(Review)

Recent Advances in Pollen Survey and Pollinosis Research in China

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Introduction

In 1873, Charies Blackley built up a cornerstone in the research of aeroallergen. He firstly confirmed that the hay fever was resulted from allergenic pollen. From then on, the researches had been widely carried out about the aeroallergens and pollinosis. Till now, at the beginning of the twenty-first century, worldwide research has progressed into a comprehensive knowledge, including biology, geology, chemistry, immunology, genetics, clinical medicine and so on. We have gotten many achievements in the epidemiology, pathophysiology, detection, diagnosis and treatment of pollinosis. However, we still can not say that we have gotten the victory in combating pollinosis. On the contrary, the allergists now have to consider pollinosis, for example ragweed allergy, as a more serious global health problem, instead of some local disease. Pollinosis has been a common worldwide disease both in developed countries and in developing countries.

China is a vast developing country inhabited by about one fifth of the world's population. There is great diversity amongst the different climatic and topographic zones in China and results in the formation of extremely variable vegetation belts. Climate, topography, and the distribution of vegetation dictate the presence of pollen in the atmosphere. This can explain the complexity and the most of aeroallergens and pollinosis research in China. On the other hand, the Chinese government has been taking opening policy since 1978. The internal and international cooperation and exchanges have been sharply increased from that decade. As parts of the results, both the environment and socioeconomics have been greatly changed. There has been a lot of migration of people from rural areas to urban settlements. Those people have, more or less, confronted the altered lifestyle, changed food structure, and high levels of pollution which are strongly doubted to induce higher allergen sensitivity. In addition, numerous original topographies have been intruded, for example, by lots of newly built railways or express roads. As we have known now, those areas usually act as a natural terrain for some kinds of weed vegetation. It can directly affect the pollen distribution and bring influence by air fluid to not only the local residents but also those living far away.

The Chinese traditional medicine had recorded the symptoms of allergic disorder two thousand years ago. However, the modern research on allergy was not far from being carried out. It is not until 1939 that an allergy clinic was set up by Qing-Song Zhang within the Peking Union Medical College (PUMC) Hospital. In 1964, Rui-Jin Gu and Shi-Tai Ye firstly published their report about pollinosis in China. They diagnosed 100 cases of pollinosis with the skin test. The *Artemisia* (sagebrush) pollinosis was considered as the major summer-autumnal pollinosis in northern China. In 1978, Zhi-Yan Gu and coworkers detected 500 pollinosis patients in the northwest of China and obtained a familiar theory. Those discoveries greatly prompted the research on aeroallergens and pollinosis of China.

From 1985 to 1989, a National Survey of Airborne and Allergenic Pollen in China (NSAAPC) was successfully completed, led by Shi-Tai Ye, the Professor of Allergology at PUMC. The data were compiled in the form of a pollen map for different regions of China (Beijing Press, Beijing, 1991), except Taiwan, Hainan Province (established in 1988), Chongqing Municipality (established in 1997), Hong Kong SAR (established in 1997) and Macao SAR (established in 1999). Undoubtedly, it is of great value for allergists and researchers to understand the species and quantity of airborne allergenic pollen in China. Moreover, it also provided a good chance to preach pollinosis to the public and attracted many more recruits to join in.

In 1981, a nasal allergy group was installed within the Chinese Society of Otorhinolaryngology. Close behind, in 1986 an affiliated subcommittee of allergology was set up within the Chinese Society of Microbiology and Immunology. The committee has coordinated four national allergy congresses since its inception. Consequently, an independent academic organization, the Chinese Society of Allergology was established in May 2001. At the same time, the First Session of China Allergology Conference was convoked in Nanchang. It declares that the allergy research in China has stepped into a new stage. In this paper, we will try to review the studies on airborne allergenic pollen and pollinosis in modern China.

Survey of Airborne Allergenic Pollen

1. A national survey in 1980s

Started from 1985 and supported by the National Natural Science Foundation, a countrywide survey on airborne allergenic pollen, the NSAAPC, was conducted in China. There were a total of 79 examining stations included in this investigation (Fig. 1). Although it might not be in-depth enough in so huge a country, it really provided a comprehensive understanding about the quantity and species of allergenic pollens in China. It is a good guidance beneficial to not only the physicians who are treating the pollinosis but also the patients who are receiving the treatments. According to this historic pollen map, we extracted a tablet to list the common airborne allergenic pollens in 29 central cites of China (Table 1).

Pollens are the male gametes of plants, and they can be divided into tree pollen, grass pollen, and weed pollen. The tree pollen, such as *Pinus*, *Platanus* and *Broussonetia*, was dominating in eastern, southern and middle China. Whereas the grass and weed pollens, such as *Cannabis*, *Humulus* and *Chenopodiaceae*, were prior in the north, northeast, and northwest. The exception was *Artemisia* pollen, which extremely widespread in the most areas, and usually acted as the primate resource of airborne allergenic pollen in China. *Ambrosia* (ragweed) pollen was recorded in 15 regions and had not become major airborne pollen, except some districts in Liaoning, Jiangsu and Jiangxi Provinces.

2. Recent survey and trends

We can only acquire limited reports about airborne allergenic pollen survey in last decade (Table 2). It is difficult to give a sweeping summary on distributing changes of pollen pattern based on this table, but it may be helpful to hint some potential trends.

Artemisia pollen still is the most important allergenic pollen, especially in northern China. The morphologic attribution of *Artemisia* pollen in China has been described by Jiang *et al* (1996). Based on exine ornamentation the pollen could be divided into two types : type Ⅰ, the basal part of spinule corrugate and extend ; and type Ⅱ, the basal part of spindle nearly rounded. The distribution of these two kinds of *Artemisia* is different. Type I mainly distributed in dry soil with high altitude and latitude while type II, on the contrary, distributed in humid areas with low altitude and latitude. This may be useful for further understanding for *Artemisia* pollen spread and pollinosis episode.

Ambrosia pollen, which was found only prevalent in few districts according to the 1980s' NSAAPC, now has become more serious in those original districts, such as in Hebei and Hubei Provinces. There are two species of ragweed in China (Liu *et al*, 1997), namely short ragweed (*Ambrosia artemisiifolia L.*) and the giant ragweed (*Ambrosia trifida L.*). The former mainly distributed in the south of China while the latter in the northeast of China. It is believed that ragweed is still in progress.

Tree pollen is likely predominant in some areas. In Chongqing, locating in the southwest of China, tree pollen occupied all the five most species of airborne allergenic pollen (Hong *et al*, 2001 ; Huang *et al*, 2002), as shown in Table 2.

An epidemiological study focused on *Cryptomeria* (cedar) pollen and the pollinosis, the Collaborative Study on Cedar Pollinosis in China (CSCPC), supported in part by grants from Japan-China Medical Association (Tokyo, Japan) and Toka Foundation for Educational and Cultural Exchanges (Tokyo, Japan), has been begun from 1995, by our Sino-Japan co-research group (Miyoshi *et al*, 1997, 1998, 1999, 2001 ; Cheng *et al*, 1997, 1999 ; Taguchi & Cheng, 2000). Some characters about cedar and cedar pollen in China have been discovered.

Two million years ago when *Cryptomeria* came into being, it lived in China and Japan without any separation as the continents of them connected to each other. *Cryptomeria* lived separately as well as the continents of China and Japan in glacier period when the sea plane rose for melting of ice. Based on

Figure 1. The map of China and survey sites (black dots) of NSAAPC in 1980s
(*source* : NSAAPC. Beijing Press, 1991)

Table 1. Common airborne allergenic pollens in the central cities of China

Area	City, Province or Autonomous region	Common airborne allergenic pollen				
		No. 1	No. 2	No. 3	No. 4	No. 5
North	Beijing	*Art.*	*CaHu.*	*Ulm.*	*Cup.*	*Che.*
	Tianjin	*Fra.*	*Che.*	*Art.*	*Gra.*	*CaHu.*
	Shijiazhuang, Hebei	*Art.*	*CaHu.*	*Gra.*	*Pop.*	*Che.*
	Taiyuan, Shanxi	*Art.*	*Pop.*	*Sal.*	*CaHu.*	*Pin.*
	Huhhot, Nei-Mongolia	*Art.*	*Pop.*	*Che.*	*CaHu.*	*Gra.*
Northeast	Shenyang, Liaoning	*Art.*	*CaHu.*	*Amb.*	*Pop.*	*Pin.*
	Changchun, Jilin	*Art.*	*Ulm.*	*Pin.*	*Pop.*	*CaHu.*
	Harbin, Heilongjiang	*Ulm.*	*Art.*	*CaHu.*	*Sal.*	*Bet.*
East	Shanghai	*Pin.*	*Pla.*	*Gra.*	*CaHu.*	*Ulm.*
	Nanjing, Jiangsu	*Pla.*	*Pin.*	*Pte.*	*Amb.*	*Gra.*
	Hangzhou, Zhejiang	*Pin.*	*Pte.*	*Cup.*	*Pla.*	*Ulm.*
	Fuzhou, Fujian	*Pin.*	*Gra.*	*Mor.*	*CaHu.*	*Cor.*
	Nanchang, Jiangxi	*Pin.*	*Cup.*	*Gra.*	*Amb.*	*Pol.*
	Hefei, Anhui	*Bro.*	*Pla.*	*Lig.*	*Pte.*	*Liq.*
	Jinan, Shandong	*Art.*	*Pop.*	*Ulm.*	*CaHu.*	*Sal.*
Middle-South	Zhengzhou, Henan	*Pla.*	*Art.*	*Cup.*	*Pau.*	*Pop.*
	Wuhan, Hubei	*Pla.*	*Pin.*	*Bro.*	*Art.*	*Que.*
	Changsha, Hunan	*Pau.*	*Lig.*	*Cup.*	*Pin.*	*Gra.*
	Guangzhou, Guangdong	*Bro.*	*Pin.*	*Euc.*	*Gra.*	*Casu.*
	Nanning, Guangxi	*Pin.*	*Cup.*	*Gra.*	*Art.*	*Che.*
Southwest	Kunming, Yunnan	*Pin.*	*Aln.*	*Cup.*	*Cast.*	*Pop.*
	Chengdu, Sichuan	*Bro.*	*Pla.*	*Pte*	*Gra.*	*Pin.*
	Guiyang, Guizhou	*Pin.*	*Fir.*	*Cup.*	*Bet.*	*Gra.*
	Lhasa, Tibet	*Sal.*	*Pop.*	*Art.*	*Gra.*	*Cup.*
Northwest	Xi'an, Shaanxi	*Art.*	*Pla.*	*Cor.*	*Pop.*	*Cup.*
	Jiuquan, Gansu	*Pop.*	*Che.*	*Ulm.*	*CaHu.*	*Gra.*
	Yinchuan, Ningxia	*Art.*	*Che.*	*Gra.*	*Pop.*	*Ama.*
	Xining, Qinghai	*Art.*	*Pop.*	*Che.*	*Ama.*	*Bet.*
	Urmuqi, Xinjiang	*Ulm.*	*Ace.*	*Che.*	*Art.*	*Pop.*

Legends) *Ace.* : *Acer* ; *Aln.* : *Alnus* ; *Ama.* : Amaranthaceae ; *Amb.* : *Ambrosia* ; *Art.* : *Artemisia* ; *Bet.* : *Betula* ; *Bro.* : *Broussonetia* ; *CaHu.* : *Cannabis-Humulus* ; *Cast.* : *Castanea* ; *Casu.* : *Casuarina* ; *Che.* : Chenopodiaceae ; *Cor.* : *Corylus* ; *Cup.* : Cupressaceae ; *Euc.* : *Eucalyptus* ; *Fir.* : *Firmiana* ; *Fra.* : *Fraxinus* ; *Gra.* : Gramineae ; *Lig.* : *Ligustrum* ; *Liq.* : *Liquidambar* ; *Mor.* : *Morus* ; *Pau.* : *Paulownia* ; *Pin.* : *Pinus* ; *Pla.* : *Platanus* ; *Pol.* : Polygonaceae ; *Pop.* : *Populus* ; *Pte.* : *Pterocarya* ; *Que.* : *Quercus* ; *Sal.* : *Salix* ; *Ulm.* : *Ulmus*.

(*Source* : NSAAPC. Beijing Press, 1991)

the Chinese Botanical Annals (Science Press, Beijing, 1978), now, there are two kinds of *Cryptomeria* species in China, namely *Cryptomeria fortunei* (*Cf*) and *Cryptomeria* japonica (*Cj*). *Cf* lives only in China while *Cj* lives in both China and Japan.

We collected these two kinds of *Cryptomeria* pollen and compared in morphology. Under optical and electronic microscope (Fig. 2), no obvious distinction was found between them (Miyoshi & Sahashi, 1998 ; Yin *et al*, 2000). Furthermore, leaf samples of *Cf* (picked from Mountain Tianmu, China) and *Cj* (picked from Yakushima and Izu Ohshima Islands, Japan) (Fig. 3) were analyzed by allozyme (Sahashi *et al*, 1999). 18 gene loci were confirmed by the use of 14 kinds of enzymes. Only enzyme LAP had allele *a* in *Cf* and allele *a*, *b*, and *c* in *Cj* (Fig. 4). Taken together, we could recognize

Table 2. Recent survey on airborne allergenic pollen in some cities of China

Area	City, Province or Autonomous region	Rapporteur, Report Year	Common airborne allergenic pollen				
			No. 1	No. 2	No. 3	No. 4	No. 5
North	Qinhuangdao, Hebei	Han *et al*, 2001	*Art.*	*Pop.*	*Amb.*	*CaHu.*	*Gra.*
East	Shanghai	Ji, 2001	*Cry.*	*Pla.*	*Gra.*	*Pop.*	*Pin.*
	Linyi, Shandong	Du *et al*, 1992	*Hum.*	*Pin.*	*Pop.*	*Art.*	*Che.*
	Zibo, Shandong	Feng *et al*, 2000	*Art.*	*CaHu.*	*Pla.*	*Pop.*	*Gra.*
Middle-South	Wuhan, Hubei	Li *et al*, 1997	*Pla.*	*Pin.*	*Cup.*	*Sal.*	*Gra.*
		Lu *et al*, 1997	*Bro.*	*Pin.*	*Pop.*	*Amb.*	*Mor.*
		Liu *et al*, 1998	*Pla.*	*Art.*	*Pin.*	*Pte.*	*Cry.*
	Nanning, Guangxi	Zhang, 1996	*Pin.*	*Mor.*	*Gra.*	*Cup.*	*Art.*
	Guilin, Guangxi	Zheng *et al*, 1993	*Bro.*	*Pin.*	*Ric.*	*Lil.*	*Cep.*
Southwest	Chongqing	Hong *et al*, 2001	*Pin.*	*Bro.*	*Cup.*	*Sal.*	*Pte.*
		Huang *et al*, 2002	*Pin.*	*Bro.*	*Cup.*	*Sal.*	*Pte.*
	Guiyang, Guizhou	Wang *et al*, 1995	*Pin.*	*Fir.*	*Cup.*	*Gra.*	*Sal.*
Northwest	Xi'an, Shaanxi	Sun *et al*, 1994	*Art.*	*Pin.*	*Ros.*	*Cup.*	*Fir.*
	Lanzhou, Gansu	Chen *et al*, 1994	*Art.*	*Che.*	*Pop.*	*Jug.*	*Pin.*

Legends) *Hum.*:*Humulus* ; *Jug.* : *Juglans* ; *Lil.* : Liliaceae ; *Ric.* : *Ricinus* ; the other abbreviations were shown in Table 1.

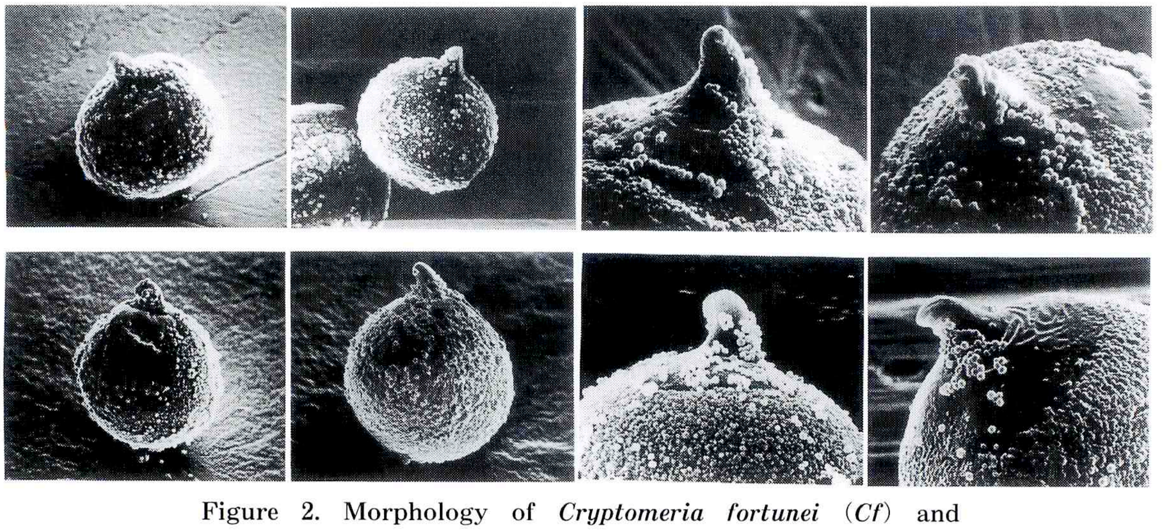

Figure 2. Morphology of *Cryptomeria fortunei* (*Cf*) and *Cryptomeria japonica* (*Cj*) pollens under SEM
Cf pollen : upper photos ; *Cj* pollen : lower photos.
(*source* : Miyoshi & Sahashi, 1998)

that although *Cf* and *Cj* grew separately in China and Japan they were in equal origin (Fig. 5).

Subsequently, a survey on cedar and cypress (Cupressaceae) pollens has been carried out by our group in Wuchang district of Wuhan City where *Cryptomeria* pollen has were found the most in 1980s' national survey. The Durham sampler was utilized in our survey. It was detected that cedar pollen began dispersing on February 29th in 2000 and March 1st in 2001, whereas cypress pollen started floating on March 5th in 2000 and February 18th in 2001. The total trapped grains of cedar pollen were 84 / cm^2 in 2000 and 194 / cm^2 in 2001, while that of cypress pollen were 502 / cm^2 in 2000 and 614 / cm^2 in 2001, respectively. The results showed that there were more cypress pollen grains than that of cedar pollen in the atmosphere of that district. Simultaneously, the positive spots of *Cry j*

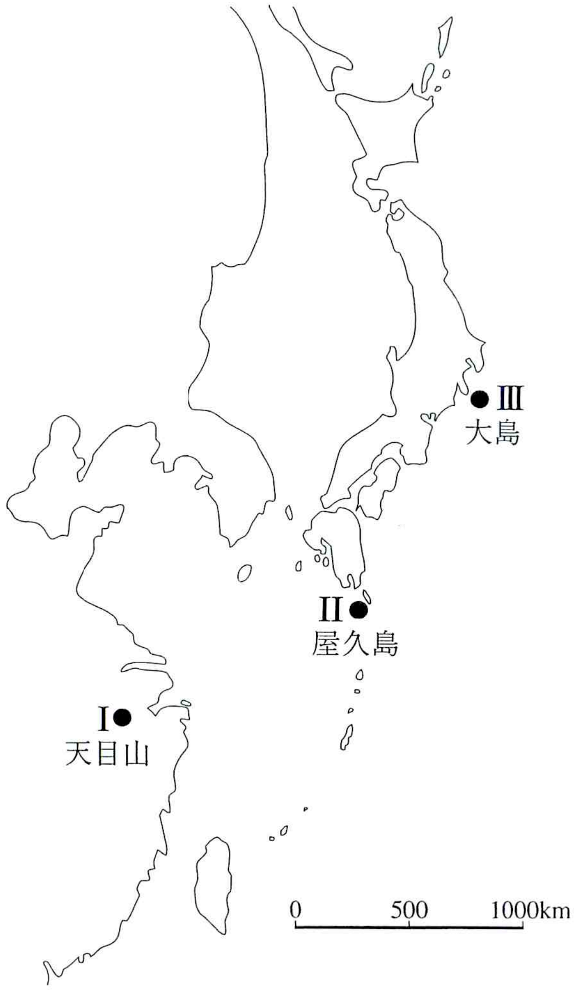

Figure 3. The collection places of *Cryptomeria fortunei* and *Cryptomeria japonica* samples

I : Mountain Tianmu, Zhejiang Province, China (altitude about 900m)

II : Yakushima Island, Kagoshima Prefecture, Japan (altitude about 1,000m)

III: Izu Ohshima Island, Tokyo Metropolis, Japan (altitude about 400m)

(*source* : Sahashi *et al*, 1999)

1, namely the major allergen element of *Cj* pollen, were counted by an aeroallergen immunoblotting technique. It was found that parts of cypress pollen grains in Wuhan were not stained by anti-*Cry j* 1 antibody, indicating that there was some cypress pollen not having the common antigens with *Cry j* 1 (Takahashi *et al*, in press).

Cryptomeria pollen was not collected in the urban of Shanghai according to the NSAAPC in 1980s. However, in 2001 Ji *et al* reported that it was the most among all floating pollens there (see Table 2). So, it is worth attracting attention to the trends of *Cryptomeria* pollen, the major offender of Japanese pollinosis, in China.

In addition, Su *et al* (1992) carried out an airborne pollen survey in Taichung, Taiwan. A total 17 families, 19 species of wind-pollinated pollens were trapped during their two-year collection (Feb. 1988 ~ Jan. 1990). They found that there was a direct relation between the amounts of pollens in air with the variables of weather conditions, especially the change of temperature.

3. Methodology on pollen survey

In China, the gravitational method is mostly adopted to collect airborne pollen. However, this method (ex. Durham sampler) is not effective enough to collect pollen grains. Furthermore, it is easily to be affected by local aspects of climate and can only provide a self-quantitative result. Supported by a China-France Cooperation Foundation, Huang *et al* (1999) recommended *Cour's* interceptor as a full-quantitative pollen analysis. Based on concentration, proportion, and radius of pollen as well as volume of air inhaled by adults per week on average, allergenic pollen amount inhaled within a week by adults during the maximum pollinating period can be further calculated. Therefore, a full-quantitative data can be provided to prevent and control pollinosis.

Some researchers discussed the relationship between the airborne pollen amount and meteorological factors. In a retrospective study, He *et al* (2001) found that the correlation coefficient for spring pollen amount with average temperature is 0.7031 ($P < 0.005$), with factual sunlight is 0.5311 ($P < 0.05$). Compared with average temperature, air pressure, humidity and water precipitate, the pollen amount in summer and autumn showed strong correlation as order by 0.7542 ($P < 0.001$), 0.7762 ($P < 0.001$) and 0.6432 ($P < 0.001$), while compared with wind speed, it showed negative ($r = -0.6142$, $P < 0.02$). A same result was also showed by univariate analysis. These results suggested that meteorological factors could significantly influence the pollen amounts in air.

In another research about the distribution of the airborne pollen, Li *et al* (2000) considered that the pollen mainly distributed in the space between 0 to 50m, and still some was found in 80m high space.

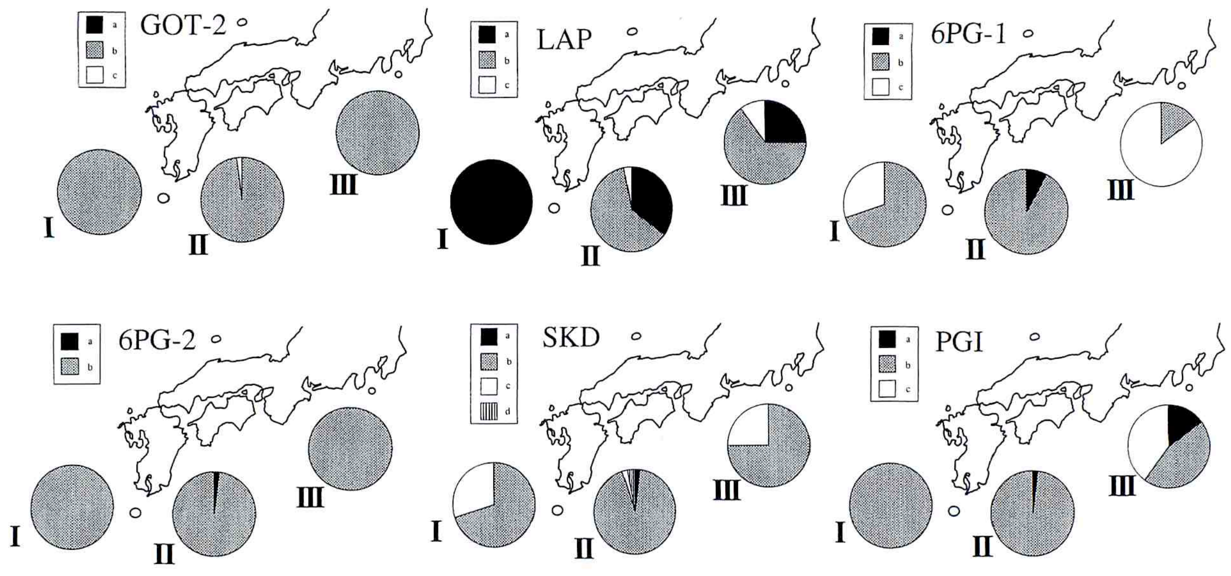

Figure 4. Allele frequencies of *Cryptomeria fortunei* and *Cryptomeria japonica* confirmed by allozyme
Sample collecting places I, II, and III were shown in Fig. 3.
(*source*: Sahashi *et al*, 1999)

Wind velocity, wind direction and temperature during the pollinating season emerged as the most influential factors. Relative humidity and distribution of high-rise also affected the space-time distribution of the airborne pollen to some extent. Their results may be useful for us to arrange monitor station and analysis the pollen data.

Epidemiological and Clinical Study on Pollinosis

1. General status

In 1970s, two large-scale epidemiological surveys on pollinosis had been completed among the local residents of northwestern China. In Urmuqi City of Xinjiang, the prevalence of pollinosis was 0.93% in 1978 (Gu *et al*, 1982). In Quanqigou district of Ningxia, the incidence was 0.03% in 1971 and sharply increased into 3.02% in 1978 (Gu & Chen, 1982). However, the overall prevalence of pollinosis in general Chinese population remains unclear.

In all the searched literature, the positive rate of allergic skin test to *Artemisia* pollen was consistently listed as the most of 5 kinds of pollen allergens in pollinosis, as shown in Table 3. *Artemisia* pollinosis, corresponding to its pollen quantity, is still very prevalent in China.

Ambrosia (ragweed), which has been alerted in China from 1980s, now has been popular in the middle-south of China and become a major allergenic pollen only second to *Artemisia* pollen (see Table 3). *Cannabis* and *Humulus* pollens rained in most of China, including the north, east, middle-south and southwest areas, and induced plenty of sensitized population there.

2. *Artemisia* pollinosis

Associations have been found, in some instances, with sensitivity to *Artemisia* aeroallergen and human leucocyte antigen (HLA) class II genes. Yang *et al* (1999) analysed the distributive speciality of HLA-DRB1 alleles in 35 allergic rhinitis patients with *Artemisia* pollen sensitization and 94 healthy controls of northeastern Han nationality. Using sequence-specific primer polymerase chain reaction (PCR-SSP), they found the frequencies of HLA-DRB1*0101.2 and HLA-DRB1*0302 alleles were significantly higher in patients than that in controls. In another study executed in *Artemisia* pollinosis patients from Beijing, the frequencies of HAL-DRB1*0301.2 and HLA-DRB4*0101 were found

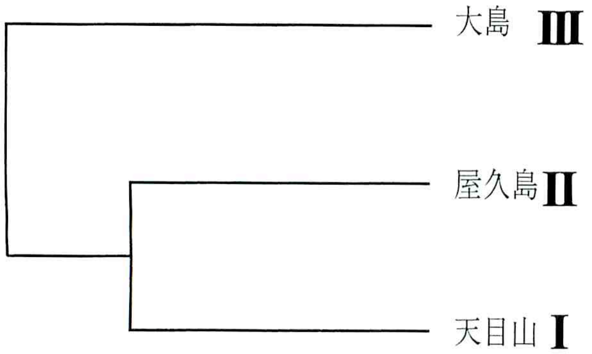

Figure 5. Genetic distance between *Cryptomeria fortunei* and *Cryptomeria japonica* calculated by UPGMA

Sample collecting places I, II, and III were shown in Fig. 3.

(*source* : Sahashi *et al*, 1999)

significantly lower in patients than that in controls (Xing & Yu, 2001).

An interesting experiment about *Artemisia* allergen was carried out by Leng *et al* (1987). They collected and extracted *Artemisia* leaves and stems before pollination time. In 52 subjects sensitive to *Artemisia* pollen, the pollen-free plant extracts were studied for allergenic activities using skin prick test, intradermal test, intranasal challenge and bronchial provocation test, and the positive responses were 92.3%, 100%, 66.7%, and 59.3%, respectively. Furthermore, in 30 seasonal asthmatics who gave negative responses to the pollen extract skin tests, and bronchial provocation showed negative results, too. It was concluded that pollen-free plant extracts did have *in vivo* allergenic activities. Analysis of the plant allergenic components *in vitro* should be included in further research on pollen allergen.

Sun *et al* (2001) discussed the possibility of two dimensional electrophoresis (2-DE) in protein analysis of *Artemisia* allergen extract. By routine method, sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE), there were four obvious bands and their molecular weights were 62kD, 52kD, 43kD, and 25kD, respectively. Then, 2-DE was used to analyzing pollen protein components. A total of 85 kinds of protein components were detected. The authors argued that 2-DE was a good method in protein analysis of *Artemisia* allergen and its potential value in allergic components needed to be further studied.

Fifty patients with both *Artemisia* pollinosis and plant food allergy were reported recently (Wen & Ye, 2002). The average age of onset of *Artemisia* pollinosis and plant food allergy was 24 years and 23 years 8 months, respectively. The common offending food were legumes, peach, peanut, and sunflower seeds. *Artemisia* pollinosis occurred prior to food allergy in 50% of the patients in comparison with plant food allergy occurred prior to pollinosis in about 29% for the patients and both of them occurred simultaneously in 21%. Nasal symptoms by inhalation of *Artemisia* pollen occurred in 96% of the patients, followed by conjunctivitis and asthma. Urticaria (66%) and oral allergy syndrome (40%) were common clinical manifestations caused by ingestion of plant food. The authors pointed out that patients with pollinosis must be in vigilance for the development of plant food allergy later.

Specific immunotherapy (SIT) for *Artemisia* pollinosis has been conducted in China. Leng *et al* (1987) reported a year round controlled trial of SIT in 50 patients with *Artemisia* pollinosis. SIT group received regular injection of *Artemisia* allergen extract for one year schedule, while control group only received systemic medication. The improvement rate was 78% in SIT group, and the nasal symptom scores were significantly improved compared with that of pretreatment and control group. Moreover, the positive decline rate of human basophil degranulation test (HBDT) in SIT group was significant in patients with improved symptoms than patients with unchanged symptoms. The results revealed that immunotherapy could induce desensitization of basophils and the induction might be allergen specific.

Wang *et al* (1997) evaluated *Artemisia* pollen-specific immuoglobulins (IgG, IgG4, and IgE) by means of enzyme-linked immunoadsorbent assay (ELISA) during rush immunotherapy in 49 patients with pollinosis. Six weeks after the beginning of course, the levels of specific IgG ($P < 0.001$) and IgG4 ($P < 0.05$) antibodies were significantly higher than those of patients before treatment. The authors concluded that rush immunotherapy might result in a rapid increase in

Table 3. Common pollen allergens in recent clinical study in China

Area	City, Province or Autonomous region	Rapporteur, Report Year	Positive rate of skin test				
			No. 1	No. 2	No. 3	No. 4	No. 5
North	Qinhuangdao, Hebei	Han *et al*, 2001	*Art.*	*Amb.*	*CaHu.*	–	–
East	Shanghai	Ji, 2001	*Mix 1*	*Mix 2*	*Mix 3*	*Amb.*	*Art.*
	Linyi, Shandong	Su *et al*, 2002	*Hum.*	*Art.*	*Pop.*	*Pin.*	–
	Zibo, Shandong	Feng *et al*, 2000	*Art.*	*CaHu.*	*Pla.*	*Pop.*	*Gra.*
Middle-South	Wuhan, Hubei	Li *et al*, 1997	*Art.*	*Amb.*	*Hum.*	*Pla.*	*Bro.*
		Liu *et al*, 1998	*Art.*	*Amb.*	*Pla.*	*Bro.*	*Gra.*
	Nanning, Guangxi	Zhang, 1996	*Art.*	*Amb.*	*Che.*	*Pin.*	–
Southwest	Chongqing	Hong *et al*, 2001	*Gra.*	*Hum.*	*Art.*	*Pin.*	*Bro.*
Northwest	Urmuqi, Xinjiang	Liu *et al*, 1996	*Fra.*	*Che.*	*Art.*	*Gra.*	*Hel.*
	Xining, Qinghai	Yang *et al*, 2001	*Art.*	*Mix 2*	*Mix 3*	*Mix 1*	–

Legends) *Hel.* : *Helianthus* ; *Mix 1* : Spring-Summer pollens ; *Mix 2* : Summer-Autumn pollens ; *Mix 3* : Winter-Spring pollens ; – : no data in the original paper ; the other abbreviations were shown in Tables 1 and 2.

IgG antibody levels. Furthermore, high specific IgG levels might implicate a clinical improvement in allergic patients due to the rush SIT.

Safety and efficacy are two important aspects in SIT. Yue *et al* (2001) reviewed 149 *Artemisia* pollinosis patients who had received SIT. A questionnaire was used in this survey. The total efficacy was 77.9%. In the maintaining stage of immunotherapy, 48.3% patients had topical side effects and 28.7% had systemic adverse reactions. The results suggested that high attention should be paid to the allergen concentration in maintaining stage of SIT.

3. *Ambrosia* pollinosis

Ambrosia (ragweed) pollinosis had generally been considered to be an exclusively North American problem before 1970s. Chinese allergists were in agreement with that there was no such problem in China because they did not found ragweed in their country. From the 1980s, the situation has changed dramatically. *Ambrosia* was detected in many districts of China and has been causing considerable health problem in an ever-increasing number of allergic patients (Yang *et al*, 1997 ; Han *et al*, 2001).

The earlier report of ragweed allergy came from Nanjing, Jiangsu Province, by Yang *et al* in 1983. They found 71.1% of allergic asthmatics showed positive skin reaction to ragweed pollen allergen, as 14.7% of investigated normal controls did. In 1985, Xia *et al* firstly reported the prevalence of ragweed pollinosis was 1.52% among general population of Shenyang, Liaoning Procince. In addition, incidence of ragweed pollinosis was reported about 1.04% in Qingdao, Shandong Province (Lu *et al*, 1994).

A campaign had been promoted to eradicate *Ambrosia* plants in China. However as soon as the campaign was stopped, ragweed quickly reconquered the cleared land and continued to spread. Nowadays, ragweed pollen has been one of the most allergenic pollens in parts of China. In the north and middle-south of China, the prevalence of positive skin reaction to ragweed pollen was only second to *Artemisia* pollen among pollinosis patients. As shown in Table 4, ragweed pollinosis seems to have existed in all areas of China. The skin test positive rate is much higher in those earlier invaded places, such as Jiangsu, Shandong, and Hubei Provinces.

According to a prevalence survey on pollinosis, carried out by our research group from 1998 to 1999 among medical students in Nanjing (Jiangsu Province), Guangzhou (Guangdong Province), Wuhan (Hubei Province), Kunming (Yunnan Province) and Xi'an (Shaanxi Province), the total positive rate of skin scratch test (SST) to ragweed pollen extract (Torii Pharmaceutical Co. Ltd., Japan) was 9.2% (see Table 4). Of 1660 subjects, 13 (0.78%) cases were diagnosed as ragweed pollinosis on the basis of questionnaire, nasal inspection, and SST (Shi *et al*, 2001).

Ambrosia pollen also has been proved to be one of the important allergens causing bronchial asthma. Lu *et al* (1994) studied airway provocation tests

Table 4. Prevalence of positive skin reaction to ragweed pollen allergen in Chinese

Area	City, Province or Autonomous region	Rapporteur, Report Year	Skin test of ragweed pollen allergen		
			Subject	n	Positive %
East	Nanjing, Jiangsu	Yang *et al*, 1983	AS	301	71.1
			NC	156	14.7
		Qi *et al*, 2001	AR	97	68.3
		Shi *et al*, 2001	MS	530	5.1
	Qingdao, Shandong	Lu *et al*, 1992	AR	624	67.7
Southeast	Kinmen, Taiwan	Tsai *et al*, 1997	AR	101	78.2
	Taipei, Taiwan	Tsai *et al*, 1997	AR	117	6.8
Middle-South	Huangshi, Hubei	Na *et al*, 2001	AR	263	54.5
	Wuhan, Hubei	Shi *et al*, 1997	AR	200	42.0
		Yang *et al*, 1997	AR	210	57.6
		Liu *et al*, 1998	AR	200	58.0
		Zhang *et al*, 2001	AR	59	32.2
		Shi *et al*, 2001	MS	309	13.9
	Guangzhou, Guangdong	Shi *et al*, 2001	MS	183	6.6
Southwest	Kunming, Yunnan	Shi *et al*, 2001	MS	293	15.4
Northwest	Xi'an, Shaanxi	Shi *et al*, 2001	MS	345	7.5

Legends) AR : allergic rhinitis patients ; AS : asthmatic patients ; MS : medical students ; NC : normal controls.

(APT) in 55 patients with ragweed pollinosis. Positive APT was found in 27 (49%) patients and dual late-phase responses in 11 patients (20%), single late-phase responses in 2 (3.6%) patients. Late-phase responses were related to the increased specific IgE and strong positive skin test.

Curiously, although there was no ragweed pollen floating in Kunming City (NSAAPC, 1991 ; Fang *et al*, 1992), ragweed pollinosis was exactly detected at there by our group (Shi *et al* 2001). The wind may play an important role in this situation. The European researcher (Jager, 1991) has reported the major parts of the ragweed pollen, when the wind blowing, could be transport by long-distance. In China, an indirect proof could be gotten from Wuchang district of Wuhan City. Although there were much more ragweed plants growing in the suburban site than in the urban, no statistic significance was found between the counts of ragweed pollen trapped in those two places (Yang *et al*, 1997). Over and above, an expressive phenomenon was shown by Zheng *et al* (1993). They were surprised to find that the total pollen counts trapped in a site surrounding by rare plants were, seriously, much more than that in another site with abundant plants.

It is evident that both the pollen load and the size of the contaminated areas are increasing. How to prevent and how to deal with ragweed pollinosis have become an emergent issue in China. Recently, some effective and available methods has been suggested which based on a better knowledge on ragweed biologic properties (Liu *et al*, 1997). Ragweed is very inclined to invading into newly annoyed places, such as the sides of newly built-up traffic routes or the nearby of new railway stations. In these places, ragweed usually forms the unique superior species in the first year. On the other hand, ragweed is sensitive to competition from other plants. It disappears in dense vegetation and/or in tree stands. Ragweed is also uneasy to survival at un-annoyed places. Now it is possible for us to identify the districts with favorable condition for permanent ragweed growth. However, it is difficult for people to eradicate ragweed, for example, planting at the railway sides with extensive "seed banks", every year. Then, importing tree or bush in those dangerous regions may mean the most cost-effective and available solution.

Ragweed pollinosis also has been proved to exited in Taiwan island. Tsai *et al* (1997) noticed a

Figure 6. Airborne quantity of *Cryptomeria* pollen and prevalence of skin scratch test positivity to *Cryptomeria japonica* pollen allergen in 5 survey sites of China
pollen count per annum*／prevalence of positive skin reaction (%)**
* NSAAPC data; ** CSCPC data.

dramatic increase in patients with allergic rhinitis in Kinmen. Most patients had characteristic seasonal variation which correlated with the pollinating season of ragweed. Then, ragweed pollen from Kinmen was collected, extracted and re-suspended for skin prick test (SPT) in both Kinmen and Taipei. Of 101 patients from Kinmen, 79 (78.2%) showed a positive response, while only 8 (6.8%) of 117 patients from Taipei responded to the same allergen. Furthermore, the SPT response rate to the most common indoor allergen, house dust mite, was detected too. The result showed a much lower rate in Kinmen than that in Taipei (25.7% vs 90.6%). It suggested that there were different aeroallergens in Kinmen and Taipei.

Using monoclonal antibodies with different specificity against the major allergenic components of ragweed pollen, Shen *et al* (1985) studied the cross-reacting with two tree pollens, two grass pollens and five other weed pollens which were common in Taiwan by the immunoblot method. It was reported that besides reacting with AgE and AgK of the ragweed pollen, the monoclonal antibody 48-5 also reacted with antigens of yellow dock (a kind of Polygonaceae) pollen with molecular weights of 40kD, 38kD, 24kD, and 21kD. From the results of allergen skin testing in 109 patients with bronchial asthma, the authors found that of 22 patients who had positive reaction to a crude extract of ragweed pollen, 18 (81.8%) also reacted to the crude extract of yellow dock pollen. It was concluded that there existed a common allergenic determinant between pollens of ragweed and yellow dock. Therefore, it may attribute to the expression of the sensitivity of patients to these two kinds of pollens.

4. ***Cryptomeria* pollinosis**

Cryptomeria pollinosis was firstly reported in

1964 in Japan and it was named as Japanese cedar (*Cryptomeria japonica*) pollinosis at that time (Horiguchi & Saito, 1964). Due to some reasons, cedar pollinosis has been increasing in Japan from 1970s. The prevalence even reached to 19.4% in Tokyo residents (Bureau of Public Health, Tokyo, 1997). Before 1990s, cedar pollinosis was consistently regarded as a unique Japanese problem because there was no the same pollinosis diagnosed in other countries. Now, this opinion is changed according to the CSCPC.

From 1995, our group completed a series of epidemiological study on cedar pollinosis in China. A total of 5820 participants (aged 6 - 24 years) were recruited in a prevalence survey on cedar pollinosis from 1995 to 2000. 3538 subjects were medical students from 5 medical colleges at Nanjing, Guangzhou, Wuhan, Kunming and Xi'an, while 2282 subjects were pupils of primary, middle, and high school from Wujiang City of Jiangsu Province, near Shanghai. The study was composed of three processes : 1) Questionnaire investigation for symptoms ; 2) Nasal inspection for signs ; and 3) Allergen skin scratch test. We found that the total prevalence of positive SST to *Cj* pollen extract (Torii Pharmaceutical Co. Ltd, Japan) was 4.1% (Yin *et al*, 2001). Of 3827 subjects examined from 1995 to 1998, 10 cases (0.26%) were diagnosed as cedar pollinosis (Yin *et al*, 1999). A link also was found between the SST positive rate of cedar pollen allergen and the pollen count among different sites (Fig. 6).

It is important to note that the first clinical case of cedar pollinosis (32-year-old, female) outside Japan was found in Nanjing on March 3rd, 1998 (Yin *et al*, 1999). Just at that time, the existence of "cedar pollinosis" in China was undoubtedly fully proved.

Recently, our coworkers performed a clinical study at Wuhan University Renmin Hospital in spring of 2000. Among 205 patients with allergic rhinitis, 28.8% was hypersensitive to *Cj* pollen allergen (Xu *et al*, 2000 ; Zhang *et al*, 2001). The results suggested that it is worth paying more attention to the trends of cedar pollinosis in China.

5. Gramineae pollinosis

In 1980s' NSAAPC, Gramineae pollens were found in nationwide. It comprised about 0.43% ~ 18.77% of the total pollen counts in a whole year. In Fuzhou (Fujian Province), Shenyang (Liaoning Province) and Shijiazhuang (Hebei Province), the rates were 18.77%, 18.36% and 17.68%, respectively. We really could not ignore the activity of Gramineae pollens to local pollinosis.

Orchard grass (*Dactylis glomerata*) is the representative allergenic species of Gramineae family. It is also regarded as one of the main allergenic pollen in the world, especially in the United Kingdom. Gramineae pollen rains have two peaks during a round year. One is in later spring and early summer, and the other is in the autumn. There are some morphologic differences between these two peaks. The pollen grains in spring-summer are much smaller than that in autumn. This makes the distribution in autumn be limited correspondingly. Thus, Gramineae pollinosis in autumn is also quite less than that in spring-summer season. Orchard grass pollen acts as an important role in the first peak.

Since 1995, our group has conducted a survey of orchard grass pollinosis in China. From 1998 to 1999, a comparative study was completed in several regions (Cheng *et al*, 2001). Among 1660 medical students, the total prevalence of positive SST to orchard grass pollen extract (Torii Pharmaceutical Co. Ltd, Japan) was 5.1%, and the prevalence of orchard grass pollinosis was 0.36%. Among allergic rhinitis patients, 17.4% showed the positive skin reaction to orchard grass pollen in Nanjing while 24.4% in Wuhan. We believe that Gramineae pollinosis is a common seasonal allergic rhinitis in Chinese population. Further observation and research is necessarily.

6. Some other pollinosis

Humulus pollen is also an important allergenic pollen in certain regions of China, such as Shandong, Shanghai. The 1980s' NSAAPC showed that *Humulus* was one of the most 5 kind pollens in 10 regions. By a recent report conducted in Shandong Province, *Humulus* was found to be the most major allergenic pollen on both its counts and allergic sensitivity (Su *et al*, 2002).

Fraxinus plants mainly distribute in the west of China, especially in northwestern China. It was the major offender in children pollinosis (Liu *et al*, 1996). Interestingly, most of the patients were the immigration from other districts.

Other tree pollens, such as *Pinus*, *Broussonetia* and *Platanus* were often found to be prevalent in certain districts of China (see Table 2 and 3). These trees were usually planted densely and quantitatively. In mature stage, the tree pollens were easy to form pollen rain and then caused a hurricane of pollinosis.

Conclusion Remarks

This paper has presented two out of many activities in the field of Allergology and Palynology going on in China. It maybe contributes to understand the seriousness of pollinosis in Chinese population. On the other hand, although those researches were mainly carried out during the last decade, most of them can only be considered as the primitive studies in certain sites. They are not efficient to demonstrate the time trends of pollinosis in China because of the short of successive data. We can only say that we have set off and begun to perceive the problems. The pollinosis in Chinese may be more serious than we think now. We still have much to do.

Grass and weed pollens now are definitely the most important aeroallergen in China. Corresponding to its widespread distribution and high allergenic sensitivity, *Artemisia* pollen still is the major offender in Chinese pollinosis. On the other hand, ragweed has imported to many districts of China and is very likely to continue. If there no effective defense strategies were executed, ragweed pollinosis will surely induce more health problems in Chinese population. Beyond that, the existence of cedar pollinosis in China has been proved by our group, although its prevalence remains very lower. Future observation on epidemic trends of cedar pollinosis in Chinese population is really needed and it also may contribute to clarify the reasons of significant increase in prevalence of Japanese cedar pollinosis over the past 2 to 3 decades.

Although a national allergenic pollen survey was carried out in 1980s, we still have not had a countrywide epidemiological survey on pollinosis in China till now. We do not know the accurate incidence and prevalence of pollinosis in Chinese population. Determination of the epidemic conditions of pollinosis and description of the epidemiological characters constitute the essential steps toward the control of this problem. So, it is very necessary to conduct a nationwide epidemiological investigation under a uniform standard.

Airborne pollen, which is round and light, travels very long distances, possibly affecting sensitive individuals some distance from the source. The problem in China is that data from all regions are not available promptly. It is either incomplete or has been published in local publications only. Thus a nationwide, at least a region-wide network on pollen monitoring and forecast is needed. In spreading season, the data should be spread via public media, such as newspapers, radio, television, or internet. This is helpful not only for the public to get the information about pollen count but also for the allergists to quest the countermeasure.

Good quality allergen extracts are still lacking in China. By now, no professional Chinese companies are producing the allergen extracts from local resource materials for clinical diagnosis and research. Furthermore, this status may extremely restrict the therapeutic levels and immunotherapy results. It is hoped that the present conditions will change in the foreseeable future.

In view of the increased incidence of allergic disorder, including pollinosis in China during the last decade, health planner and policy makers have started realizing the significance of preventive measures in tackling this new health problem. Moreover, another important key in preventing this disease is to politically progress the effective educational programs addressing the public in China. Then, prophylactic treatment can be started two to three weeks before the pollen season to prevent priming by allergen.

Nowadays, pollen allergy has already become a worldwide health problem. Global prevention of allergy in the new century is the common aim for all allergists. By all means, international cooperation and exchanges are essential for good results.

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中国における空中花粉調査および花粉症研究の進歩

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中国は，世界で初めてアレルギーの記録された国の一つである．しかし，中国における空中花粉調査および花粉症研究の歴史は，比較的に浅いと言わねばならない．1939年，北京協和医学院にアレルギークリニックが設置されたが，1964年までヨモギ花粉症の確証例が初報告されてきた．1980年代に入って，花粉症の原因花粉が次々と発見されている．ヨモギ属花粉が，中国の主に北部地方の最も重要な空中花粉であることは，いくつかの疫学調査によって改めて実証されている．

中国は広大で植物の種類も多種にわたるため，地域によって空中花粉の飛散に大きな差異がみられる．花粉症の原因花粉の全貌を把握する目的で，1985年から1989年にかけて全国79観測場所で花粉飛散状況調査が行われ，その成果は「中国気伝致敏花粉調査」という単行本（北京出版社，1991）として集大成された．本調査の結果，中国の主な空中原因花粉（学名のABC順）はカエデ属，ハンノキ属，ヒユ科，ブタクサ属，ヨモギ属，カバノキ属，コウゾ属，アサ属，クリ属，モクマオウ属，アカザ科，ハシバミ属，ヒノキ科，ユーカリ属，アオギリ属，トネリコ属，イネ科，カナムグラ属，イボタノキ属，フウ属，クワ属，キリ属，マツ属，プラタナス属，タデ科，ポプラ属，サワグルミ属，コナラ属，ヤナギ属，ニレ属など30種類であった．北部（華北・東北・西北）地方では草本花粉が圧倒的多数を占めたことに対し，東部と中南（華東・華中・華南）地方では樹木花粉が主な原因花粉になった．ヨモギ属花粉は例外で，その分布はほぼ中国の全域に広がっている．近年，ブタクサ属花粉は急速に蔓延し全国多くの地域に飛躍的に波及され，ある地域でヨモギ属花粉に取って代わる傾向がある．

空中花粉調査が注目された折に，花粉症につきまして疫学や臨床研究が行われている．1978年新疆自治区首府のウルムチ市の調査では，一般住民の花粉症有病率は0.93%となった．なお，寧夏自治区泉七溝地区における，花粉症の発症率は1971年には0.03%たったそれは1978年の時点で3.02%に増加しており，8年間に100倍に急増したとされる．最近の動向について，われわれのグループは江蘇省をはじめとする5つの地域でブタクサやカモガヤ，スギ花粉症などの調査結果を報告しているが，残念ながら，今まで全国レベルの疫学調査が行われておらず，中国人全体の花粉症有病率に関する報告はない．

スギはこの地上に出現したのは約200万年前のことであった．「中国植物誌」の記載によって，中国では *Cryptomeria fortunei*（*Cf*）と *Cryptomeria japonica*（*Cj*）という2種類のスギが植生している．一方，スギ属花粉の飛散は，1980年代中国の全国調査ではいくつかの地域にみられた．1995年から，われわれ共同研究グループは中国におけるスギ花粉症の実態調査を行っている．*Cf* と *Cj* の花粉を光顕そして走査電顕で観察し，これらを比較検討すると，両者間に花粉形態学的な相違はほとんど認められなかった．なお，中国の天目山と日本の屋久島・伊豆大島で採集したスギの針葉を，酵素多型による遺伝子解析からは *Cf* と *Cj* は品種程度の分化しかなく，別種に分類する必要性は示唆されなかった．疫学的には，中国の児童・青少年において鳥居製のスギ花粉アレルゲンエキスに陽性反応を示す症例がみられ，その感作率は4.1%であった．さらに臨床の場でも，われわれは日本以外における初めてのスギ花粉症症例を発見してきた．これらの事実から，スギ花粉症は日本独特のものとは断言できない．

近年，花粉症などアレルギー疾患は，中国も含め世界諸国に増加しつつあり，大きな健康問題となっている．したがって，国際的交流や共同研究は花粉症を克服するための努力に重

要な一環である．中国における空中花粉調査および花粉症研究の今後の進展に，大きな期待を寄せている．

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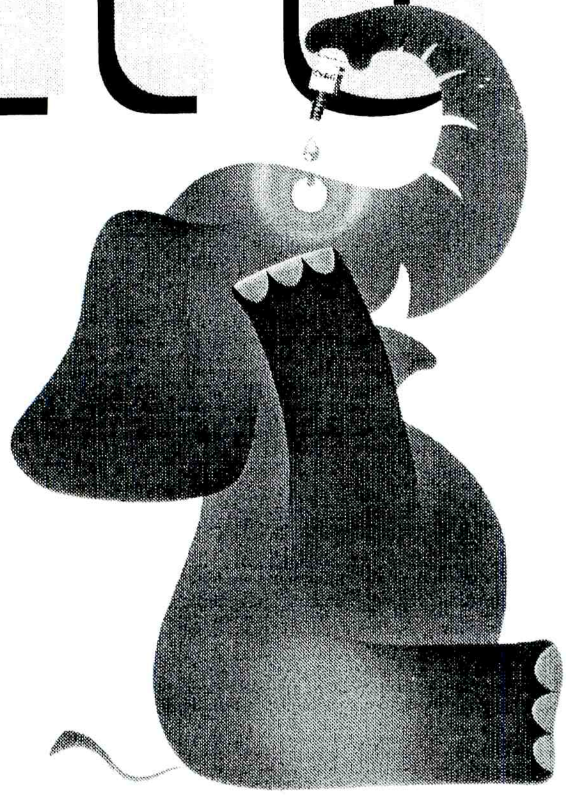
It's EYE



禁忌(次の患者には投与しないこと)
本剤の成分に対し過敏症の既往歴のある患者

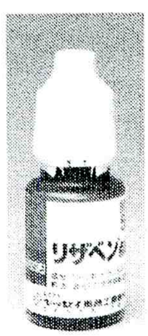
効能・効果
アレルギー性結膜炎
用法・用量
通常,1回1〜2滴を1日4回(朝,昼,夕方及び就寝前)点眼する。
使用上の注意
1.重要な基本的注意
重症例には本剤単独では十分な効果が得られないので,他の適切な治療法への切替えあるいはそれとの併用を考慮し,本剤のみを漫然と長期に使用しないこと。
2.副作用
329例中5例(1.52%),5件の副作用がみられ,その内訳は刺激感,眼瞼皮膚炎,眼瞼炎,角膜上皮糜爛,しみるであった(承認時までの集計)。

	頻度不明	0.1〜5%未満
過敏症(注)	接触性皮膚炎(眼周囲)	眼瞼皮膚炎,眼瞼炎
眼	結膜充血,眼瞼腫脹	刺激感,瘙痒感

注):発現した場合には,投与を中止するなど適切な処置を行うこと。
3.妊婦,産婦,授乳婦等への投与
妊娠中の投与に関する安全性は確立していないので,妊婦(特に約3カ月以内)又は妊娠している可能性のある婦人には投与しないことが望ましい。[動物実験(マウス)で,本剤の経口大量投与により,骨格異常例の増加が認められている。]
4.小児等への投与
低出生体重児,新生児,乳児に対する安全性は確立していない(使用経験がない)。
5.適用上の注意
1)投与経路:点眼用にのみ使用すること。
2)点 眼 時:容器の先端が直接目に触れないように注意すること。
眼周囲等に流出した液は拭き取ること。

リザベン点眼液の特性

1. 季節性および通年性のアレルギー性結膜炎に効果を示す点眼液です。
2. 瘙痒感、眼脂、結膜充血をはじめ、結膜濾胞(ろほう)も改善します。
3. pH7.0〜8.0、浸透圧比0.9〜1.1の点眼液です。
4. ケミカルメディエーター(ヒスタミン、ロイコトリエン等)の遊離を抑制します*(in vitro)*。
5. 副作用発現率は1.52%(5/329例)でした。
副作用の内訳は刺激感(0.3%)、眼瞼皮膚炎(0.3%)、眼瞼炎(0.3%)、角膜上皮びらん(0.3%)、しみる(0.3%)でした。
(承認時までの集計)



アレルギー性結膜炎治療剤

指定医薬品

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