

Process and Current Status of the Epidemiologic Studies on Cedar Pollinosis in Japan

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This paper reviews the present situation and future aspects of epidemiologic studies on Japanese cedar pollinosis. Increase of allergic rhinitis patients is observed in both the Patient Survey and the Reports on the Surveys of Social Medical Care Insurance Services, however, these surveys are conducted when cedar pollens do not pollute the air. Many have reported on the prevalence of pollinosis in limited areas but only a few nationwide epidemiologic surveys have been conducted. Most of the studies were conducted at special medical facilities such as university hospitals. There is a high possibility that patients who visit the specific facilities do not exactly represent the actual number of patients and epidemiologic pictures of pollinosis in Japan. The rapid advances in laboratory test methods may change the diagnostic criteria and increase the number of reported patients. Therefore, the prevalence of Japanese cedar pollinosis in Japan has not been determined yet. Determination of the prevalence of cedar pollinosis and description of the epidemiologic pictures constitute the essential steps toward the control of this clinical entity. Thus it is necessary to conduct an epidemiologic survey on Japanese representative samples with a standardized survey form with clear and concise diagnostic criteria.

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It has been reported recently that the number of patients suffering from allergic diseases, such as asthma, atopic dermatitis, and allergic rhinitis, is increasing in Japan¹⁻⁴⁾. The related factors supposed to have swelled after the Second World War ; the mite and house dust due to changes in housing conditions, air pollution due to the industrialization. Cedar pollen caused by forestation policies after the Second World War have been cited to explain these epidemiologic trends in particular⁵⁻¹⁰⁾.

Among the allergic conditions, pollinosis is defined as ocular and nasal symptoms that develop paroxysmally upon contact with pollens: these symptoms are seasonal and occur repeatedly each year. Clinical symptoms mainly involve the nose and eyes and consist of typical features of allergic rhinitis such as sneezing, excessive nasal secretion, nasal congestion, and intranasal itching; and those of allergic conjunctivitis symptoms such as conjunctival itching, redness, lacrimation, sensation of having foreign bodies in the eye, and photophobia^{11,12)}.

Allergic reaction to pollen was originally considered to be extremely rare in Japan. It was even believed that the disease was nonexistent in the Japanese Archipelago before the Second World War. The first case of allergy to pollen (ragweed pollinosis) was reported by Araki in 1961^{13,14)}, which was followed by the discovery of cedar pollinosis in the Nikko area of Tochigi Prefecture in 1964¹⁵⁾. During the succeeding period between 1961 and 1970, major pollen antigens, such as ragweed, cedar, grasses, Japanese hop, mugwort, and alder, were discovered^{16,17)}. Later in the 1980s, new pollen antigens, such as those found in association with certain professions, were reported¹⁸⁻²⁷⁾.

MATERIALS AND METHODS

As described above, the history of pollinosis in Japan goes back only 40 years or less. An overwhelming number of these allergy patients suffer from cedar pollinosis and an increase in

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the number of ambulatory patients has been reported throughout the country (except in Hokkaido and Okinawa). More recently there has been notably heightened public interest, culminating in activities such as forecasting the pollen count during the season when cedar pollens are rampant in the atmosphere.

In this study, we review the surveys and reports published in this country. The major reports on the statistical observations on the number of patients with pollinosis or allergic rhinitis were retrieved from CD-ROMs by Igaku Chuo Zasshi (*Japana Centra Revno Medicina*) and Medline for the literature which contained terms pollinosis as key words search of the publications. The former retrieved the literature published for the 10 years between 1987 and 1997, the latter did from 1970 to

1997. For those reports that were published prior to retrieval, we selected those that were included in the major domestic academic periodicals.

In 1979, the 9th revision to the "International Statistical Classification of Diseases, Injuries, and Causes of Death" was adopted to the Patient Surveys and Reports on the Surveys of Social Medical Care Insurance Services that are prepared by Statistics and Information Department, Minister's Secretariat of the Ministry of Health and Welfare; and as a respiratory tract disease, allergic rhinitis was included in classification (B) of the Disease Classification Table. Thus it became possible to see whether the number of patients with allergic rhinitis is on the increase in the surveys.

Table 1. Reports on the numbers of cedar pollinosis patients in Japan.

Author(s)	Publication Year	Setting	Area	Diagnostic Criteria											
				Que	IDT	Total IgE	RAST	RIST	ELISA	NPT	Eosinophil mucus	blood	X-ray	Naso scope	Other
Yanohara K, et al ²⁸⁾	1976	outpatients	Kyoto	○	○	○					○	○	○		
Arai T. ²⁹⁾	1980	outpatients	Ibaragi	○	○	○					○	○	○	○	○
Uchikoshi S, et al ³⁰⁾	1981	outpatients	Wakayama		○						○	○	○	○	
Ogino S, et al ³¹⁾	1981	outpatients	Osaka	○	○	○	○				○	○	○	○	criteria modified in halfway
Koyama K, et al ³²⁾	1983	outpatients	Aichi	○											
Hori T, Ohyama H. ³⁷⁾	1985	Agricultural Cooperative	Matsukawa, Nagano	○	○	○									
Hanada T, et al ³³⁾	1986	outpatients	Matsukawa, Nagano	○	○	○	○	○			○	○	○		criteria modified in halfway
Hori T, Ohyama H. ³⁸⁾	1986	junior high school	Matsukawa, Nagano	○		○	○								
Ishizaki T, et al ³⁹⁾	1987	general population	Nikko, Tochigi	○	○	○	○								
Saito Y, et al ³⁴⁾	1988	outpatients	Kyoto		○	○	○				○				
Kishikawa R. ⁸⁾	1990	outpatients	Fukuoka City	○											
Nakamura S. ⁴⁰⁾	1990	students and staff	Oita Univ.	○		○	○								
Baba K, et al ⁴¹⁾	1991	general population	Mibu, Tochigi	○											
MHW ⁴²⁾	1992	general population	All Japan	○											
Sadanaga Y, et al ³⁵⁾	1992	outpatients	Kumamoto	○	○	○	○	○			○	○	○	○	○
Nishima S, et al ³¹⁾	1993	elementary school	Western Japan	○											
Nakamura S. ³³⁾	1993	students	Oita Univ.	○		○	○								
Sadanaga Y, et al ⁴⁴⁾	1994	high school	Kumamoto	○		○	○	○							human leukocyte antigen NHI records
Ozawa K, et al ⁴⁵⁾	1994	NHI insured	Aichi												
Okuma M. ⁴⁶⁾	1994	elementary school	Okinawa	○											
Yamazaki M, et al ⁴⁷⁾	1994	health check up	Aichi			○	○								Quida! Allergy Screen Test
Yokoshima K, et al ³⁶⁾	1995	outpatients	Tokyo	○		○	○				○	○	○		
Mori A. ⁴⁸⁾	1995	students 6-18 years old	Mibu, Tochigi	○		○	○				○			○	
Usami A, et al ⁴⁹⁾	1995	outpatients	Shizuoka	○		○	○								
Tamura K, et al ⁵⁰⁾	1995	NHI insured	Ibaragi												NHI records
Usami A, et al ⁴¹⁾	1996	students 6-18 years old	Shizuoka	○											
Nakamura S. ³¹⁾	1996	freshmen	Oita Univ.	○		○	○								
Arita M, et al ⁵²⁾	1997	infants 1-2 years old	All Japan	○											
Iwata T, et al ⁵³⁾	1997	infants 5-6 years old	Bunkyo-ku, Tokyo	○		○	○				○				
Hosoi S, et al ⁵⁴⁾	1997	students 6-15 years old	Kyoto	○											

MHW : the Ministry of Health and Welfare, Que : Questionnaire, IDT : Intradermal test, RAST : Radioallergosorbent test, RIST : Radioimmunosorbent test

ELISA : Enzyme-linked immunosorbent assay, NPT : Nasal provocation test, NHI : National Health Insurance

RESULT

Since the initial discovery of pollinosis in Japan, many have reported that the numbers of patients visiting health facilities seeking treatment for pollinosis are increasing²⁸⁻³⁵. It is estimated that from 5 to 20 % of population exhibits symptoms those are specific to pollinosis^{3, 4, 36-54}. But the studies were conducted in a university^{40, 42, 50}, a town^{36, 37, 39, 47}, a city^{53, 54}, a couple of towns or cities^{38, 46}, a prefecture^{4, 44, 45, 48, 49}. Only a couple of nationwide epidemiologic surveys^{3, 41, 51, 52} have been conducted on allergic diseases, not specific to this disease entity.

Table 1 is the list of reports on the numbers of cedar pollinosis patients in Japan. The target population is different from study to study. Some are infants^{52, 53}, some are students^{3, 4, 38, 43, 44, 46, 48, 51, 54}, some are the member of specific organization^{37, 40, 45, 47, 50} and some are patients who visited medical facilities^{8, 28-36, 49}, only a couple of studies are general population^{39, 41, 42}.

Some use only questionnaire^{3, 4, 8, 32, 41, 42, 46, 52, 54}, and some use laboratory tests alone (e.g., detection of specific IgE antibodies)^{30, 34, 47}, and others use both^{28, 29, 31-33, 35-37, 39, 40, 43, 44, 48, 49, 51, 53}. Most of the surveys at medical facilities perform laboratory tests. Two surveys conducted in Aichi Prefecture⁴⁵ and in Ibaragi Prefecture⁵⁰ used the receipts from the National Health Insurance for the month of May to estimate the number of patients with pollinosis.

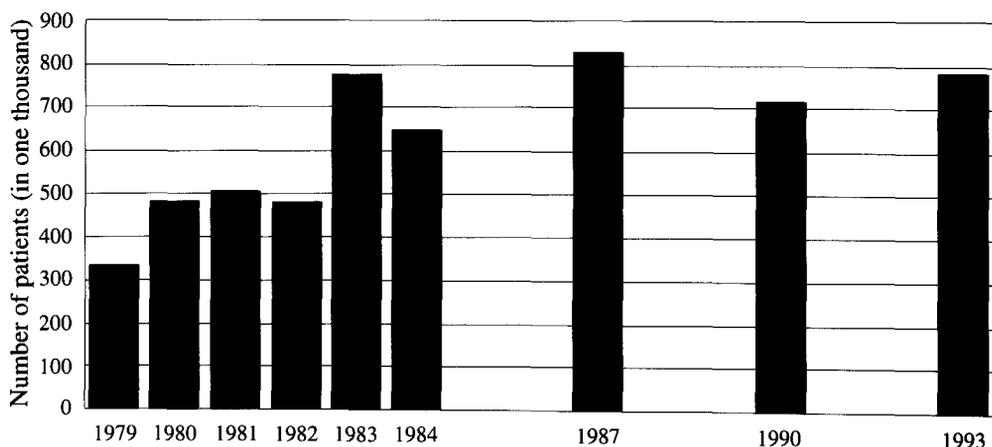
Figure 1 shows annual fluctuations in the estimated number of patients with allergic rhinitis, according to the "Patient

Surveys" taken between 1979 and 1993. After 1983, the method was altered : the survey was conducted in July every year until 1983, after 1983, in October once in every 3 years. Figure 2 presents the number of Medical care bills of allergic rhinitis, the total amount of medical care benefits assigned to the treatment, and frequency of consultation, according to the aforementioned "Reports on the Surveys of Social Medical Care Insurance Services" between 1979 and 1985. Starting with the 1986 survey, National Health Insurance was added to the original subject of the survey. The results are shown in Figure 3.

In both the Patient Survey and the Reports on the Surveys of Social Medical Care Insurance Services, the number of patients with allergic rhinitis increased from 1979 to 1984, then it reached a plateau.

DISCUSSION

There are several problems that we must consider in statistical examination of the number of patients who visited specific facilities, university hospitals for example, in estimating prevalence. First, in urban areas with many medical facilities available, it is highly unlikely that all patients will visit certain medical service facilities; and tabulation only for these facilities means that only part of the patient population of the area (where these facilities are located) is being observed. Furthermore, in the medical service system in Japan, where patients preserve the absolute right to select medical facilities, they may not necessarily choose the organizations that are con-



Source ; Patient Survey, Statistics and Information Department, Minister's Secretariat, Ministry of Health and Welfare

* The patient survey were conducted every year from 1979 to 1983, and every three years since 1984 with alteration of survey methods

Figure 1. The estimated number of one-day allergic rhinitis patients by year.

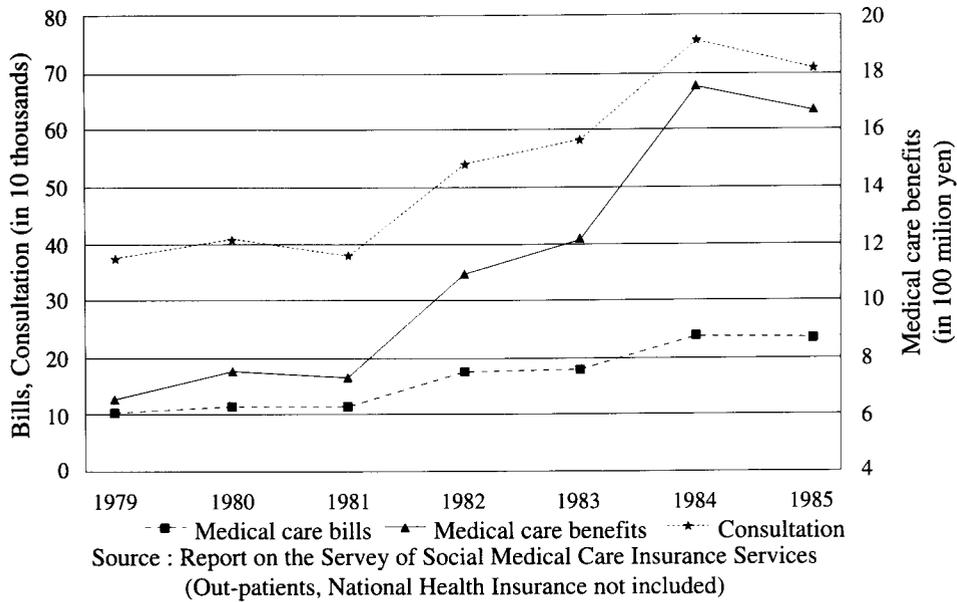


Figure 2. Yearly changes in number of bills, total amount of medical care benefit and frequency of consultation for allergic rhinitis based on one-month invoice in June 1979-1985.

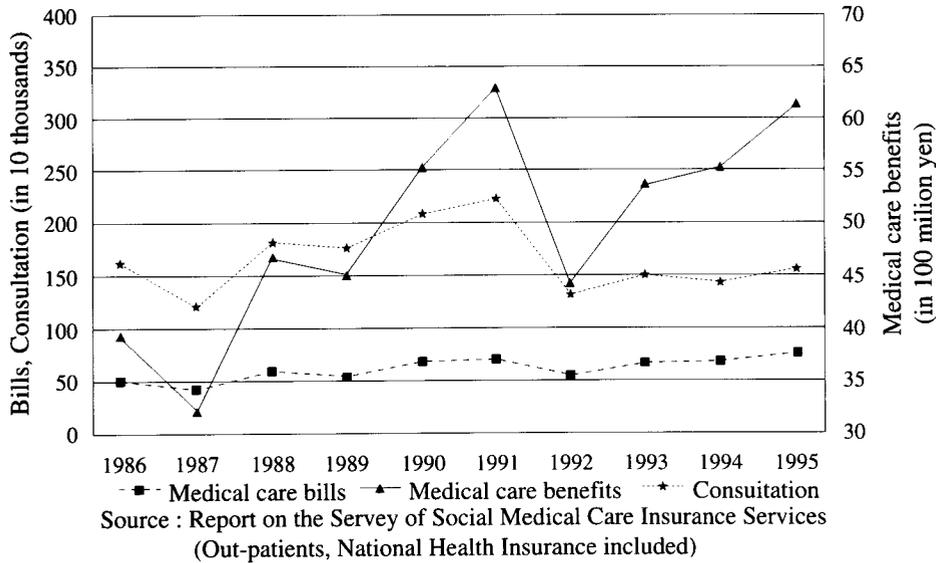


Figure 3. Yearly changes in number of bills, total amount of medical care benefit and frequency of consultation for allergic rhinitis based on one-month invoice in June 1986-1995.

sidered to be equipped with a capacity to manage allergic diseases when the patients suspect that they have pollinosis.

Therefore there is a high possibility that the number of

patients who seek help at specific facilities does not represent the actual number of patients in the area. It is indeed problematic to assume that an increase in the number of patients visit-

ing medical facilities is related to a nationwide rise in the incidence. But only a very few pointed out the problems⁵⁵⁾.

The next is that diagnostic criteria changed from year to year. Along with progress of test methods, laboratory test methods changed very rapidly. Thus, the reproducibility of test methods should be evaluated. For example, the cedar pollen extract for the intradermal test was improved in the first half of the 1980s and its potency was greatly increased over its predecessor^{4,56)}. With the rise in the potency of the diagnostic antigens designed for intradermal tests, some of those patients who produced negative results in a test using the old pollen extracts may react positively to a test using the newer, more potent antigen. It is possible that the potency of the antigen may have been compromised even before it was used if the manner in which the antigen for the intradermal test is stored is less than satisfactory⁵⁶⁾. Only a few studies^{4,51)} took the trouble to provide accurate standardization of antigen potency before analyzing and discussing the epidemiologic characteristics of the data.

In both the Patient Survey and the Reports on the Surveys of Social Medical Care Insurance Services, it should be noted, that the date of Patient Survey was altered from July to in October, while the latter reports are based on a compilation of the details of invoices received for the month of June each year (most of these invoices are believed to be for treatment given in the month of May). We must be alert to the fact that neither data are for the period between February and April when cedar pollens pollute the air and that all cases of allergic rhinitis are classified as pollinosis.

Estimating the fluctuations in the number of patients with patient surveys or bills from medical facilities to health insurance plans has some problems. Because the diagnosis is given by individual physicians based on their own judgement at multiple health service facilities. There is no problem in compiling data based on reports of the number of patients from multiple facilities, if nationally uniform diagnostic criteria are adopted at diagnosis. We should consider a possible discrepancy in the diagnostic criteria between facilities specializing in allergic diseases and those specializing in other diseases or between physicians who are interested in allergic diseases and those who are not.

The increase in the number of patients with cedar pollinosis has attracted public attention. It is necessary that immediate nationwide policies should be implemented to control allergic diseases that are represented by cedar pollinosis. In spite of this publicly recognized need, it became evident from the past reports that even the figures for nationwide prevalence are still of a speculative nature. In formulating policies concerning pollinosis, it is absolutely essential that the prevalence of cedar pollinosis, a representative allergic diseases, be determined accurately in this country. In view of the reports that we evaluated, we came to the conclusion that the following should be

noted in future surveys:

(1) The denominator and numerator must be clearly defined in conducting epidemiologic surveys.

When the subjects are patients that seek help at specific medical facilities (as in past reports), it is possible that the patient population was not necessarily composed of local residents, depending on such factors as available forms of transportation and types of medical facilities. It has been said that the age of patients is predominantly in the 20s and 30s of year^{29-33, 35-37, 41, 42)}. In the areas where the average age of inhabitants is higher than in the others, the number of patients may be small and yet the number of patients in the 20s and 30s may be greater. It is necessary to consider the population composition of a particular area before the analysis of prevalence.

(2) Clear definition of the diagnostic criteria

Uniform, reproducible diagnostic criteria must be decided before evaluating the prevalence of cedar pollinosis because prevalence fluctuates with diagnostic criteria^{56,57)}. It is possible only with uniform criteria to compare the area-specific prevalence and the trends of annual fluctuations. A lack of uniform criteria may even lead to an erroneous theory on the cause-effect relationship concerning the pathogenesis of cedar pollinosis.

To consider the seasonal change of symptom and specificity of antibody at once, diagnostic criteria should consist both questionnaire and laboratory tests. To maintain the reproducibility of the diagnostic criteria, the liability of the questionnaire⁵⁸⁾ should be tested and standard allergen extracts⁵⁹⁾ must be used in the laboratory tests.

(3) Effects extending to other areas

The significance of the results that come out of a study on the prevalence of cedar pollinosis, above anything else, is an accurate determination of the number of affected patients (which has only been estimated up to now) and comprehension of the epidemiologic characteristics of the disease. In addition, the outcome of a study may offer a key to find factors that may exacerbate pollinosis or those that serve as the background for the onset of the disease.

Prevalence is one of the most basic informations and it is often treated lightly. Increases in the number of patients with cedar pollinosis have been reported by several medical facilities but accurate nationwide data are yet to be determined. If the condition is allowed to continue as it is, one can only estimate the sociological effects of cedar pollinosis (e.g., societal loss due to a reduction in productivity of the affected patients), instead of arriving at specific and more applicable management policies.

Even if a drastic measure is to be applied to prevent cedar pollinosis, it is impossible to confirm the actual reduction in the number of patients and to judge the efficacy of the measure unless there is a method for accurate determination of the

nationwide prevalence of the disease. Thus determination of the prevalence of cedar pollinosis and description of the epidemiologic pictures constitute the first essential step toward the control of this clinical entity.

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