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Research Article

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Longitudinal Investigation on Allergenic Conifer Pollen in Japan for Successful Prevention and Treatment against Japanese Cedar Pollinosis

Reiko Kishikawa[1*], Chie Oshikawa[1], Eiko Koto[1], Akemi Saito[2], Norio Sahashi[3], Nobuo Soh[4], Toshitaka Yokoyama[5], Tadao Enomoto[6], Toru Imai[6], Koji Murayama[6], Yuma Fukutomi[2], Kazuo Akiyama[2],Terufumi Shimoda[1] and Tomoaki Iwanaga[1]

Abstract

In Japan allergic people has been recognized increasing according to the increase of Japanese cedar, *Cryptomeria japonica* (JC) pollinosis since first reported in 1964. We have detected allergenic airborne pollen when Japanese government has begun to investigate the background and treatment on JC pollinosis as a serious social problem since July1986. Urgently the gravitational method with Durham's sampler has been adopted to know huge number of JC and cypress family, Cupressaceae family (Cypress) pollen grains as causative agent. The area of national artificial forest of over 31 years old has become about 7 times from1970. We have estimated annual fluctuation of Japanese important allergenic pollen, with climatic factor during about 30 years for successful treatment of pollinosis in near future.

There are institutions in fifteen locations monitoring airborne pollen by Durham's sampler in Japan between the latitude of 30 to 40 degrees north. Airborne pollen samples were collected at each institute and were sent to our hospital on a daily basis. We counted pollen grains per cm^2 through microscope, classifying and summarizing them. From 1986 to 2014 we have referred to the change in meteorological condition at the close to 9 of the pollen monitoring locations and estimated statically.

JC and Cypress pollen counts have shown huge but remarkable annual fluctuation and they have been increasing gradually according to over 31 y-old conifer planting area expanding. The mean temperature in summer time, JC male flower formation, has a significant correlation with next year pollen counts. The pollination season has started earlier in north and later in central Japan gradually through a changing on mean temperature.

In Japan allergenic conifer pollen counts have been increasing because of over 31 y-old conifer plantations area increase through the climate change about 30 years. Moreover, it has changed the start of pollination season.

Keywords

Allergic airborne pollen; Japanese cedar pollinosis; Climate change

Introduction

In Japan allergic people has increased according to the increase of Japanese Cedar (JC) pollinosis since 1964 when the first case was reported [1]. Planting of Japanese cedar, *Cryptomeria japonica* D. Don trees were promoted throughout broad areas in Japan except Okinawa Prefecture and the most of Hokkado district since nineteenth century, especially after II War. The area of national artificial forest of over 31 years old has become twice during 1900 to 1970 [2]. Generally the amount of JC pollen production is proportional to the area of JC forests aged over 31 years. And planting of trees of the Cypress, Cupressaceae family (mainly *Chamaecyparis obsta*), was promoted as same as JC. Japanese government has begun to take preventive measures against JC pollinosis since1986. Because JC and Cypress pollen antigen has become one of the serious nationwide social problems for Japanese people with pollen allergy in a few decades. We have had to detect allergenic airborne pollen since July1986 urgently. The gravitational method with Durham's sampler has been suitable to know huge number of JC and Cypress pollen grains.

Japan is covered with a forest area about 70%. The conifer pollen grain is the most important allergic causative agent. During February to April/May, firstly JC, next Cypress pollination was observed. Many patients with rhino conjunctivitis due to the allergic conifer have exacerbated every spring. The prevalence of allergic rhinitis has begun to increase. Especially the patients with JC pollinosis has increased rapidly. In 1998 the prevalence of JC pollinosis was 16% average and became to 26.5% average in 2008 [3]. Also regional deviation due to environmental condition was observed, too. So we have studied annual fluctuation of Japanese important allergenic pollen and estimated them with climatic factor for prevent against JC and Cypress pollinosis at each area longitudinally.

Method

There are institutions in fourteen locations monitoring airborne pollen by Durham sampler in Japan between the latitude of 30 to 40 degrees north (Figure 1). We estimated the pollen count and climatic data close to nine pollen monitoring locations. These are north region, Tohoku and Hokuriku district (Sendai 140°54'E38°16'N, Niigata139°1'E 37°54' N, Toyama 137°12'E36°43'N), central region, Kanto, Tokai and Kinki district (Sagamihara 139°22'E 35°34'N, Hamamatsu 137°43'E34°45'N, Tsu 136°31'E34°44'N, Wakayama 135°10'E34°14'N) and south-west region, Kyushu district (Fukuoka 130°26'E33°42'N, Kumamoto 130°42'E32°49'N).

We have collaborated the facilities for monitoring. Sendai (Tohoku University), Niigata (Fujisaki Clinic, Tsukioka Clinic), Toyama (Toyama University),Takasaki (Sato Clinic), Sagamihara (NHO Sagamihara 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 Foresty Agency). And Japan Weather Support Center, Environmental Ministry, Fukuoka Prefecture Medical Association, Japan Medical University, Oita University and Worcester University have supported our investigation.

At each institute daily airborne pollen sample was collected by Vaseline coated glass slides which were fixed in the Durham's sampler and exchanged every morning, as a rule. The sampling slides were sent to our clinical institute. After staining the samples with saturated basic fuchsine (Calberla's stain) we identified the pollen grains at 400-power and counted them at 100-power through microscope. For the Durham's method, pollen counts were standardized expressing

***Corresponding author:** Reiko Kishikawa MD, PhD, Department of Allergology, the National Hospital Organization Fukuoka Hospital 4-39-1 Yakatabaru Minami-Ku Fukuoka Japan (zip cord) 811-1394, Tel: +81 92 565 5534; Fax: +81 92 566 0702; E-mail: kishi@mfukuoka2.hosp.go.jp

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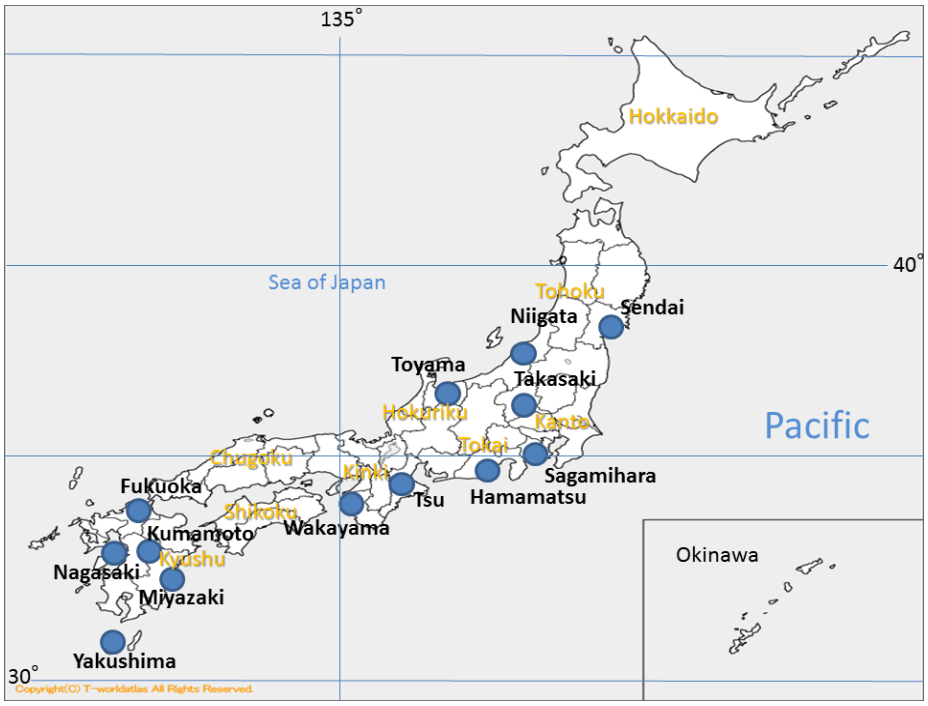

Figure 1: The locations of airborne pollen monitoring by Durham's Sampler.

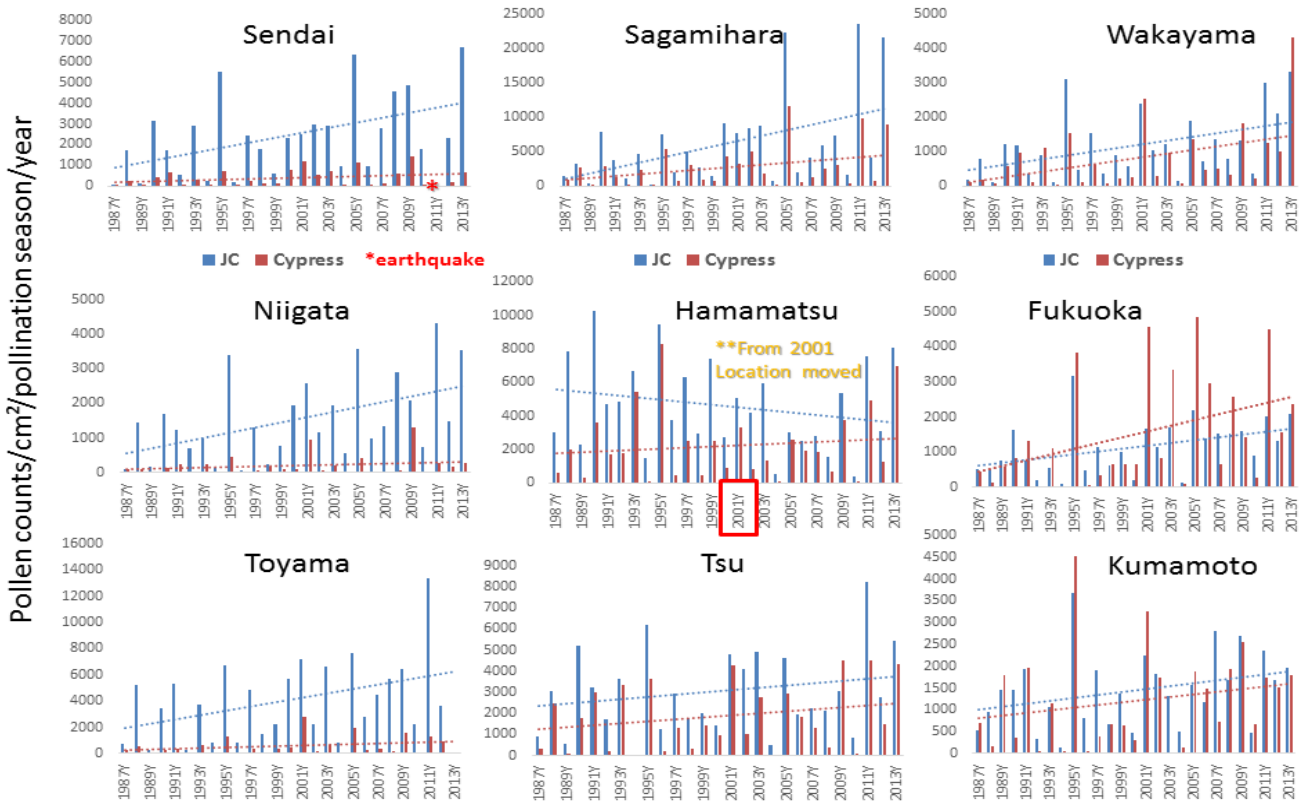

Figure 2: Annual fluctuation of conifer pollen counts (JC, Cypress) from 1987 to 2013 at 9 locations in Japan.

them as the number of pollen grains per cm^2, classifying and summarizing them [4]. From 1986 to 2014 we have referred to the annual change in monthly mean temperature using Japan Weather Association Home Page database. We have estimated annual JC and Cypress total pollen count and annual starting day of JC pollen dispersing with climatic conditions statistically by student t test.

Result

Annual pollen count and climate change

Figure 2 shows Annual fluctuation of the conifer pollen counts (JC, Cypress) from 1987 to 2013 at the 9 locations in Japan. Each vertical line shows pollen counting per cm^2per year and horizontal line shows year. We did not express pollen counting logarithmically because it is difficult to show the annual fluctuation visually. JC pollen counting is blue bar and Cypress red. The each dotted line shows approximation line. JC and Cypress pollen counts have shown huge but remarkable annual fluctuation and they have been increasing gradually. The pollen counts/cm^2/year is different from each location. In Sagamihara the most of all JC pollen counts was observed and next in Toyama, Hamamatsu followed. In Tohoku district Cypress pollen counts were less than the other region and in Kyushu cypress pollen counts have become increasing more than that of JC.

Each vertical line shows pollen counting per cm^2per year and horizontal line shows year. Both of JC and Cypress pollen counts have shown huge but remarkable annual fluctuation and they have been increasing gradually. The pollen counts/cm^2/year is different from each location. In Sagamihara the most of all JC pollen counts were observed.

Figure 3 shows annual change of mean temperature at the 9 cities in July and August when JC and Cypress male flower formation from 1986 to 2014 in Japan. Each vertical line shows mean monthly temperature and horizontal line shows year and the dotted line shows the approximation. The monthly mean temperatures are going to be rising of all area without exception.

In summer time JC and Cypress male flower formed. In the figure 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 going to be rising of all area without exception.

Table 1 shows the correlation ship between the mean temperature in summer time and the next annual total pollen counting of JC and Cypress. There are significant positive correlation between the annual summer mean temperature and the next total pollen counts of JC and Cypress especially in July (<0.05 to <0.0001). The higher summer temperature, the more these conifer pollen counts have become larger significantly.

Generally product of the conifer pollen grains correlates with the previous summer climate condition especially temperature and humidity. There are significant positive correlation (<0.05 to <0.0001) between the annual summer mean temperature and the next total pollen counts of JC and Cypress especially in July.

Annual starting day and climate change

Figure 4 shows Annual change of starting day in JC pollination at the 9 locations from1987 to 2014. Each vertical line shows days from 1st January and horizontal line shows year. And the dotted line shows the approximate. The starting day is going to be earlier in Tohoku (Sendai, Niigata), Hokuriku (Toyama) district, and later in Kanto (Sagamihara), Tokai (Hamamatsu) and Kinki (Tsu, Wakayama) districts. In Kyushu districts (Fukuoka, Kumamoto) are almost still.

Figure 5 shows the annual change of monthly Mean temperature of January and February just before and after JC pollination season at the 9 cities from 1986 to 2014. Each vertical line shows monthly mean temperature and horizontal line shows year. The dotted line shows the approximate. It has become a gradual fall in January and rise in February although the changing range is so small in Hokuriku or almost no change in Tohoku district.

Each vertical line shows monthly mean temperature and horizontal line shows year. The dotted line shows the approximate, the fluctuation tendency. It has become a gradual fall in January (blue line) and rise in February (red line) although the changing range is so small in Hokuriku or almost no change in Tohoku district.

Table 2 shows the correlation between starting day of Japanese cedar pollination and the mean temperature in January (blue line) and February (red line) when the JC pollen grains are near beginning to disperse from 1987 to 2014. In February we found significant negative correlation ship between the starting day and winter mean temperature (P=0.03 to p<0.0001). Especially they are distinguish in Sendai, Niigata and Hokuriku, north of Japan (p=0.0003 to p<0.0001). In January there are weak negative significant correlation ship between them in Sagamihara, Hamamatsu and Tsu (p=0.03 to p=0.003). Through winter climate change during about 30 years the starting day become earlier in north region and later in central region, the colder winter and the later beginning of JC pollinated season.

Table shows the correlation between starting day of Japanese cedar pollination and the mean temperature in January and February when the JC pollen grains are near beginning to disperse from 1987 to 2014. In February we found significant negative correlation ship between the starting day and winter mean temperature (P=0.03 to p<0.0001).

Discussion

Characteristics of hay fever in Japan

Japanese people had little conception on hay fever (pollinosis) historically. Before World War II some of researchers have reported and noticed to the presence of ragweed hay fever in Japan as same as USA [5]. Araki has reported airborne pollen and a patient with severe ragweed hay fever in Tokyo in 1961[6,7]. And then various kinds of cases such as grass, Japanese hop, mugwort and occupational hay fever were reported one after another during about one decade. In 1964 hypersensitivity to JC pollen was reported first as an allergic disease peculiar to Japan [1]. Thereafter, increasing number of patients suffering from JC pollinosis have been diagnosed in all Japan since the 1980s according as the over 31-y old JC plantation area increasing. Japanese people have recognized as a serious nationwide social problem and Japanese government has taken the countermeasure against the harmful pollinosis since 1986. Cypress pollen has strong cross reactivity to JC. Cypress pollen grains were recognized as one of important allergens as well as JC but weak allegenicity although JC has classified to Cupreccaseae family after genome analysis recently. In such circumstances we have had to investigate airborne pollen dispersion by monitoring its start, intensity and duration as a one of successful approaches to the national problem urgently. Gravitational sampling by Durham's sampler as a technically simple method which used already by our predecessors was immediately available and easy

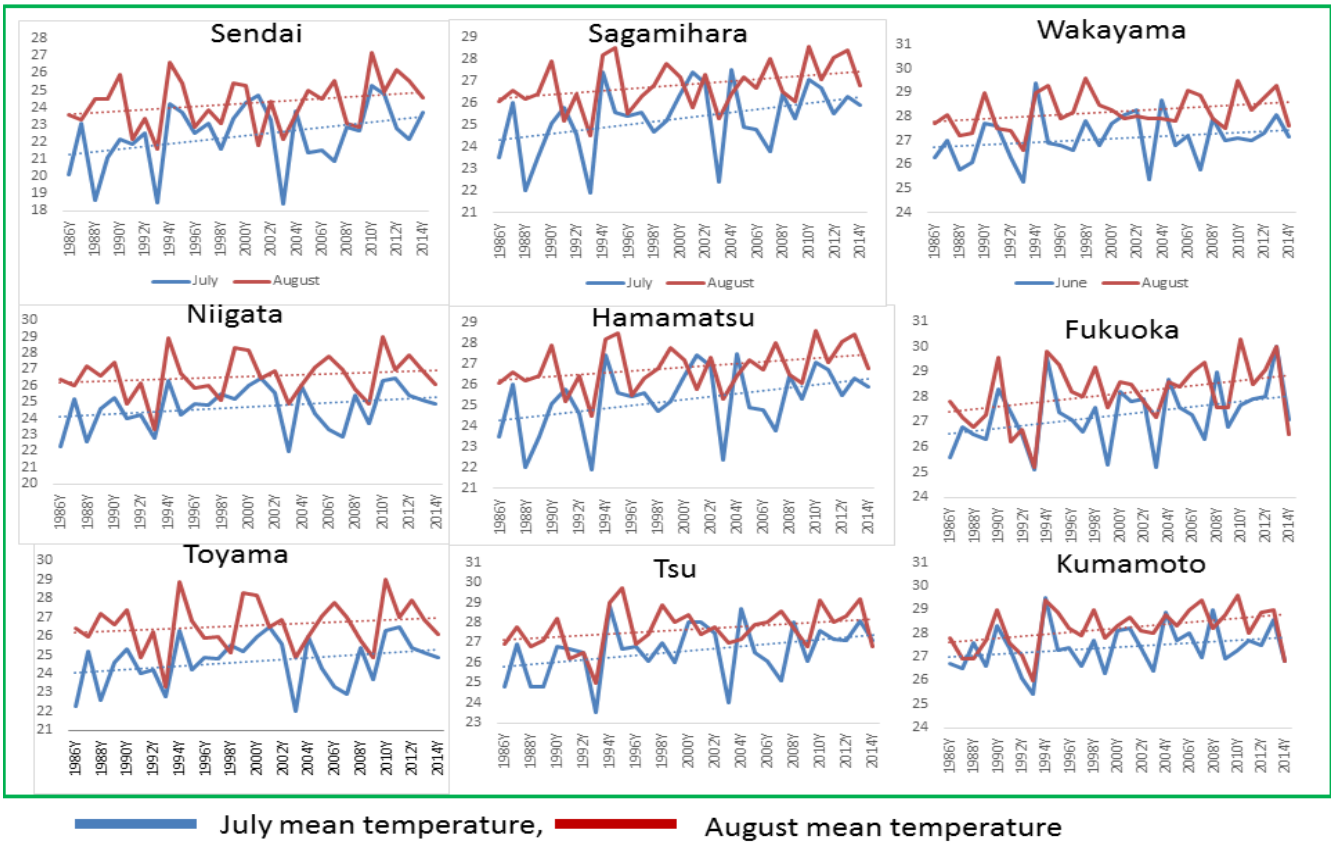

Figure 3: Annual change of mean temperature in July and August from 1986 to 2014 in Japan.

Table 1: Correlation between Total pollen counts of conifer pollen from 1987 to 2013 and the previous year of July, August mean temperature in male flower formation.

Japanese Cedar					
City	**July**		**August**		
Sendai	r=0.463	p<0.05		NS	p=0.064
Niigata	r=0.583	p<0.01	r=0.607		p=0.001
Toyama	r=0.629	p<0.001	r=0.676		p<0.001
Sagamihara	r=0.534	p<0.005	r=0.384		p<0.05
Hamamatsu	r=0.405	p<0.05		NS	p=0.064
Tsu	r=0.626	p<0.001		NS	p=0.815
Wakayama	r=0.570	p<0.005	r=0.476		p=0.05
Fukuoka	r=0.742	p<0.0001	r=0.652		p<0.0001
Kumamoto	r=0.780	p<0.0001	r=0.578		p<0.005
Cypress Family					
City	**July**		**August**		
Sendai	r=0.501	p<0.01		NS	p=0.121
Niigata	r=0.438	p<0.05		NS	p=0.248
Toyama	r=0.678	p<0.001	r=0.462		p<0.05
Sagamihara	r=0.551	p<0.005	r=0.453		p<0.005
Hamamatsu	r=0.466	p<0.05		NS	p=0.092
Tsu	r=0.673	p<0.001		NS	p=0.098
Wakayama	r=0.407	p<0.05		NS	p=0.216
Fukuoka	r=0.615	p<0.005	r=0.558		p<0.005
Kumamoto	r=0.729	p<0.0001	r=0.441		p<0.05

applicable by clinicians, who had a little knowledge on aerobiology in 1960s. For this reason the gravitational method using

Durham's sampler has become the most popular monitoring technique in Japan. Also this technique is suitable to huge number of JC and Cypress pollen grains every day for the information of pollen dispersing to the patients with Pollinosis. And then we have already reported strong positive correlation between Durham's and Burkard's conifer pollen counting in 2009 [8,9]. In 1986 we have started this investigation at 47 institutes each prefecture in Japan and 14 institutions of all have continued to investigate until 2014. On the other hand more than 31 years aged JC planting area has occupied about 70% of all the national JC forest because of unused of the timber (Figure 6). A large quantity of these conifer pollen grains has continued to product in our country however new JC and Cypress planting area has decreased.

More than 31 years old JC trees have become to product a large quantity of pollen grains. This Figure has made from the released annual data of the national forest area of planting in the Forestry Agency by Toshitaka Yokoyama from 1970 to 2007.

Meteorological condition affects this conifer pollen product

For the effective treatment and prevention of many patients with JC pollinosis it is important to monitor this conifer allergen and inform the medical doctors and patients by every measure such as mass communications quickly. JC and Cypress pollen product have been influenced by annual climate conditions especially

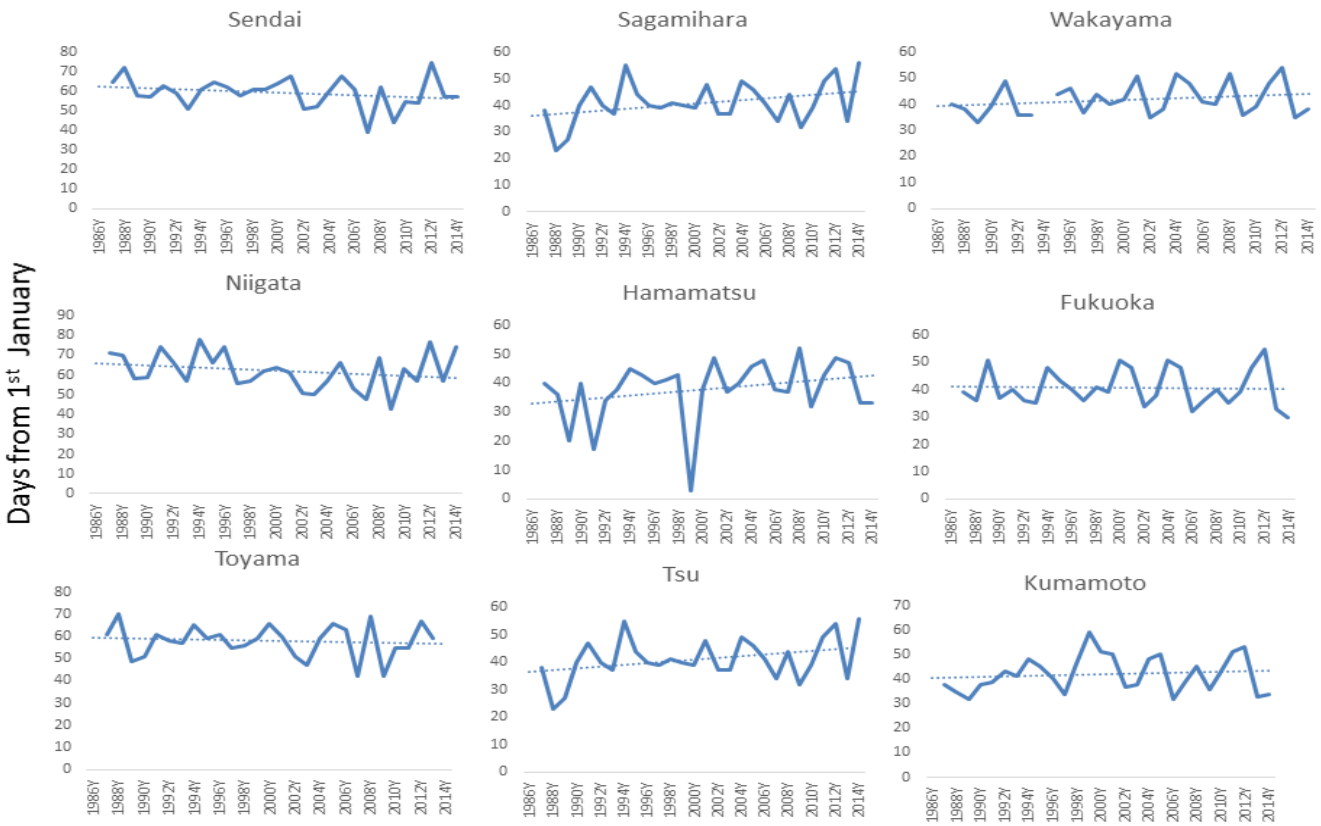

Figure 4: Annual change of starting day in Japanese cedar pollination from 1987 to 2014. Each vertical line shows days from 1st January and horizontal line shows year. The starting day from 1st January is going to be earlier in Tohoku (Sendai, Niigata), Hokuriku (Toyama) district, and later in Kanto (Sagamihara), Tokai (Hamamatsu) and Kinki (Tsu, Wakayama) districts. In Kyushu districts (Fukuoka, Kumamoto) is still.

Table 2: Correlation between starting day of Japanese cedar pollination and mean temperature near pollinated season from 1987 to 2014.

City	January	Average Temperature		February	Average Temperature	
Sendai	Y=3.541X+65.50	r=0.498	p=0.007	Y=5.482X+71.66	r=0.757	p<0.0001
Niigata	NS		p=0.210	Y=4.852X+77.09	r=0.637	p<0.0003
Toyama	NS		p=0.217	Y=4.664X+73.33	r=0.827	p<0.0001
Sagamihara	Y=4.803X+70.32	r=0.549	p=0.003	NS		p=0.551
Hamamatsu	Y=4.679X+66.74	r=0.409	p=0.031	NS		p=0.969
Tsu	Y=0.505X+61.45	r=0.444	p=0.020	NS		p=0.117
Wakayama	Y=4.316X+73.31	r=0.410	p=0.030	NS		p=0.183
Fukuoka	NS		p=0.444	NS		p=0.134
Kumamoto	NS		p=0.190	NS		p=0.148

summer time when the male flower forms remarkably. JC and Cypress pollen product is relative to higher temperature and lower humidity condition of the former summer of male flower formation. And the start of pollination has been influenced by meteo close to male flower matured term. Moreover male flower formation and dispersal of pollen depend on whether condition and geographic features. So we estimated the regional pollen data with some of meteorological conditions and hoped to predict this pollen dispersal trend in near future through the climate change properly. Generally the more pollen counting and the longer the pollen were dispersing duration. This time we did not estimate pollen dispersal duration and meteorological condition, next chance we have to check them.

Annual pollen counting and climate change

Both of JC and Cypress pollen counts have shown huge but remarkable annual fluctuation almost parallel in each location and they have been increasing gradually except in Hamamatsu. In Hamamatsu the pollen monitoring location has moved far from the first place. The pollen counts/cm^2/year is different from each location. In Sagamihara the most of all JC pollen counts were observed but less than 1,000 to more than 20,000 pollen grains/cm^2/season were counted. Everywhere pollen counting has been remarkable fluctuations. But in Tohoku district Cypress pollen counts were less than that of other region and the increasing pollen counting is not remarkable. Because planting of Cypress tree has been less extensive, prevailing from Fukushima Prefecture in the north to western part

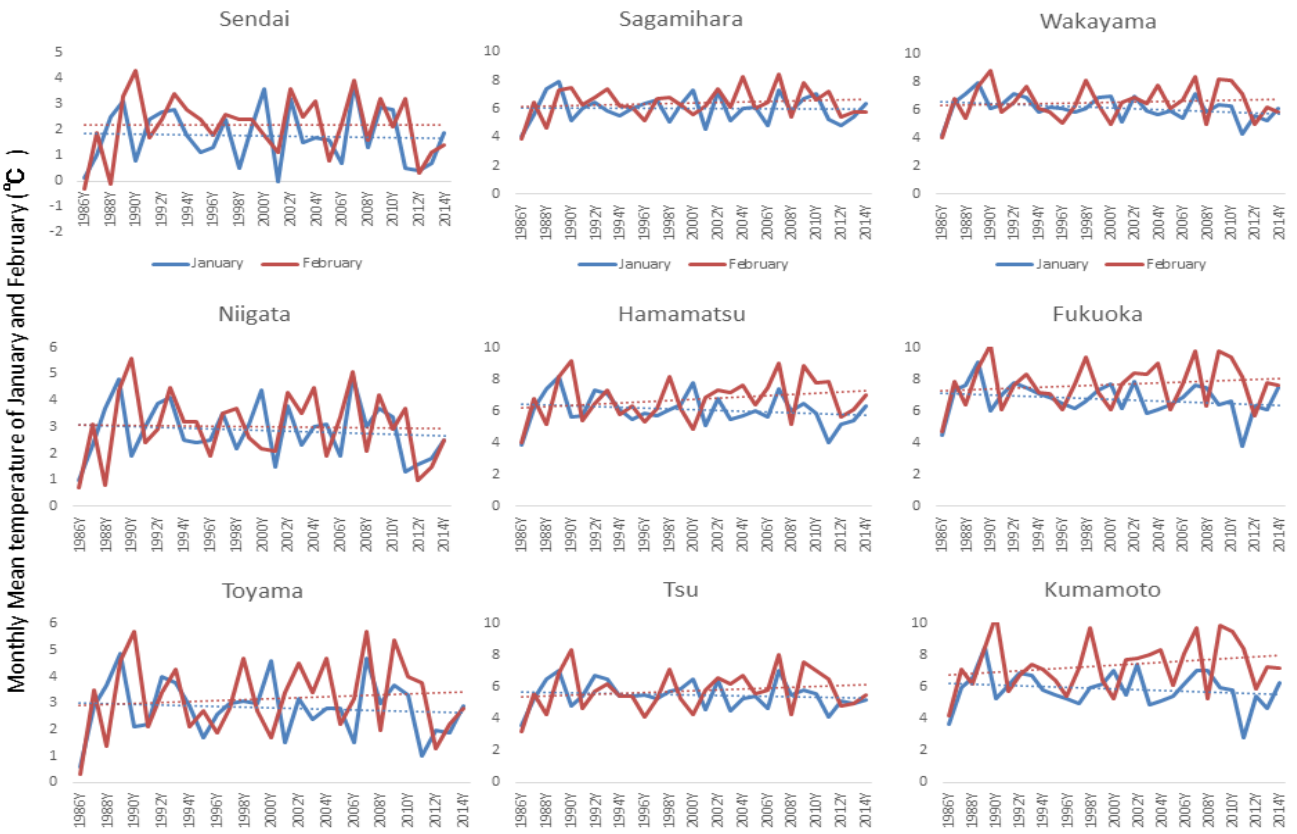

Figure 5: The annual change of Monthly Mean Temperature of January and February from 1986 to 2014.

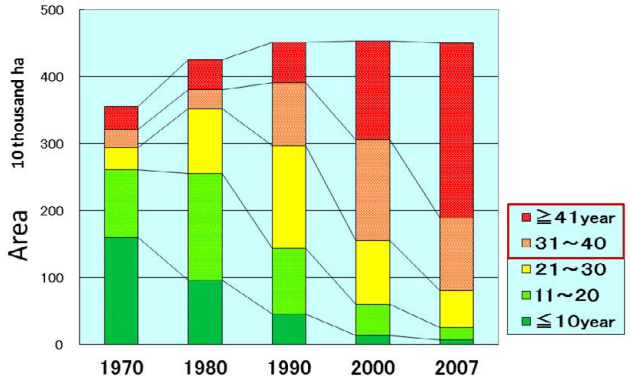

Figure 6: Japanese Cedar plantation National Forest in Japan.

of Japan Islands. In Kyushu districts Cypress pollen count have become increasing more than that of JC. But total Cypress pollen counting is more in Kanto and Tokai districts than that in Kyushu. The monthly mean temperatures are going to be rising of all area. There is significant positive correlation between the annual summer mean temperature and the next total pollen counts of JC and Cypress especially in July. The higher summer temperature the more these conifer pollen counts significantly even in Tohoku. JC antigen has cross reactivity and stronger allergenisity. And the production of JC pollen grains is larger in Kanto and Tokai districts where a large population living. It concerned that there are many serious patients with JC pollinosis including rhino conjunctivitis but also systemic allergic symptoms and related food allergy such as oral allergic syndrome [10], against all of generation exposed JC pollen antigen. Cypress antigen has contributed to effect human health too.

Annual starting day of JC pollen dispersing and climate change

It is important to know the starting of pollination before season related to successful treatment. Now the prediction of starting of JC pollen dispersal everywhere is essential measure for JC pollinosis.

The starting day is going to be earlier in north of Japan, and later in central Japan where huge pollen grains dispersing. We thought that JC pollination season would be going to start at almost same time in near future. On climate conditions it has become a gradual fall in January and rise tendency in February although the changing range is so small in Hokuriku and Tohoku district. JC male flower need low temperature for the dormancy in winter and next higher temperature become to start pollination after the dormancy. We found significant negative correlation ship between the starting day and winter mean temperature. Especially they are distinguish in north of Japan in February nevertheless annual mean temperature has not become changed clearly. This inconsistency of earlier change of the starting day and less temperature fluctuation in February has to be solved by conifer forest specialist hereafter. Moreover we need to estimate

with another climatic factor. In January there are weak significant correlation ship between them in Sagamihara, Hamamatsu and Tsu, Currently the colder winter and the later in JC pollinated season.

Economic importance of prediction

The total expenses came to more than 3 billion dollars for treatment patient with JC pollinosis and associated diseases [11]. So, the Japanese government has worked for the preventive measures. In medical and Health Welfare fields the continuous research for allergy and Immunology including JC pollinosis. Moreover Forest Agency, Ministry of Environment have many projects, they are nonproductive pollen cedar bleeding [12], promoting of comfortable forest around big cities, nationwide information network and prediction pollen dispersing precisely. Now we have full pollen network system by Durham's Sampler. We have more than 4 hundred locations observed JC and Cypress pollen count. About 100 stations work as nationwide pollen information by Japan Weather Association. We can get the data everyday by TV, newspaper, Radio, website and mobile in season. On the other hand real time monitor for selected JC and Cypress pollen grains has developed in one decade and informed hourly pollen data by website in Minister of Environment system. But we have many problems to continue useful and popular pollen information and forecast against changing JC pollinosis prevention for a long duration through a climate change.

Perspectives and Conclusion

Allergenic conifer pollen count has been increasing in Japan due to the 31 year old conifer plantation area. Moreover, it has changed the start of pollination. Accordingly we need to study the climate change by allergenic pollen grains in detail and also to apply the result as a successful tool for preventing JC pollinosis from aerobiology side.

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Author Affiliations

Top

[1]*Department of Allergology, the National Hospital Organization Fukuoka Hospital, Fukuoka, Japan*

[2]*The National Hospital Organization Sagamihara Hospital, Sagamihara, Japan*

[3]*Toho University, Funabashi, Japan*

[4]*Soh ENT clinic, Fukuoka, Japan*

[5]*Forestry and Forest Products Research Institute, Tokyo, Japan*

[6]*NPO Association of Pollen Information, Tokyo, Japan*