

Effect of Climate Change on Allergenic Airborne Pollen in Japan



Reiko Kishikawa, MD, PhD^{a,*}, Eiko Koto^b

KEYWORDS

• Allergenic pollen • Climate change • Japanese Cedar • Pollinosis • Immunotherapy

KEY POINTS

- Japanese representative allergenic airborne pollen-related allergic diseases include Cupressaceae in early spring, the birch family and grass in spring and *Artemisia* in autumn.
- The number of Cupressaceae (Japanese Cedar and Cypress) pollen grains is very large.
- An increase in the amount of conifer airborne pollen grains and an earlier start to disperse were observed, related to climate change.
- In addition, an increase in the number and severity of patients with Japanese Cedar pollinosis has been observed.
- Medical pollen information, medication, and sublingual immunotherapy have all been enhanced. Recently, pollen-food allergic syndrome has become of increased interest.

INTRODUCTION

We introduce the important allergenic pollen in Japan according to longitudinal monitoring of airborne pollen all over Japan.

We recognized conifer pollen as the most important because of continuing increase to an already huge number of patients suffering from Japanese Cedar pollinosis.

With a focus on “climate change and allergic diseases,” as recommended by Professor Jae-Won Oh, we report long-term survey results of Japanese Cedar (JC) and Cypress family (Cypress) pollen and the related meteorologic conditions in Japan.

Botanically the classification system of Angiosperm Phylogeny Group is gradually taking over from the Copeland/Engler classification system by DNA analysis.¹ In this system, JC belongs to Cupressaceae. However, in Japan, JC is more strongly antigenic than other members of the Cypress family. With this in mind, and due to the

^a Department of Allergology, National Hospital Organization Fukuoka National Hospital, 4-39-1 Yakatabaru Minami-Ku, Fukuoka 811-1394, Japan; ^b Clinical Research Institute of National Hospital Organization, Fukuoka National Hospital, 4-39-1, Yakatabaru Minami-ku, Fukuoka 811-1394, Japan

* Corresponding author.

E-mail address: kishikawa.reiko.td@mail.hosp.go.jp

difference in morphology and term of dispersion, we classified JC separately from other cypresses.

Also, the important allergic pollen grains in Japan have been attracting attention related to pollen-food allergies.

HISTORY

Japanese people had little conception of hay fever (pollinosis) historically. Before World War II, some researchers had reported on and drawn attention to the presence of ragweed hay fever in Japan as being similar to the United States.² In 1960, the first case of severe ragweed hay fever was reported with airborne pollen in Tokyo.²⁻⁴ Over the next decade various types of cases such as grass, Japanese hop, mugwort, and occupational hay fever were reported in succession. In 1964, hypersensitivity to JC pollen was reported for the first time.^{2,5}

Since the 1970s, the number of patients with JC pollinosis has increased markedly with the huge number of airborne conifer pollen grains dispersing in early spring. This is also influenced by hereditary factors for immune-response and air pollution.⁶ In 1986, the Japanese government began to take preventive measures against JC pollinosis and started to investigate JC and Cypress family (Cypress) pollen as an important causative allergen. Planting of JC trees, *Cryptomeria japonica* D. Don trees was promoted throughout broad areas of Japan except in Okinawa Prefecture since the nineteenth century, especially after World War II. The area of national artificial forest more than 31 years old doubled in the 1970s.⁷ Generally the amount of JC pollen production is proportional to the area of JC forests aged over 31 years. By 2017, more than 90% of the area was of this age.⁸ Planting of trees of the Cypress, Cupressaceae family (mainly *Chamaecyparis obsta*)⁹, was also promoted in the same way as JC.

METHOD

We have had to detect allergenic airborne pollen since July 1986. The gravitational method with Durham's sampler has been used.

AIRBORNE POLLEN MONITORING

We have monitored airborne pollen all year round at 26 locations in the Japanese archipelago between the latitudes 30 to 40° north (Table 1). At each institute a daily airborne pollen sample was collected by Vaseline-coated glass slides that were fixed in the Durham's sampler, usually exchanged every morning.

The sampling slides were sent to our hospital and pollen number counted per cm² after staining. They were then classified by main pollen grains as a causative agent of pollinosis through the microscope. For the Durham's method, pollen counts were standardized to express them as the number of pollen grains per cm², classifying and summarizing them.¹⁰ For convenience, the number of collected pollen was compiled every 6 months, with the January to June samples classified as spring pollen and the July to December as autumn pollen even if from the same family.

ESTIMATING ALLERGIC CONIFER POLLEN COUNT AND CLIMATIC DATA

In addition, we estimated the pollen count and climatic data close to 9 pollen monitoring locations.^{11,12} These are northern regions, Tohoku and Hokuriku (Sendai, Niigata, Toyama); central regions, Kanto, Tokai and Kinki (Sagamihara, Hamamatsu,

Table 1

Geography of pollen monitoring, height of Durham sampler from ground and investigation duration at each institute from north to south of Japan

Institute	City	Latitude	Longitude	Height(m)	Beginning	Duration (Year)
Wagatsuma children clinic	Sapporo	43.05525	141.3455	16→7	Aug 1986	19
Hakodate Hospital	Hakodate	41.78677	140.744	12	Jul. 1995	7
Akita University	Akita	39.74729	140.0834	20	Aug 1986	6
West Taga Chest Hospital	Sendai	38.25416	140.8414	12	Aug. 1986	4
Tohoku University	Sendai	38.25416	140.8414	20	Jul. 1986	31
Fukushima Chest Hospital	Fukushima	37.74891	140.37	8	Mar. 1990	2
Fujisaki Clinic	Niigata	37.92084	139.0533	3	Jan. 1987	29
Tsukioka Clinic	Niigata	37.92084	139.0533	8	Jul. 1986	21
Toyama University	Toyama	36.69124	137.2201	20	Jul. 1986	27
Tokyo Hospital	Kiyose	35.76606	139.506	16	Jul. 1986	6
Sato Clinic	Takasaki	36.32537	139.0162	6	Jan. 1998	21
NHO Sagamihara Hospital	Sagamihara	35.48806	139.1608	20	Oct1986	28
Tokai Pollinosis Institute	Hamamatsu	35.68907	139.7874	37→6	Jul. 1986	33
NHO Mie Hospital	Tsu	34.71911	136.5168	8	Jul. 1986	32
Osaka Medical University	Osaka	34.70251	135.4965	40	May. 1986	7
Wakayama Redcross Hospital	Wakayama	34.22198	135.1661	16→18	Jan. 1987	31
Matsue Chest Hospital	Matsue	35.46905	133.0616	8	Sep. 1986	18
East Kochi Chest Hospital	Kochi	33.55201	133.5383	10	Jan. 1987	15
Kyushu University	Fukuoka	33.57979	130.4024	21	Jul. 1986	28
NHO Fukuoka Hospital	Fukuoka	33.57979	130.4024	16	Jul. 1986	33
Nagasaki University	Nagasaki	32.76542	129.8663	16	Jul. 1986	29
Kumamoto University	Kumamoto	32.78852	130.7149	40	Jul. 1986	29
Fujimoto-Hayasuzu Hospital	Miyakonojo	35.66897	139.4777	21	Jul. 1986	20
Miyazaki University	Miyazaki	31.90738	131.5525	5	Jul. 1986	29
Hokusatsu Hospital	Oguchi	32.03073	130.5871	5	Jul. 1986	19
Kumage Branch Office	Yakushima	30.25635	130.5028	8	Jan. 1998	21

Table 1 shows the geographic location of each pollen monitoring institute, the height of the sampler from the ground, and pollen investigation duration from north to south of Japan.

Tsu, Wakayama); and in the south-west, Kyushu district (Fukuoka, Kumamoto) as shown in [Table 2](#). We referred to the annual change in monthly mean temperature using the Japan Weather Association Home Page database. We have estimated annual total pollen counts and yearly starting day of JC pollen dispersal with climatic conditions statistically. Stata (StateCorp LLC, USA/ Lightstone Co. LTD, Tokyo, Japan) was used for statistical analysis.

RESULTS
Representative Airborne Pollen as Allergenic Agent

*Tree pollen*¹²: As [Fig. 1](#) shows, tree total pollen count at each location was averaging 889 ~ 13,116 pollen grains per year. JC pollen was most common, at 40%, with the Cypress family next at approximately 20%, together more than 60% of pollen in the sample. These pollen counts increased with the annual fluctuation. In Hokkaido, the prevalence of birch family pollen in the count was larger.

*Herbaceous pollen*¹³: Total herbaceous pollen counts at each location were extremely small compared with tree pollen, averaging 73 ~ 650 pollen grains ([Fig. 2](#)). The Sagamihara location had the highest count. Spring grass pollen gave the largest count, at 30% of the total collected. *Artemisia* pollen is scarce, but it is found across the country, with 6 ~ 40 pollen count per cm² in autumn. *Ambrosia* was less in evidence than *Artemisia* except in Sagamihara and Miyazaki (333,88).

Annual Conifer Pollen Grains Count and Climate Change

[Fig. 3](#) shows the annual fluctuation of the conifer pollen counts (JC, Cypress) at the 9 locations in Japan (see [Table 2](#)). Each vertical line shows pollen counts per cm² per year and horizontal line shows year. We did not express pollen counts logarithmically because it is difficult to show the annual fluctuation visually. JC pollen counts are indicated by the blue bar and Cypress by the red. Each dotted line shows the approximation line. Both pollen counts have been increasing gradually over time. The pollen counts per cm²/year are different for each location. In Sagamihara, the highest JC pollen count was observed. In Tohoku, Cypress pollen counts were lower than in other regions, and in Kyushu, Cypress pollen counts have increased.

Table 2 The locations of airborne pollen monitoring by Durham's Sampler over a long period. There are 9 institutions in Sendai, Niigata, Toyama, Sagamihara, Hamamatsu, Tsu, Wakayama, Fukuoka, and Kumamoto						
NO	City	District	Institute	Latitude	Longitude	Survey Period (year)
1	Sendai	Tohoku	Tohoku University	38.25416	140.8414	31
2	Niigata	Hokuriku	Fujisaki Clinic	37.92084	139.0533	29
3	Toyama	Hokuriku	Toyama University	36.69124	137.2201	27
4	Sagamihara	Kanto	NHO Sagamihara Hospital	35.48806	139.1608	28
5	Hamamatsu	Tokai	Tokai Pollinosis Institute	35.68907	139.7874	33
6	Tsu	Kinki	NHO Mie Hospital	34.71911	136.5168	32
7	Wakayama	Kinki	Wakayama Red cross Hospital	34.22198	135.1661	31
8	Fukuoka	Kyushu	NHO Fukuoka Hospital	33.57979	130.4024	33
9	Kumamoto	Kyushu	Kumamoto University	32.78852	130.7149	29

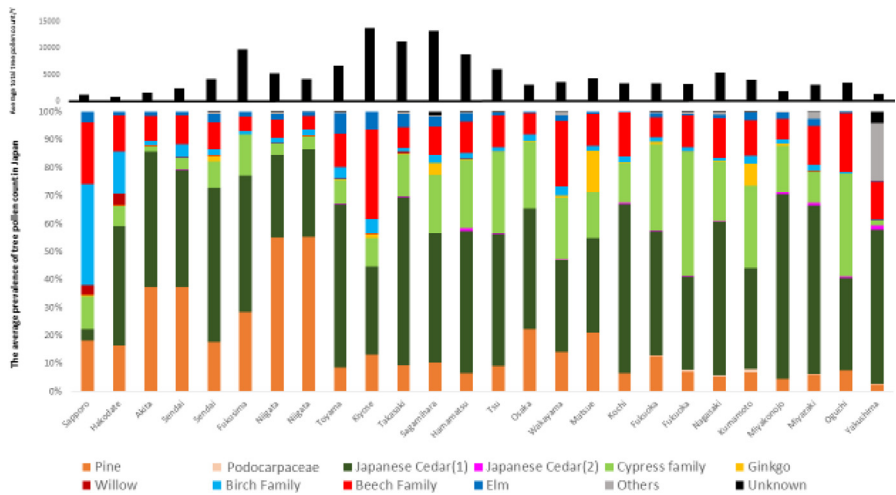


Fig. 1. Mean total pollen counts and mean prevalence of allergic tree pollen count at each location from Sapporo to Yakushima. The upper histogram shows mean total pollen counts. The Kiyose and Sagaminara locations had the highest counts. Each bar chart shows mean prevalence of pollen count. At all locations with the exception of Sapporo city, JC and Cypress family pollen were the most prevalent pollen at approximately 60% of the total. In Sapporo, the prevalence of birch pollen count was greater.

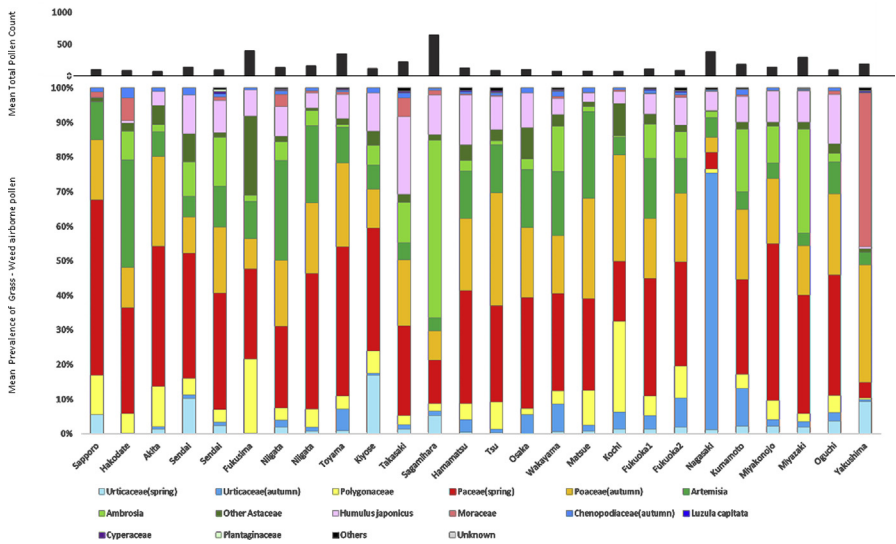


Fig. 2. Mean total pollen counts and mean prevalence of allergic herbaceous pollen counts at each location from Sapporo to Yakushima. The upper histogram shows mean total pollen counts. The Sagaminara location had the greatest count. The lower bar chart shows mean prevalence of pollen counts at each location. The red element shows grass (Poaceae) pollen in spring at each location: it was the largest element with a mean of 30%. Ambrosia in Sagaminara and Urticaceae in Nagasaki stood out in particular.

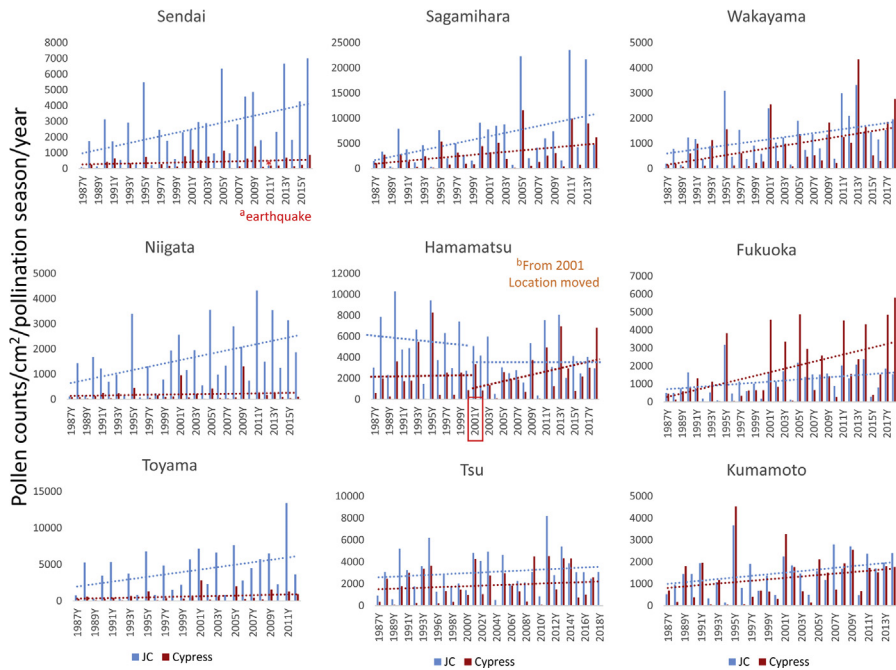


Fig. 3. Annual fluctuation of conifer pollen counts (JC, Cypress) from 1987 to, at the longest 2018, at 9 locations in Japan. Each vertical line shows pollen counts and the horizontal line shows the year. Both pollen counts have shown remarkable annual fluctuation and totals have been increasing gradually. In Sagami-hara, the highest JC pollen count was observed. ^a The East of Japan Earthquake March 11, 2011. ^b In Hamamatsu the monitoring location was moved in 2001.

Fig. 4 shows the annual change in mean temperature at the 9 cities in July and August when JC and Cypress male flower buds are growing. Each vertical line shows mean monthly temperature and the horizontal line shows year and the dotted line shows the approximation. The monthly mean temperatures rise in all regions without exception.

Table 1 shows the correlation between the mean temperature in summer and the next year's annual total pollen count. There are significant positive correlations between the annual summer mean temperature and the next year's total pollen counts of JC and Cypress especially the counts in July ($P < .05$ to $< .0001$). The higher the summer temperature, the more significantly conifer rose in these pollen counts.

Annual Japanese Cedar Pollination Starting Day and Climate Change

Fig. 5 shows the annual change of starting day in JC pollination. Each vertical line shows days since January 1, and each horizontal line shows the year.

The dotted line shows the approximate. The starting day is earlier in Tohoku (Sendai, Niigata), Hokuriku (Toyama), and later in Kanto (Sagami-hara), Tokai (Hamamatsu), and Kinki (Tsu, Wakayama) regions. In Kyushu districts (Fukuoka, Kumamoto), they are almost static.

Fig. 6 shows the annual change of monthly mean temperature of January and February just before and after the JC pollination season. Each vertical line shows

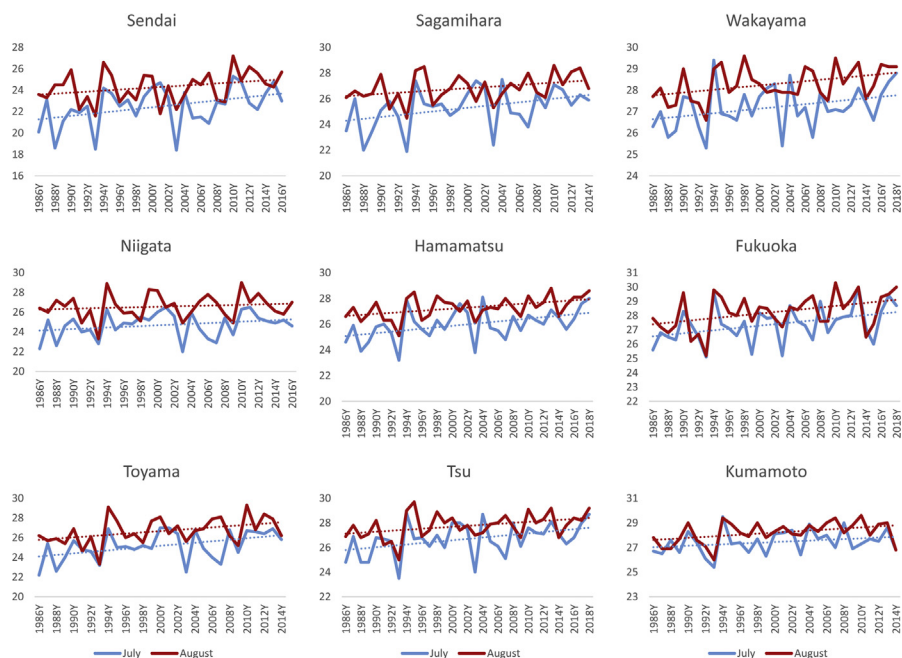


Fig. 4. Annual change of mean temperature in July and August from 1986 to, at latest, 2018 in Japan. In summer, the JC and Cypress male flower bud forms. The vertical line shows mean monthly temperature and horizontal line shows year, and the dotted line shows the approximation. In July and August the monthly mean temperatures are rising of all areas without exception.

monthly mean temperature and the horizontal line shows the year. There has been a gradual fall in January and rise in February, although the change range is very small in Hokuriku and there is almost no change in Tohoku regions.

Tables 3 and 4 show the correlation between the start day of JC pollination and the mean temperature in January (blue line) and February (red line) when the JC pollen grains are nearly beginning to disperse. In February, we found a significantly strong negative correlation between the starting day and mean temperature ($P = .05$ to $P < .0001$), in Sendai, Niigata, and Toyama, north of Japan. In January there are weak negative significant correlations in Sagami-hara, Hamamatsu, and Tsu ($P = .03$ to $P = .003$). Due to winter climate change over 30 years, the starting day has become earlier in northern regions, and later in central Japan.

DISCUSSION

In 1986, we started these investigations at 47 institutes, one in each prefecture in Japan, and 26 institutions have continued to investigate for more than 2 years (see **Table 1**). For the first 9 years, we investigated using a research fund of the Ministry of Health.¹⁴ After that, we continued monitoring airborne pollen on a Voluntary basis.

The Appearance of Pollen-Food Allergic Syndrome/Oral Allergic Syndrome

In our country, airborne pollen of the JC and Cypress, the birch family, grass in spring, *Artemisia* and *Ambrosia* in autumn are representative pollens causing allergic diseases.

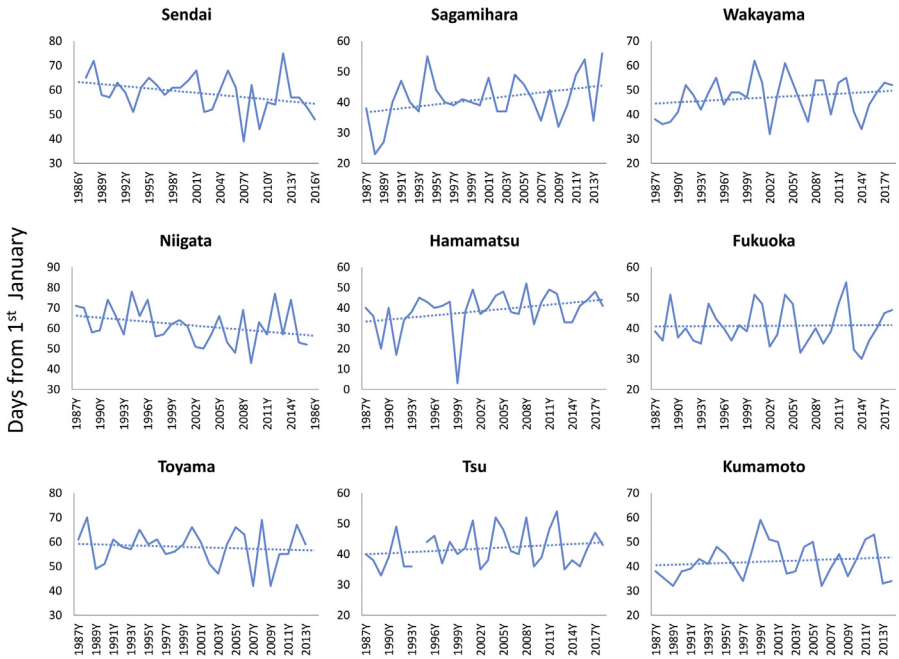


Fig. 5. Annual change of starting day in JC pollination from 1987 to, at the latest, 2018. Each vertical line shows days from January 1 and the horizontal line shows year. The start day, counting from January 1, is earlier in Tohoku (Sendai, Niigata), Hokuriku (Toyama) district, and later in Kanto (Sagami-hara), Tokai (Hamamatsu) and Kinki (Tsu, Wakayama) districts. In Kyushu districts (Fukuoka, Kumamoto) it is static.

The amount of JC and Cypress pollen is very large. People with pollen allergies have rhinoconjunctivitis mainly in each pollination season with allergic pharyngitis, asthma, and allergic dermatitis exacerbation. However, from approximately 2000, rose family fruit food allergy due to the birch pollen antigen in Hokkaido¹⁵ was reported and the number of patients with pollen-food allergic syndrome (PFAS) has increased with increasing birch family pollen production.¹⁶ In Kanto region and West Japan also, alder and mugwort PFAS with pollinosis has been reported.^{17,18} In Kyushu, trees of alder pollen (from the birch family) are counted in very small numbers. But adult and infant patients with rose family fruit food allergy¹⁹ are consulted. In Kyushu there are trees of the beech family such as oak, and the pollen production from these is increasing.²⁰ There is cross-reactivity between the beech and birch family pollen antigen²¹ but this is not yet proven to be related to PFAS/oral allergic syndrome (OAS).²² However, this suggests that we need to carefully examine the rhinoconjunctivitis and PFAS/OAS related to these possibly problematic trees and herbaceous pollen. The number of articles on PFAS has increased from approximately 2000, and the review articles reported until then that the main symptoms were mainly rhinoconjunctivitis and respiratory in Europe and the United States.^{23,24} We believe the number of PFAS patients has increased²⁵ with the increase in pollen antigen related with climate change.

Japanese Cedar Pollinosis Has Been the Most Important for a Long Time

Japan has extensive forests, with 70% total coverage of the country as a whole. The conifer pollen grain continued to be the most important allergic causative agents.

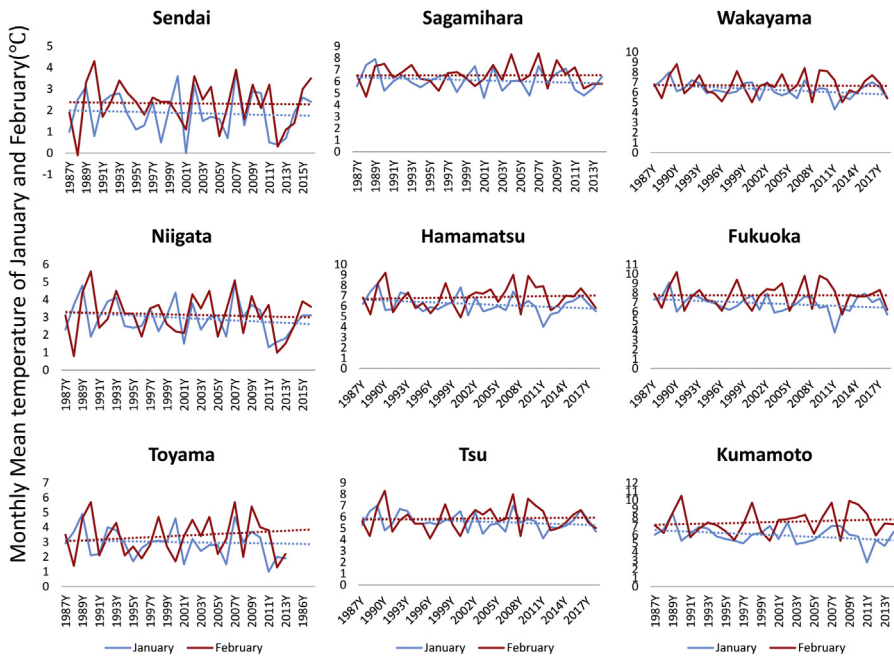


Fig. 6. The annual change of monthly mean temperature of January and February from 1986 to, at latest, 2018. Each vertical line shows monthly mean temperature and horizontal line shows year. The dotted line shows the approximation. It gradually falls in January (blue line) and rises in February (red line), although the change range is very small in Hokuriku and there is almost no change in Tohoku region.

National JC forests are aging because they are no longer being used for timber. Cypress pollen has strong cross-reactivity to JC. Many patients with allergy to conifer have exacerbated symptoms every spring. In 1998, the prevalence of JC pollinosis was 16% on average but rose to 26.5% on average, with a particular increase in infants with JC pollinosis, by 2008.²⁶

Gravitational Monitoring Is Primitive but Adequate for Pollen Information

Durham's sampler was a technically simple method used by our predecessors, as it was immediately available and easy applicable by allergy professional clinicians in the 1960s.²⁷ Durham's sampler has become the most popular in Japan. This technique is now almost outdated but is still suited to gathering daily information about huge numbers of pollen grains, for the medical benefit of patients with pollinosis. We reported a strong positive correlation between Durham's and volumetric sampler (Burkard's sampler) conifer pollen counting in 2009.²⁸ We now have more than 400 locations observing JC and Cypress pollen count to gather nationwide pollen information.

Meteorologic Conditions Affect Conifer Pollen Production

JC and Cypress pollen production is related to higher temperatures and lower humidity conditions in the previous summer, when male flower formed. The start of pollination has been influenced by meteorologic conditions around the time of male flower maturation. Male flower bud formation and dispersal of pollen depends on weather

Table 3 Correlation between total pollen counts of conifer pollen from 1987 to, at latest, 2018 and the previous year's July and August mean temperature in male flower bud formation					
City	Duration (Y)	July		August	
Japanese Cedar					
Sendai	n = 30	r = 0.397	P<.05	r = 0.145	P = .443
Niigata	n = 30	r = 0.639	P<.001	r = 0.452	P<.05
Toyama	n = 26	r = 0.652	P<.001	r = 0.639	P<.001
Sagamihara	n = 28	r = 0.613	P<.001	r = 0.499	P<.01
Hamamatsu	n = 32	r = 0.390	P<.05	NS	
Tsu	n = 31	r = 0.696	P<.0001	NS	
Wakayama	n = 32	r = 0.630	P<.001	r = 0.491	P<.01
Fukuoka	n = 32	r = 0.736	P<.0001	r = 0.668	P<.0001
Kumamoto	n = 28	r = 0.737	P<.0001	r = 0.638	P<.001
Cypress family					
Sendai	n = 30	r = 0.558	P = .0014	NS	
Niigata	n = 30	r = 0.718	P<.0001	r = 0.414	P<.05
Toyama	n = 26	r = 0.694	P<.0001	r = 0.546	P<.01
Sagamihara	n = 28	r = 0.598	P<.001	r = 0.475	P<.05
Hamamatsu	n = 32	r = 0.539	P<.01	r = 0.446	P<.05
Tsu	n = 31	r = 0.597	P<.001	r = 0.390	P<.05
Wakayama	n = 32	r = 0.627	P<.001	r = 0.414	P<.05
Fukuoka	n = 32	r = 0.676	P<.0001	r = 0.650	P<.0001
Kumamoto	n = 28	r = 0.656	P<.001	r = 0.505	P<.01

Spearman's rank correlation coefficient.

Generally production of conifer pollen correlates with the previous summer's climate condition with the temperature and humidity. There are significant positive correlations between the annual summer mean temperature and the following year's total pollen counts especially the July temperature

Abbreviation: NS, not significant.

conditions and geographic features. We estimated the regional pollen data under some meteorologic conditions and hope to predict these pollen dispersal trends in coming years as the climate changes.

Annual Pollen Counting and Climate Change

As Fig. 3 shows, for both of pollen, annual fluctuation has been measured in each location. In Sagamihara the highest JC pollen count was observed, but fewer than 1000 to more than 20,000 pollen grains per cm²/season were counted. Everywhere pollen counting has seen remarkable annual fluctuations. In Tohoku, Cypress pollen counts were less than that of other regions. In Kyushu, Cypress pollen counts have increased more than those of JC. Monthly mean temperatures are going to rise in all areas. There is a significant positive correlation between the annual summer mean temperature and the next year's total pollen counts especially in July when the male flower bud is formatted. The higher the summer temperature, the more these conifer pollen counts increase. The production of both types of pollen grains are higher in the Kanto and Tokai regions where a large percentage of the population lives. In those regions exposed to large amounts of pollen antigen, there are many patients

Table 4
Correlation between starting day of Japanese Cedar pollination and mean temperature near pollinated season from 1987 to, at latest, 2018

City	Years	January Average Temperature		February Average Temperature	
Sendai	30	$r = -0.500$	$P = .005$	$r = -0.774$	$P < .0001$
Niigata	30	NS		$r = -0.645$	$P = .0001$
Toya ma	27	NS		$r = -0.827$	$P < .0001$
Sagamihara	28	$r = -0.549$	$P = .003$	NS	
Hamamatsu	32	$r = -0.373$	$P = .036$	NS	
Tsu	31	$r = -0.414$	$P = .021$	NS	
Wakayama	32	$r = -0.397$	$P = .025$	NS	
Fukuoka	32	NS		NS	
Kumamoto	28	NS		NS	

Spearman's rank correlation coefficient.

Table 4 shows the correlation between starting day of JC pollination and the mean temperature in January and February when the JC pollen grains are nearly beginning to disperse. In February we found significant negative correlation between the starting day and winter mean temperature.

Abbreviation: NS, not significant.

with serious rhinoconjunctivitis, including systemic allergic symptoms and related food allergies such as PFAS/OAS.^{29–31}

Annual Starting Day of Japanese Cedar Pollen Dispersing and Climate Change

It is important to know the starting date of pollination before the season for successful treatment. Currently the prediction of the start of JC pollen dispersal everywhere is an essential measure for treating JC pollinosis.

The start day is earlier in the north of Japan, and later in central Japan where there is a huge dispersal of pollen. We believe that JC pollination season will commence at almost the same time at each region in the near future.

JC male flowers need low temperatures to produce dormancy in winter followed by higher temperature to trigger pollination after the dormancy period. We found significant negative correlation between the start day of pollination and winter mean temperature. This is especially clear in the north of Japan in February.

Since approximately 1994, a little JC pollen dispersion has been monitored from October to December,³² and the number of pollen grains is increasing. We believe this may be one of the effects of climate change.

Social and Medical Background of Japanese Cedar Pollinosis Treatment

The total cost of treatment of patients with JC pollinosis and associated diseases is \$3 billion.³³ For this reason, the Japanese government has worked to find preventive measures. In the medical and health welfare fields there is continuous research into allergy and immunology including JC pollinosis. In addition, the Forest Agency and the Ministry of Environment have many projects, including nonproductive pollen cedar bleeding,³⁴ promoting of comfortable forest without JC/Cypress around big cities, a nationwide information network, and the precise prediction of pollen dispersal. We now have a full pollen network system by Durham's Sampler. Real-time auto monitor for selected pollen grains has been developed over the past decade in the Ministry of Environment. However, there are many problems in making a useful, popular, and long-lasting pollen information and forecast system to prevent pollinosis

exacerbation. On the other hand, sublingual immunotherapy of JC has been developed and the therapeutic effect was seen.^{35,36} This method is suitable for all patients in all age groups. In addition, improved medication has been introduced every year adding to treatment of pollinosis guidelines.²⁶ Continuous efforts to overcome pollinosis in all generations are still ongoing in our country.

Perspectives and Conclusion

In Japan, allergenic conifer pollen counts have been increasing because areas with aged conifer plantations and also through the effects of climate change over 30 years. We need to know the allergenic pollen grains and to apply the results to deal with it. PFAS due to allergenic pollen is likely to increase in all generations.

Clinics care points

- Antigen avoidance: Daily pollen forecast is useful. In addition, we must understand the types of important pollen antigens and the pollination season.
- Early treatment for successful treatment: we must obtain information for predicting the start of cedar pollen dispersal and start treatment before dispersal.
- We should continue treatment during the dispersal period to prevent the exacerbation and aggravation of comorbidities such as bronchial asthma, pollen dermatitis, and PFAS.

ACKNOWLEDGMENTS

The authors thank many collaborators and around people related these study for a long time following Sendai (Tohoku University Otolaryngology Laboratory), Niigata (Fujisaki Clinic, Tsukioka Clinic), Toyama (Toyama University), Takasaki (Sato Kei Clinic), Sagami-hara (NHO Sagami-hara Hospital), Hamamatsu (Tokai Pollinosis Institute), Tsu (NHO Mie Hospital), Wakayama (Wakayama Red Cross Hosp.), Fukuoka (Kyushu University), Kumamoto (Kumamoto University), Miyazaki (Miyazaki University) and Yakushima (Kagoshima University, The Forestry Agency), and Japan Weather Support Center, Environmental Ministry, Fukuoka Prefecture Medical Association, Japan Medical University, Oita University. We appreciate the Ministry of Health and Welfare funds from 1986 to 1995 for monitoring airborne pollen survey.

Also the authors thank to Honor director of our hospital the late Hitoshi Nagano, Sankei Nishima, MD, PhD, the late Mitue Katuta, MD, PhD, Yoshinori Wagatsuma, MD, PhD (Wagatsuma children clinic), the late Takao Shida, MD, PhD (Sagami-hara National Hospital), Honor Professor Estelle Levetin (The University of Tulsa, Tulsa, Oklahoma), Honor Professor Randy Goldberm, Associate Professor Terumi M. Horiuti and Edward Brooks (University of Texas Medical Branch, USA), Honor Professor Jean Emberlin (Worcester University, UK).

Moreover, the authors thank the respected collaborators for about 30 years, Norio Sahashi, PhD, Nobuo Soh, MD, PhD, Toshitaka Yokoyama, PhD, Tadao Enomoto, MD, PhD, Toru Imai, MD, PhD, Koji Murayama, PhD, Atsushi Usami, MD, PhD, Hide-toyo Teranishi, MD, PhD, Yoko Fujisaki, MD, PhD, Akemi Ishii, Secretary, and the late Motoo Suzuki, PhD (NPO Pollen Information Association), Akemi Saito, PhD, Yuma Fukutomi, MD, PhD, Masami Taniguchi, MD, PhD (NHO Sagami-hara National Hospital), Yasuhiro Samjima, MD, PhD (Kumamoto University), Takao Fujisawa, MD, PhD (NHO Mie National Hospital), Chie Oshikawa, MD, PhD, Akiko Sugiyama, MD, Koki Okabe, MD, Takehito Fukushima, MD, PhD, Kaoru Kojima, Tec, Makiko Oda, Tec,

Terufumi Shimoda, MD, PhD, Satoshi Honjo, MD, PhD, Makoto Yoshida, MD, PhD, and Tomoaki Iwanaga, MD, PhD (NHO Fukuoka National Hospital).

Thank you for English Proofreading, Nick May.

REFERENCES

1. Yonekura K, Murata H, supervisor. Higher plant classification Scheme. Tokyo (Japan): Hokuryukan; 2010. p. 13–28, 34–6. [in Japanese].
2. Ishizaki T. History a University of Texas Medical Branch nd definition of hay fever. In: Ishizaki T, editor. Pollen allergy of Circumstance and treatment. Tokyo (Japan): Hokuryukan; 1979. p. 1–7 [in Japanese].
3. Araki H. Studies on Pollinosis 1. Pollen Survey in Tokyo its Neighboring District. Arerugi 1960;9:648–55 [in Japanese].
4. Araki H. Studies on Pollinosis II.Sensitization with pollen in Japan. Arerugi 1961; 10:354–70 [in Japanese].
5. Saito Y, Horiguchi S. Japanese Cedar pollinosis in Nikko Japan. Arerugi 1964;13: 16–8 [in Japanese].
6. Ishizaki T, Koizumi K, Ikemori R, et al. Studies of prevalence of Japanese cedar pollinosis among the residents in a densely cultivated area. Ann Allergy 1987;58: 265–70.
7. Yokoyama T, Kanazasi T. Annual change in the area of Japanese Cedar forest as a source of allergic pollen. In: Muranaka M, Taniguchi K, editors. Immune- goblin E antibody and environmental factors. Tokyo: Medical Tribune; 1990. p. 67–78 [in Japanese].
8. Yokoyama T. A bite note of Japanese Cedar pollinosis,p6. Available at: http://www.tokyo-eiken.go.jp/kj_kankyo/kafun/hitokuti/.
9. Makino T, Honda S, editors. Makino's illustrated flora in colour. Tokyo: Hokuryukan; 1982. p. 810.
10. Sahashi N, Nishima S, Kishikawa R, et al. Standardization of procedures for atmospheric pollen counts and pollen forecast in Japan. Jpn J Palynol 1993;39: 129–34 [in Japanese].
11. Kishikawa R, Oshikawa C, Koto E, et al. Longitudinal investigation on allergenic conifer pollen in japan for successful prevention and treatment against Japanese Cedar Pollinosis. Expert Opin Environ Biol 2016;5:2.
12. Kishikawa R, Koto E, Oshikawa C, et al. Longitudinal monitoring of tree airborne pollen in Japan- regional distribution and annual change of important allergenic tree pollen. Arerugi 2017;66:97–111.
13. Kishikawa R, Koto E, Oshikawa C, et al. Long-term results of airborne pollen surveys in the Japanese archiago from the perspective of pollen antigen. – regional and annual variation of important herbaceous pollen antigen in Japan-. Arerugi 2019;68:1221–38 [in Japanese].
14. Nishima S, Okuda M, Shida T, et al. Edi: Ministry of Health and Welfare pollen research Group, pollen survey in the Japanese Islands data Base. Tokyo: Kyowakikaku; 2000. p. 1–261.
15. Asakura K, Honnma A, Yamasaki T, et al. Relationships between oral allergy syndrome and sensitization to pollen antigen, especially to Mugwort. Arerugi 2006; 55:811–9.
16. Kobayasi T, Takeuchi S, Yasaka M. Trends in annual counts of *Betula* pollen from six cities in Hokkaido. Jpn J Palynol 2013;59:59–67 [in Japanese].

17. Maeda N, Inomata N, Morita A, et al. Correlation of oral allergy syndrome due to plant-derived foods with pollen sensitization in Japan. *Ann Allergy Asthma Immunol* 2010;104:205–10.
18. Adachi A, Horikawa T. Local differences of oral allergy syndrome with pollinosis: a comparison between Hanshinkan and Higashiharima in Southhyogo. *Alerugi* 2006;55:811–9.
19. Masumoto N, Teduka J, Nanishi M, et al. Pollen food allergy syndrome in five-year-old boy after moving house at the foot of the mountain: a case report. *Alerugi* 2018;67:1027–32 [in Japanese].
20. Kishikawa R, Yokoyama T, Sahashi N, et al. Effect of climate change on Fagaceae airborne pollen in Japan as allergic causative agent associated with food allergy. *J Geogr Nat Disast* 2016;6:3.
21. Koya K. A study on pollinosis : III. The significance of oak (genus *Quercus*) in pollinosis. *Alerugi* 1970;19(918–30):933–93 [in Japanese].
22. ALLERGEN NOMENCLATURE, WHO/IUIS Allergen Nomenclature Sub-Committee ,WHO/IUIS Allergen Nomenclature Home Page. Available at: <http://www.allergen.org/>.
23. Carlson G, Coop C. Pollen food allergy syndrome (PFAS): A review of current available literature. *Ann Allergy Asthma Immunol* 2019;123:359–65.
24. D'Amato G, Spieksma F, Liccardi G, et al. Pollen-related allergy in Europe. *Allergy* 1998;53:567–78.
25. Lee SC, Kim SR, Park KH, et al. Clinical features and culprit food allergens of Korean adult food allergy patients: a cross-sectional single-institute study. *Allergy Asthma Immunol Res* 2019;11:723–35.
26. Committee on Practical guidelines for the Management of Allergic Rhinitis in Japan: Epidemiology of Japanese cedar pollinosis in Japan, practical guidelines for the management of allergic rhinitis in Japan. Tokyo: Life Science; 2015. p. 7–13 [in Japanese].
27. Saito A, Murakami A, Fukutomi Y, et al. Fifty-year record of airborne pollen in Sagami-hara, Japan. *Jpn J Palynol* 2017;62:75–85.
28. Kishikawa R, Sahashi N, Saito A, et al. Japanese Cedar airborne pollen monitoring by Durham's and Burkard Samplers in Japan- Estimation of the usefulness of Durham's Sampler on Japanese Cedar pollinosis. *Glob Environ Res* 2009;13: 55–61.
29. Inuo C, Kondo Y, Tanaka K, et al. Japanese cedar pollen-based subcutaneous immunotherapy decreases tomato fruit-specific basophil activation. *Int Arch Allergy Immunol* 2015;167:137–45.
30. Bonds R, Sharma GS, Kondo Y, et al. Pollen food allergy syndrome to tomato in mountain cedar pollen hypersensitivity. *Mol Immunol* 2019;111:83–6.
31. Sénéchal H, Keykhosravi S, Couderc R, et al. Pollen/fruit syndrome: clinical relevance of the cypress pollen allergenic gibberellin-regulated protein. *Allergy Asthma Immunol Res* 2019;11:143–51.
32. Taira H, Teranishi H, Kenda Y. Sugi (*Cryptomeria japonica* D. Don) pollen scattering out of season. *Alerugi* 1992;41:1466–71 [in Japanese].
33. Ogino S. Loss of work productivity in patients with Japanese Cedar pollinosis. *Jpn J Occup Environ Allergol* 2015;22:25–31 [in Japanese].
34. Saito M, Goto S. Doubling the production of male sterile Japanese cedar (*Cryptomeria japonica* D. Don) seedlings by application of micro-cutting technique. *Jpn J FGTB (Forest Genetics and Tree Breeding)* 2019;8:1–7 [in Japanese].

35. Yuta A, Ogihara H, Miyamoto Y, et al. The enhanced clinical efficacy by treated years and the sustained efficacy after treatment of sublingual immunotherapy for Japanese cedar pollinosis]. *Arerugi* 2010;59:1552–61 [in Japanese].
36. Okamoto Y, Okubo K, Yonekura S, et al. Efficacy and safety of sublingual immunotherapy for two seasons in patients with Japanese cedar pollinosis. *Int Arch Allergy Immunol* 2015;166:177–88.