

Studies of prevalence of Japanese cedar pollinosis among the residents in a densely cultivated area

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Prevalence studies of Japanese cedar pollinosis in densely planted areas were performed using pollen counts, patient studies, and population surveys with questionnaires. The incidence of pollinosis was increased and appeared to be related to dispersed pollen, which resulted in high immunologic responses. Onset of symptoms was influenced by hereditary factors as well as pollution from automobile exhausts.

INTRODUCTION

Japanese cedar (*Cryptomeria japonica*) is one of the important sources of lumber for construction. Its cultivation is therefore popular throughout Japan, especially on mountains. Airborne pollen of this tree is the main cause of pollinosis in Japan. Since pollinosis was first reported by Horiguchi and Saito,¹ this cedar has become a focus of interest among Japanese, and researchers have investigated it from the clinical,^{2,3} aerobiologic,^{4,5} and immunologic^{6,7} aspects. Recently, Koizumi et al⁸ reported an adjuvant effect of car exhausts on specific IgE production in mice.

Horiguchi and Saito³ and Furuuchi⁹ have reported the main symptoms of allergy to Japanese cedar to be sneezing, rhinorrhea, nasal obstruction, anosmia, conjunctivitis, hyperlacrimation, itching of nose and eyes, dermatitis, throat irritation and cough and fever due to inflammation.

Geographic areas of pollination in Japan have been published by Nagano et al¹⁰ from which the period of Japanese cedar pollinosis is known. These studies show that the prime pollination period of Japanese cedar is February and March in Tokyo, and March through April

in the Nikko-Imaichi district. Epidemiologic research has been limited only to hospitalized or ambulatory patients. The present report is a population study on Japanese cedar pollinosis (Jap. CP) in the Nikko-Imaichi district. This district includes mountains and plain areas covered with Japanese cedar forests, city and farming areas with poor plantation or the complete absence of these trees, and three inter-city roads densely lined with Japanese cedars greater than 300 years in age. This report examines quantitative aspects of related pollinosis in a group of patients studied at a local general hospital in Nikko and Dokkyo University Hospital, and a population survey on Jap. CP by a questionnaire in 1984.

SUBJECTS AND METHODS

Pollen Counting by Gravity Sampler

Durham samplers were used under standard conditions in different environments, eg, at Nikko General Hospital (city area); Imaichi Health Center (near the inter-city roads), a local clinic in the cedar forest area; Dokkyo University Hospital; one of author's home in Utsunomiya (Prefectural Capital); and Tokyo University Hospital. The period of pollen collection was February through April. Slides were collected at 9 AM every day. During this period, over

90% of fallen pollen was Japanese cedar, the remaining was white birch and others. No mold was detected. The pollen count was microscopic and expressed as the number/cm².

Clinical Study on Japanese Cedar Pollen

The patients having Jap. CP in Nikko and Dokkyo University Hospital from March through April, 1984-1985 were skin tested by the scratch method with 15 allergens (described in the results), using a serial endpoint titration response and RAST titers and subjective symptoms were also evaluated. For skin tests, Ishizaki's criteria¹² were used according to methods described previously by the Japanese Society of Allergology.

The Population Survey Through the Questionnaire

The subjects were randomly selected per familial unit from a list of total residents in the Nikko-Imaichi district (approximately 100,000). Of 817,631 families (77.2%) responded, which included 1,527 males and 1,606 females.

The questionnaire was distributed and explained thoroughly. After completion, the questionnaires were collected by local stationary health volunteers, who were educated at the Imaichi Health Center and licensed by local authorities. Most of them had previously been in-

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structed by the authors concerning the purpose of this survey and interview techniques. All individuals less than 50 years old in sampled families were generally knowledgeable on health matters and could give accurate answers to the questionnaire items.

The Questionnaire

The questionnaire is shown in Table 1. The sample group was subdivided into five sample groups according to environmental differences: (1) those families living within 200 m from main inter-city roads, which are densely lined with old cedar trees and where traffic is heavy all day long; (2) those in or near cedar forests; (3) those in the city or farming fields where cedar trees are few; and (4) those living in high land without cedars (>1000 m above sea level).

Follow-up Study to Confirm the Survey Results

There are two pathogenetic factors

important in enhancing sensitization by Japanese cedar pollen: the quantity of pollen in the air and local air pollution by automobiles. Accordingly, pollen counts were performed in different environments during April of 1985 (pollination period shifted into April). Jap. CP patients in Nikko Hospital and Dokkyo University Hospital in 1985 were tested by serial endpoint dilution skin tests and by RAST titers.

RESULTS

Pollen Counts of Japanese Cedar in the Nikko-Imaichi District

The pollination period of Japanese cedar previously was in March and April in the Tochigi prefecture. Japanese cedar is the main pollen during this period (over 90%). The quantitative pollen counts and the pollination period, however, have shifted each year. Accordingly, the

extremely high samples in 1976 (maximum) and low samples in 1982 (minimum) occur at two places (Nikko and Utsunomiya) (Fig 1). The curves of daily pollen counts were markedly high in Nikko in both years with the highest periods in the middle of March. The Nikko-Imaichi district is one of the most pollinated areas while Utsunomiya and Dokkyo University Hospital, located far from this area, and have poor cultivation density of Japanese cedar.

Clinical Features of Japanese Cedar Pollen

Ishizaki¹³ reported clinical features of 147 cases of pollinosis during 1984-1985. These patients were tested with pollen allergens including three animal danders and four airborne molds via the scratch method.

As can be seen in Fig 2, the highest incidence was in March in Tokyo (45 cases). Seventy-three percent of patients in this month were afflicted by Jap. CP. From March through April in 1985, 153 cases of pollinosis were reported from Nikko Hospital and 39 from the Dokkyo University Hospital. All cases in both hospitals received scratch tests with various allergens. The results

Table 1. QUESTIONNAIRE on Jap. C. Pollinosis

Section or street: Segawa

Householder: N.K.

1, May, 1984

Inquiries	House holder	1	2	3	4	5	6
Sex	♂ f	m ♂	♂ f	m ♂	♂ f	m ♂	♂ f
Age	55	53	28	26	2	76	23
Family relation	wife	son	son's wife	grand son	Mother	Employee	
Suffering Period							
February							
first decade						○	
middle d.						○	
last d.	○					○	
March							
first d.	○			○		○	
middle d.	○		○	○			
last d.	○		○	○			
April							
first d.	○		○	○		○	
middle d.	○		○	○		○	
last d.			○	○			○
Nasal Symptoms							
Sneezing	○			○		○	
Rhinorrhea	○			○			○
Nasal obstruction	○			○			○
Itching or Pain	○		○				
Cough			○				
Eye Symptoms							
Redness of Eye				○			○
Eye Mucus							
Tear Secretion	○						
Dazzling			○				
Itching	○						
Throat							
Redness of Throat			○				
Pain	○						
Others							
Allergic History				○		○	
Asthma						○	
Urticaria	○						
Dermatitis			○				
Remarks							

Through year

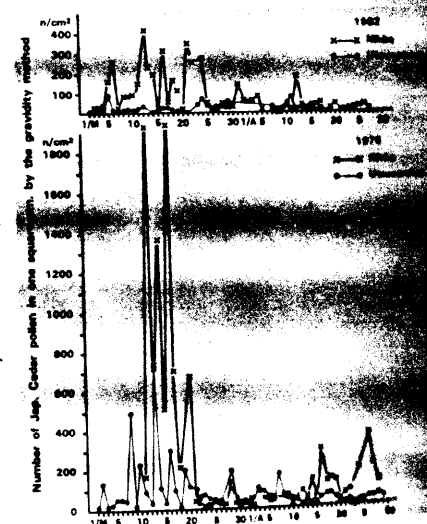


Figure 1. Pollen counting of Japanese cedar in March and April at Nikko and Utsunomiya (Prefectural Capital).

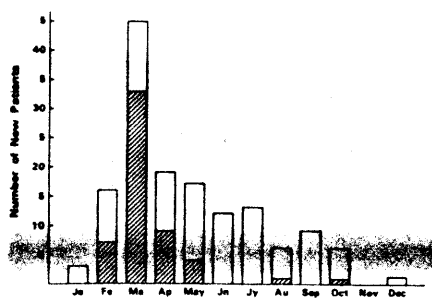


Figure 2. Distribution of new patients of pollinosis per month at an eye clinic in Tokyo in 1984-85 (147 cases in total).

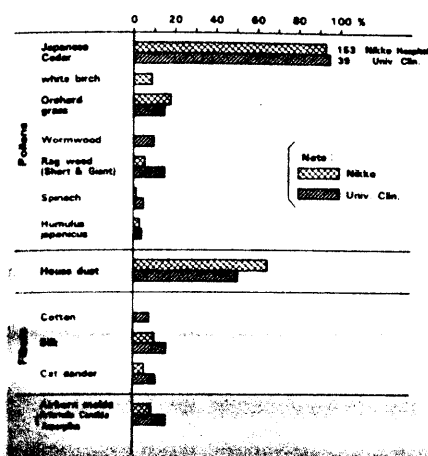


Figure 3. Incidences of positive reaction by various allergens in the patients of pollinosis in February-April.

are summarized in Fig 3. Although they responded to various allergens, 95% of them were positive to Japanese cedar pollen, while the rates to others remained low except house dust (about 60%). Jap. CP patients showed their symptoms up to the end of April, so that Jap. CP is considered the main pollen in March through April in the Nikko-Imaichi district.

Population Survey Through the Questionnaire

Analysis of subjected groups on sexes and age differences. As is shown in the upper panel of Fig 4, the numbers of both sexes are almost the same. There is no difference in age distributions between them. In the lower panel of Fig 4, the age distribution in five different environments are listed. There was

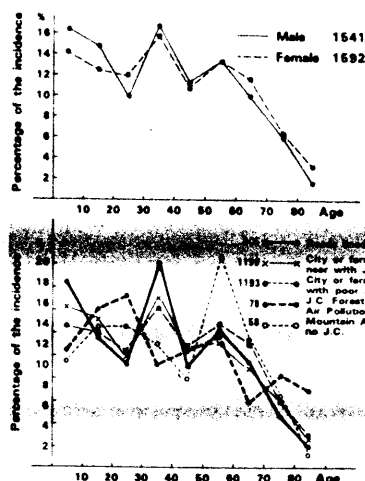


Figure 4. Age and sex distributions of the subjected people per different environments.

the same tendency in age distributions among four groups, except in the mountain-resident group that had more older people. With those results, a comparison of these incidences of Jap. CP between different environments (without any correction) is possible.

Criteria for selecting actual cases of pollinosis due to Japanese cedar pollen. The survey via the questionnaire has only one short coming and that was that all the possible symptoms were assigned to the Jap. CP group when a subject had not been examined clinically. To avoid this, strict criteria for the determination of this pollinosis were adopted, ie, patients complaining of three nasal symptoms (ie, sneezing, rhinorrhea, and nasal obstruction) or of three eye symptoms (ie, redness of eye, hyperlacrimation, and itching of eye) during the pollination period of March and April which were classified into the Jap. CP group. Others who had seasonal or perennial complaining of nasal or ocular symptoms were assigned to an undefined symptom group. A remarkable difference was detected as shown in Fig 5. The age distribution of Jap. CP was mainly located in the younger age groups, under 40 years old. On the other hand, that of the undefined group, over 15 years old continues almost at the same level regardless of the

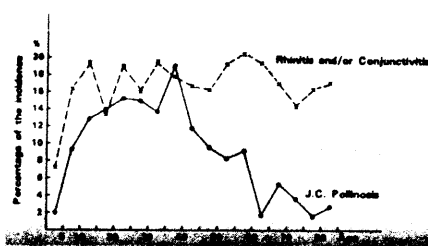


Figure 5. Age distribution of incidences of Japanese cedar pollinosis compared with that of undefined symptom group (rhinitis and/or conjunctivitis).

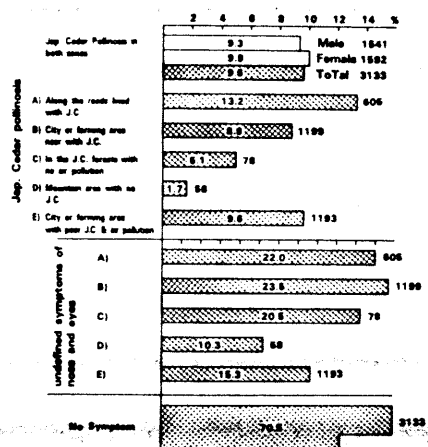


Figure 6. Incidences of Japanese cedar pollinosis and undefined symptoms among the residents in different environments.

age. In both figures, incidences under 10 years old were at a low level. Accordingly, criteria for detecting actual cases of Jap. CP appear to be reasonable.

Comparison of incidences of Japanese cedar pollinosis in different environments. A summary of incidences for different sexes and environments is shown in Fig 6. Shown on the left of this figure are characteristics of the incidence rates (%) in different environments. Also shown in this figure in the upper half are data related to Jap. CP and in the lower half, data from an undefined group, the group with no discernible symptoms. As can be seen in Fig 6, the incidence of Jap. CP is 9.6% of the total population (3,133) and no differences between sexes were seen. Among Jap. CP (A) the incidence is the highest, ie,

13.2% among residents located contiguous to the inter-city roads where old cedar trees are prevalent; (B) those in the city and farming areas near the forests, 8.8%; (C) those in the forests with no traffic remains at 5.1%; and (D) those in the mountains with no cedar trees (over 1,000 m above sea level) is 1.7%. The differences in incidences above listed are all significant statistically by χ square test ($P < .01$ to $.05$). (E) But the incidence of those who live in the city and farming areas with poor concentrations of cedar trees was 9.6%, nearly the same as in (B).

The incidence in the undefined group varied with a different pollen pattern. It was almost identical in groups A, B, and C. It was lowest in D and a median value in E. The reason(s) for these differences could be attributed to various causes ie, other pollens, coincidental to upper respiratory tract infection, as well as other factors.

It should be also noticed that 70.5% of the whole subject population was free of Jap. CP and other undefined symptoms. This could be attributed to the absence of sensitization by Jap. CP.

The age of onset of Japanese cedar pollinosis related to hereditary factors. All subjects under 10 years of age were divided into two groups: those whose parents suffered from nasal and ocular symptoms and those not suffering from these symptoms.

The Jap. CP incidence per each age is shown in Fig 7. Children under 3 years were free from Jap. CP regardless of parents' symptomatology. Those having parents with no symptoms are almost free from this pollinosis up to 6 years of age. Those having parents suffering from Jap. CP beyond 3 years of age showed increases commensurate with their age. In total, the incidence of Jap. CP among children with parents having symptoms was 12.3% (14/114) while the incidence of those patients having parents with no symptoms was only 3% (4/129).

These differences were statistically significant by χ square test ($P < .01$). A second analysis was performed to evaluate the possible role of hereditary factors.

The parents-child relationship of Jap. CP was evaluated in the following studies in all subjects. The total number evaluated up was 1,318. The incidence of Jap. CP among those having parents with symptoms was found to be as high as 16.2% (100/617), while those from parents with no symptoms was 6.1% (43/701). These differences were statistically significant by χ square test ($P < .01$). Accordingly, a hereditary factor appears to be important for the onset of Jap. CP.

Comparison of symptoms of Japanese cedar pollen from the survey results and patients statistics. In this

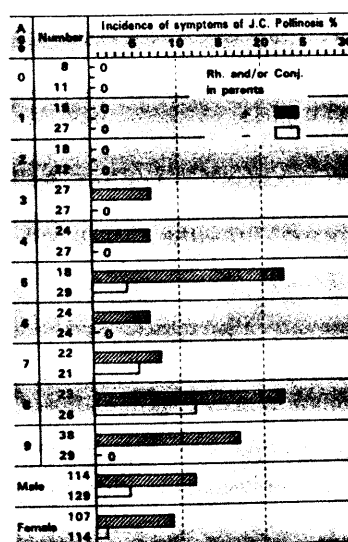


Figure 7. Parent-child relationship on the onset of symptoms.

Table 2. Incidences of each symptom among Jap. C. Pollinosis

	Questionnaire Analysis			Patients statistics in Univ. Clinic
	Male 138	Female 165	Total 303	Total 525
Sneezing	90.6%	87.3%	88.8%	88.6%
Rhinorrhea	98.1%	85.5%	87.1%	81.9%
Nasal obstruction	81.2%	76.4%	78.5%	70.5%
Itching or Pain	44.9%	41.2%	42.9%	56.2%
Cough	25.4%	32.7%	29.4%	22.9%
Redness of eye	46.4%	40.0%	42.9%	31.4%
Eye mucus	36.2%	29.1%	32.3%	16.4%
Tear Secretion	51.4%	56.4%	54.1%	34.3%
Dazzling	26.8%	30.3%	28.7%	never asked
Itching	73.2%	78.2%	75.9%	81.9%

survey, three major nasal and/or eye symptoms were used as diagnostic criteria for the detection of Jap. CP. Since such patients were mainly detected by these three nasal symptoms, these nasal responses are mostly positive as shown in Table 2. Those are getting only through the questionnaire, so that their incidences should be compared with the patient statistics in Dokkyo University Hospital.

The number of Jap. CP cases detected was 303 from the survey and 525 from the University Hospital. The symptoms are sneezing, rhinorrhea, nasal obstruction, itching or pain of nose, cough, redness of eye, eye mucus, tear hypersecretion, dazzling, and itching of eye. The incidences in both groups concerning nose are quite similar to each other, and eye symptoms are similar in both groups. From this table, the main symptoms of Jap. CP are sneezing, rhinorrhea, nasal obstruction, and itching of eye although other symptoms are also of importance.

Follow-up Studies for Confirming the Survey Results

There are several findings from the survey, but those findings should be confirmed by further research. Accordingly, two studies were performed during the pollination period in 1985 in the Nikko-Imaichi district and others.

Daily pollen counts at different environments in April 1-20, 1985. In 1985, the pollination period in the subjected district was shifted April so that daily pollen counting

was done in April at different sites: (A) Imaichi Health Center, located alongside the inter-city main roads with old Jap. cedar trees; (B) Nikko General Hospital in the city area near the forests; (C) a local clinic, located in the forest area with no traffic air pollution; and (D) Tokyo University Hospital with no cedar trees.

All curves of daily pollen counts in the four places are listed in Fig 8. Those curves are different from each other. The quantity of pollen on the slide was at markedly high levels (1,000 to 3,000 per cm² in a day) in both (A) and (C), while pollen counts decreased to a lower level in (B) and remain at the smallest level in (D).

No differences were detected in pollination between the forest area and the region with contiguous road-side cedar trees, even though there were marked differences in the incidence rates of Jap. CP. This may suggest that a second factor enhancing sensitization by the pollen might exist.

Comparative study on Japanese cedar pollen in Nikko Hospital and Dokkyo University Hospital. Patients with Jap. CP at Nikko Hospital and Dokkyo University Hospital in 1985 were tested by RAST titers to Japanese Cedar pollen and by endpoint serial dilution skin tests using Japanese cedar pollen allergen injected intradermally. Fig 9 shows a difference of the endpoint curves between Nikko Hospital (80) cases and University Hospital (57 cases) in February through April, 1985.

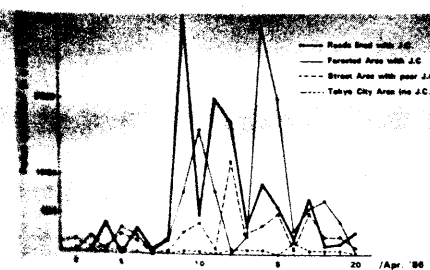


Figure 8. Daily pollen counts of Japanese cedar during April 1 to 20, 1985 in different areas.

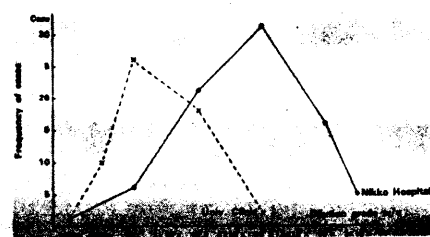


Figure 9. Distributions of endpoints of intradermal skin test of Japanese cedar pollen among patients in Nikko Hospital (80 cases) and in the University Clinic during the season March and April (57 cases) in 1985.

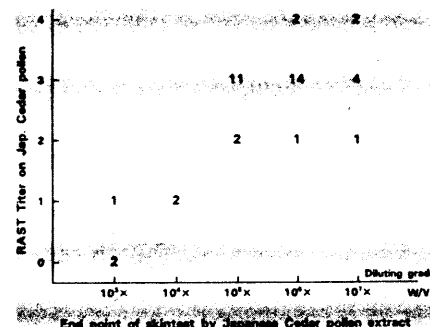


Figure 10. Correlation between RAST titer and endpoint on Japanese cedar pollen allergen.

Serial 3-fold dilutions starting from 1000x dilutions of the allergen extracts (wt/vol) were performed. The results suggested that patients in Nikko Hospital were more highly sensitized than those in the University Hospital, because the peak dilution of Nikko Hospital was a million dilutions in contrast to that of the University Hospital, which remained at ten thousand dilutions. The ranges of the distribution of both groups were different in different areas. As can be seen in Fig 10, there was a close relationship between the RAST titer and the endpoint of skin test. Its correlation coefficient was $r = +0.725$ with significance of $P < .001$. Accordingly, the patients of Jap. CP in the subjected district appeared to be highly sensitized.

DISCUSSION

The Nikko-Imaichi district consists of mountains, forests, rice fields, and city areas. Although the former

two regions are covered densely with Japanese cedar trees, the other areas are poorly cultivated with this type of tree. Japanese cedar pollen is dispersed widely over the whole prefecture, and its quantity in the air is very high in the mountain region (less than 1,000 m above sea level), neighboring cities, and rice field areas as detected by results density.

The results of the skin test on pollinosis patients in the Nikko-Imaichi district in March and April indicate that the main causes of pollinosis is Japanese cedar pollen (over 90%) and house dust (60%). Other allergens play a relatively minor role. A population survey using a questionnaire to detect the prevalence of Jap. CP in this district appeared reasonable. Before performing this survey, previous education for health volunteers aimed at getting correct answers from sampled families also appeared to be reasonable.

The rate of families who responded was sufficient for (77.2%) two statistical analyses. The total subject number of 3,133 was also adequate for prevalence analysis.

The results of the survey indicated an incidence of Jap. CP as high as an average of 9.6%. There were no differences between sexes. The pollinosis was prevalent among younger people under 40 years of age. Environmental factors appeared to influence the incidence: the highest incidence was seen among residents alongside the inter-city main road lined with older cedar trees and having heavy automobile traffic all day long. On the other hand, residents in the cedar forest with less intense automobile traffic showed a low incidence. Pollen counts at both areas were almost identical in quantity, air pollution by automobile exhausts should be considered as an enhancing factor.

The analysis of the hereditary relationship to Jap. CP suggests that at least 3 years may be necessary for establishment of sensitization in the

children who have allergic constitution for the pollinosis.

The immunologic study on the patients in Nikko Hospital and Dokkyo University Hospital (as a control) indicated that patients in Nikko were highly sensitized by the pollen. The measurement by serial endpoint skin titration with Japanese cedar pollen are highly correlated with RAST titer of this allergen.

The results gained from the questionnaire survey showed that symptoms of Jap. CP obtained from the survey were similar to the patient statistics obtained from Dokkyo University Hospital. It may be concluded that the present studies have clarified the prevalence of Jap. CP in Nikko-Imaichi district from various aspects.

CONCLUSION

A prevalence study of Jap. CP in a highly endemic area was performed. Annual pollen counts revealed that Japanese cedar pollen was dispersed in large quantity in the air and that Jap. CP is very common in 9.6% of the population. Its main symptoms are sneezing, rhinorrhea, nasal obstruction, itching or pain of nose

and eye. Jap. CP patients in Nikko-Imaichi district are more highly sensitized than patients in the control areas. The population survey using a questionnaire methodology suggested that hereditary factor(s), air pollution, and automobile exhausts enhanced the sensitization responsible for the onset of Jap. CP. These factors were confirmed by comparison of pollen counts in different environments as well as immunologic follow-up of the patients.

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