ten years before her admission, and had about 300 pigeons. Therefore, the diagnosis of hypersensitivity pneumonitis, specifically pigeon breeder's lung was made. Although smoking is considered to suppress occurrence of hypersensitivity pneumonitis, this patient was a heavy smoker. Reported cases of hypersensitivity pneumonitis in a smoker without stopping smoking are rare.

Key Words: Pigeon breeder, a heavy smoker, hypersensitivity pneumonitis

INTRODUCTION

Hypersensitivity pneumonitis is a diffuse interstitial lung disease caused by inhaled antigens, such as spores of fungi and bird droppings. Pigeon breeder's lung is a hypersensitivity pneumonitis caused by inhalation of pigeon droppings. In Mexico pigeon breeder's lung is the most common interstitial lung disease, it is very rare in Japan[1-3]. We describe a 47-year-old woman, a smoker, who developed subacute hypersensitivity pneumonitis 10 years after her husband began breeding pigeons.

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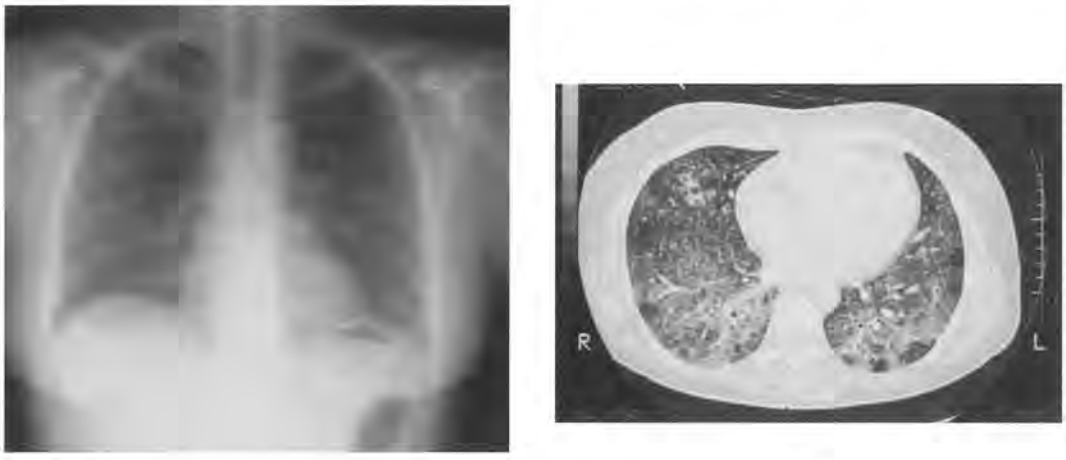
CASE REPORT

A 47-year-old woman was transferred to our hospital due to marked hypoxemia (PaO_2 36.3Torr) and diffuse ground glass appearance in chest roentgenography. Her husband began keeping pigeons 10 years before her admission, and had about

300 pigeons. Breeding pigeons was her husband's hobby, and she rarely entered the pigeon house. However, the pigeon house was next to her house, pigeon feathers often came into her house. The patient smoked about 20 cigarettes a day since 20 years of age.

She noted coldness and an increased fever six months before admission. Dry cough and dyspnea developed two months before admission. Since her dry cough and dyspnea worsened, she was admitted to another hospital. On the admission, her body temperature was 38.0℃ and arterial blood gas analysis showed marked hypoxemia (PaO_2 36.3Torr) and normocapnea. Chest roentgenography showed diffuse ground glass appearance (lower lung field dominant). She was diagnosed as having pneumonia and was treated with antibiotics. Her symptoms improved slightly within one week. The chest roentgenographic and CT findings were different from usual pneumonia, so she was transferred to our hospital for a complete of investigation. When she was admitted to our hospital, she complained of dyspnea and dry cough. Fine crackles were heard in both lungs, and marked erythema on her face and neck was observed. Laboratory data are shown in Table 1. Inflammatory change and slight liver dysfunction were detected. There was no evidence of autoimmune disease in the general status or serological test. Chest roentgenography showed diffuse ground glass appearance in the lower lung field of both sides (Fig 1A). However, the condition was slightly improved compared with that demonstrated in previous hospital. Chest CT findings showed ground glass appearance with geographic deviation (Fig 1B). Arterial blood gas analysis showed marked hypoxemia (Table 1). Pulmonary function test showed diffusion disorder pattern (Table 2).



(A) (B)

Fig. 1 Chest roentgenography (A) and chest CT (B): When the patient was admitted to our hospital, roentgenography and CT showed diffuse ground glass appearance.

Bronchoalveolar lavage fluids (BALF) were analyzed (Table 3). The total cell count obtained from BALF increased and many lymphoid cells were seen. T cell subset CD4/8 in BALF was higher than the normal upper limit. Pigeon dropping antibody in BALF was weakly positive. Transbronchial lung biopsy was performed and the specimen showed alveolitis that involved thickening and inflammatory cellular infiltration in alveoli (Fig 2). There was no evidence of fibrosis or granuloma. These findings suggested that this disease was compatible with hypersensitivity pneumonitis. Therefore, the patient was observed with no therapy and her symptoms, chest roentgenographic findings and arterial blood gas slowly

Table 1. Laboratory data of the subject

WBC	3100/μℓ	CRP	0.3 mg/dℓ
(Neu)	39.1 %	ESR	60 mm/h
(Lym)	48.2 %		
RBC	446×10⁴/μℓ	RF	(-)
Hb	14.4 g/dℓ	ANA	(-)
Ht	49.2 %	Anti Sm Ab	(-)
Plt	31.1×10⁴/μℓ	Anti SS-A Ab	(-)
		Anti SS-B Ab	(-)
TP	7.5 g/dℓ	Anti RNP Ab	(-)
Alb	4.2 g/dℓ	Anti Scl 70 Ab	(-)
LDH	534 IU/ℓ		
GOT	36 IU/ℓ	pH	7.49
GPT	42 IU/ℓ	$PaCO_2$	35.5 Torr
CK	17 IU/ℓ	PaO_2	48.9 Torr
BUN	12 mg/dℓ	HCO_3	26.1 mEq/ℓ
Cr	0.5 mg/dℓ	SaO_2	87.7 %
Na	139 mEq/ℓ		(O_2 1ℓ /min)
K	4.3 Eq/ℓ		
Cl	104 Eq/ℓ		

Table 2. Pulmonary function test

VC	1.95 ℓ
%VC	73.3 %
FEV1.0	1.62 ℓ
FEV1.0%	87.6 %
%DLCO	58.3 %

Table 3. Analysis of bronchoalveolar lavage fluids

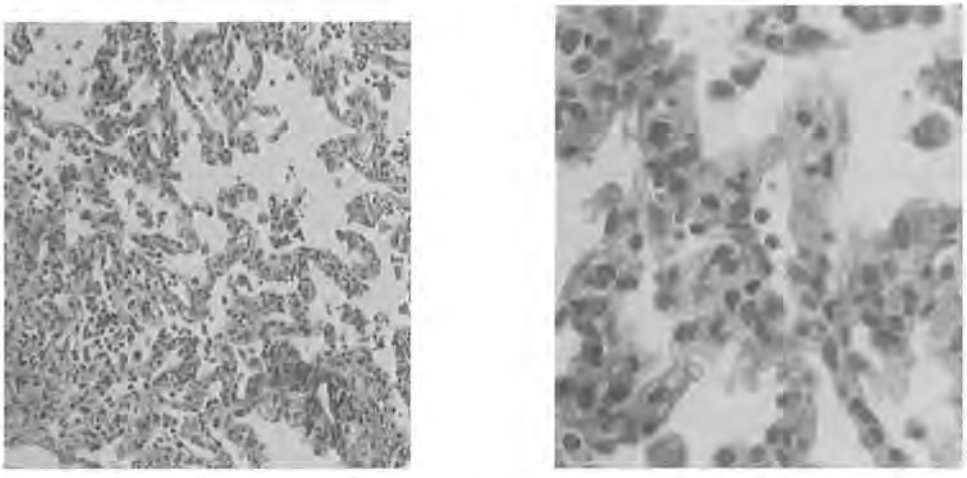
Recovery rate	63.3 %
Cell count	6.4×10⁵/mℓ BALF
(Lymph)	70.7 %
(eos)	12.4 %
CD 4/8	2.64

improved. The antigen exposure test at her house was performed. When she returned home, she noted coldness, dyspnea and an increased fever. She returned to the hospital and arterial blood gas analysis showed reduction of PaO_2, and increased inflammatory markers such as CRP and WBC. The result of antigen exposure test and the fact that her husband kept many pigeons close to their house support that her disease was pigeon breeder's lung. Despite escaping from the antigen about one month after antigen exposure test, recovery of clinical findings (symptom, chest roentgenography, etc.) was very slow. Therefore oral steroidal treatment (30 mg/day of prednisolone) was started. After one month of therapy, the symptoms markedly improved and ground glass appearance on chest roentgenography and CT disappeared (Fig 3). Her husband disposed of the pigeons, and she was discharged three months after her admission.

DISCUSSION

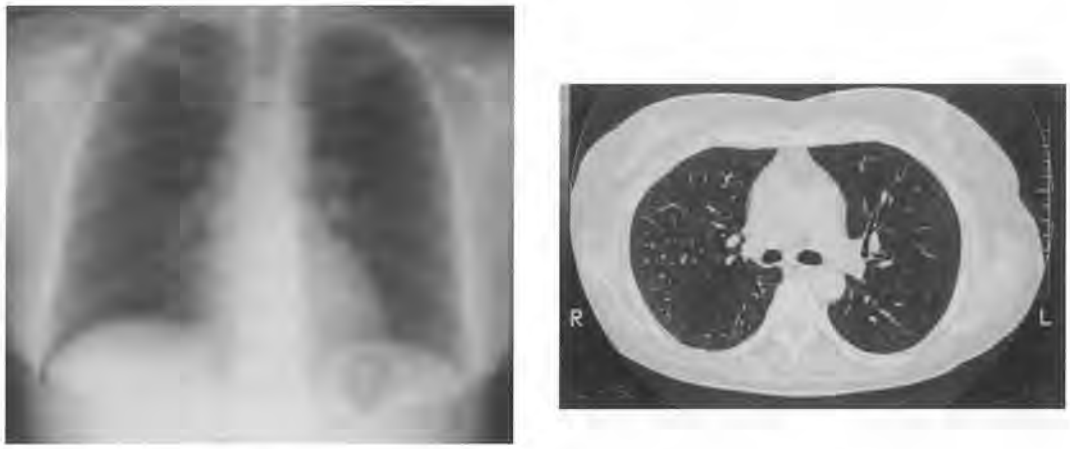
Hypersensitivity pneumonitis, also known as extrinsic allergic alveolitis, is an interstitial lung disease caused by type III or type IV allergic reaction to inhaled antigens such as fungi, bird droppings, bacteria and chemical substances. Pigeon breeder's lung is caused by IgA contained in the faeces or feathers of pigeons, and it is a very rare disease in Japan.

Our patient initially noted increased fever and coldness and noted cough and dyspnea. In patients with pigeon breeder's lung, as in all types of hypersensitivity pneumonitis, increased fever, dry cough and dyspnea are the main clinical symptoms[3]. Clinical symptoms in this patient were compatible with hypersensitivity pneumonitis. Ground glass appearance shown by chest roentgeno-



(A) (B)

Fig. 2 Photomicrographs (H-E stain, A; X100, B; X400) of lung biopsy material obtaine by transbronchial lung biopsy, showing lymphocytic infiltration and edematous thickening of alveolar septa.



(A) (B)

Fig. 3 Chest roentgenography (A) and chest CT (B) after oral steroidal therapy: The ground glass appearance was completely reduced by oral steroidal therapy.

graphy and chest CT also indicated hypersensitivity pneumonitis. However the pathological findings were not typical for hypersensitivity pneumonitis because in TBLB, alveolitis was detected but Masson body and granuloma which are considered as features of hypersensitivity pneumonitis were not found. But this patient recovered from clinical symptoms such as fever, coldness, cough and dyspnea without therapy. When she returned home, these symptoms recurred immediately. Clinical course was typical acute or subacute hypersensitivity pneumonitis. Granulomatous lesions in hypersensitivity pneumonitis are not so often detected in the acute phase. Because the disease phase in this patient progressed relatively acutely, it was assumed that Masson body and granulomatous lesions could not be detected. In addition, eruptions appeared on her face on admission. We did not perform a skin biopsy, so we could not determine whether these eruptions were associated with the antigen exposure. However, we suspected that they were related to hypersensitivity pneumonitis because the eruptions gradually disappeared by avoiding antigen exposure. Because hypersensitivity pneumonitis is caused by type III or type IV allergic reaction to inhaled antigens, it is precious to find the specific antigen. To find the specific antigen, some immunological tests are available, like precipitins to pigeon products. In this patient, pigeon dropping antibody in BALF was weakly positive. Although *Trichosporon cutaneum* antibody test was not performed, her CD4/8 ratio was higher than normal upper limit and her hypersensitivity pneumonitis occurred in winter. These facts indicated that this hypersensitivity pneumonitis was not summer type hypersensitivity pneumonitis. We estimated that pigeon droppings were related to occurrence at her hypersensitivity pneumonitis, because she lived under the circumstance of

pigeon dropping exposure during about 10 years.

This patient was a heavy smoker, while smoking is considered to reduce the occurrence of hypersensitivity pneumonitis in general. Some clinical and animal experimental data showed that cigarette smoking reduced the levels of specific antibody for some inhaled specific antigens, like spores of *T. cutaneum*, pigeon droppings[4-7]. These data suggest that cigarette smoking reduces the ability for antibody production. In addition, because the numbers of alveolar macrophages, their levels of superoxide production, and phagocytosis were markedly increased in smokers, it is considered that the clearance of inhaled antigen in smoker is more enhanced than that of non-smokers[8]. Cigarette smoking is thought to reduce the occurrence of hypersensitivity pneumonitis through these mechanisms. On the other hand, it is known that injury in alveolar and airway epitheliums by cigarette smoking or viral infection induces the absorption of the inhaled antigen, and systemic sensitization to the antigen is apt to be established.[9-11] The mechanisms of reduction of the hypersensitivity pneumonitis-occurrence by cigarette smoking still have remained unclear. In this patient, the levels of pigeon dropping antibody in BALF and serum were weakly positive, while hypersensitivity pneumonitis occurred. One possibility is that cytokines produced by macrophages and T lymphocytes, played a major role in the occurrence of her hypersensitivity pneumonitis. It is the fact that activated macrophages produce various cytokines, such as Interleukin-1, that is produced by activated macrophage and is known to mediate granuloma reaction. Recent study revealed that interferon-γ is necessary for the expression of hypersensitivity pneumonitis[12]. It is possible that cytokines produced by activated macrophages and T lymphocytes induced inflammatory reaction in lung without the influence of immune complex. Second possibility is that minor doses antibody reacts to pigeon droppings and caused hypersensitivity pneumonitis occurrence. It is possible that the immune complex produced by antigen antibody reaction in the minor doses adhere to lung and strongly activate complement factors or several cytokines, which cause inflammation in lung.

In general, the exposure time to the antigen and the amount of inhaled antigen are thought to be the major factors for the occurrence of hypersensitivity pneumonitis. Furthermore, hypersensitivity pneumonitis may be caused by the complicated association of many factors such as genetic background of the host[13], the characteristics of the antigen, and other modified factor like smoking.

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