



**\*Correspondence**

**Akira Awaya,**  
Dermatology & Epidemiology Research  
Institute (DERI), 4978 Totsuka-cho,  
Totsuka-ku, Yokohama, Kanagawa  
244-0003, Japan.

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Trend of asthma death, 1978-1996, Kawasaki disease(KD), allergic rhinitis, Influenza(flu), onset, fluctuation, pollen exposure, pollen dispersal, pollen scatter, pollen counts, pollen level, a large amount of pollen release e-Stat

**Abbreviations**

pollen exposure: PE; Kawasaki disease: KD; Influenza: flu

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## In Japan, asthma mortality declined from 1950 to 2019, but halted in 1978 and continued to stall till 1996, plateauing at high levels. Notably, 1978 marked the onset of widespread pollen dispersal in Japan, suggesting increased pollen exposure may have influenced asthma severity, contributing to symptom changes, worsening, and exacerbations during this period nationwide

Akira Awaya<sup>1,2\*</sup>, Yoshiyuki Kuroiwa<sup>3-5</sup> and Tatsuya Yamashita<sup>6</sup>

<sup>1</sup>Dermatology & Epidemiology Research Institute (DERI), Yokohama, Kanagawa, Japan

<sup>2</sup>Graduate School of Nanobioscience, Yokohama City University, Yokohama, Kanagawa, Japan

<sup>3</sup>Department of Neurology and Stroke Center, University Hospital Mizonokuchi, Teikyo University School of Medicine, Kawasaki, Kanagawa, Japan

<sup>4</sup>Department of Medical Office, Ministry of Finance, Japanese Government, Chiyoda-ku, Tokyo, Japan

<sup>5</sup>Department of Neurology, Yokohama City University Graduate School of Medical Sciences, Kanazawa-ku, Yokohama, Japan

<sup>6</sup>200-10 Fukudomari, Naka-ku, Okayama-City, Okayama, Japan

**Abstract**

**Background:** While examining a bar graph showing asthma deaths in Japan since 1950, the author noticed that the steady downward trend had temporarily shifted to a sharp increase in 1995, and suspected that this phenomenon might be an extremely useful clue in investigating the cause of death from asthma. 1995 was the year that saw the largest amount of pollen ever recorded at that time. The author found in 2003 the association between pollen dispersal levels and the onset of Kawasaki disease (KD) during 1970 to 2003 and has reported on the phenomena in four papers by 2016. Subsequently, the author analyzed the correlation between the dynamics of seasonal influenza cases and fluctuations in pollen counts within Kanagawa Prefecture during the period from 1991 to 2002. As a result, the author discovered that seasonal influenza outbreaks occur annually 10 months after the peak pollen exposure period, similar to KD.

**Methods:** The author then created a graph by merging a line graph showing the trend in asthma deaths with a line graph analyzing the correlation between seasonal influenza patient numbers and pollen count fluctuations within Tokyo and Kanagawa Prefectures.

**Results:** The declining trend in asthma deaths was interrupted in 1978, the year that marked the beginning of massive pollen dispersal in Japan. During this period from 1978 to 1996, asthma deaths fluctuated, but peaks in asthma-related deaths were observed three times around 1980, 1983, and 1985-6.

Remarkably, three peaks in the number of KD cases occurred at almost the same time in 1979, 1982 and 1985-6, coinciding precisely with three peaks in pollen dispersal counts. An astonishing phenomenon existed: three independent metrics—the number of asthma deaths, the number of KD patients, and the number of hay fever sufferers—showed a perfect correlation, demonstrating three simultaneous increases in peak numbers at precisely about the same time.

Peaks in pollen dispersal continued in 1988, 1990, and 1993. As a result of this sustained exposure to pollen, a growing number of patients have developed severe chronic conditions, placing them at risk of dying from asthma.

**Conclusions:** The author interpreted the reason for the transient surge in asthma deaths in 1995 as follows: patients in this asthma death reserve group were exposed to the largest-ever mass pollen exposure at the time, occurring in early spring 1995. This exposure caused them to die one after another each month, as if clearing out a stockpile.

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## Introduction

(1) It has become clear that 2018 was a year with a high number of patients suffering from various diseases in Japan, including Kawasaki disease (KD), cancer, and designated intractable diseases.

The pollen count in Tokyo was highest in 2005, followed by 2011. 2018 ranked as the third-highest pollen count year on record, trailing 2011 by a narrow margin [1].

According to the 2018 Tokyo Metropolitan Government fixed-point weekly reports, the total number of KD cases over 52 weeks reached a record high [2]. A nationwide survey in 2018 later revealed that the total number of KD patients nationwide also reached a record high, matching the total number of patients in Tokyo [3].

Meanwhile, the National Cancer Statistics Survey also reported in spring 2021 that the number of new cancer cases in 2018 was the highest on record [4].

Similarly, the number of patients registered for designated intractable diseases in 2018 also showed a steady increase [5]. Whether 2018 was also a notable year for the incidence of other diseases besides designated intractable diseases remains to be seen, pending further research by others.

(2) Utsumi et.al reported in the paper of Pediatrics titled “Rate of asthma prescriptions for children and adolescents during the 2018 floods in Japan”, that “The 2018 Japan floods increased the demand for asthma inhalers among flood victims, underscoring the general implication that natural disasters can increase the incidence of asthma” [6]. To this publication we added comment [7] that the increase in asthma exacerbation during the 2018 Japan floods might be also associated with increased pollen dispersal, as the correlation between pollen dispersal and asthma deaths in 1995 implies.

In this paper, we analyzed and demonstrated the emergence and progression of the sudden surge in KD patients accompanying the onset of massive pollen dispersal in Japan since 1978, alongside the dynamics of asthma deaths that occurred in parallel and synchronously.

(3) On the other hand, KD, first reported at a scientific conference in Japan in 1962, has long been considered a disease involving some form of microorganism [8]. However, in 2003, the author compared and analyzed the annual trends in KD patient numbers from nationwide surveys with fluctuations in pollen counts using line graphs. This led to the consideration that KD may be a disease triggered by pollen exposure [9,10].

Subsequent cross-correlation and trend analyses revealed that KD exhibited peaks in onset approximately 9–10 months and 3–4 months after pollen exposure, with an average time to onset of 21.4 months [11].

Furthermore, we conducted multiple comparison analyses and discovered that the incidence of KD is suppressed during seasonal influenza epidemics [12], reporting four papers on this topic by 2016 [9-12].

The author conducted a 20-year correlation analysis between fluctuations in pollen counts and nationwide patient numbers for 40 designated intractable diseases (1974-2014) and 24 types of cancer and malignant tumors (1975-2015). As a result, we found a statistically significant correlation. Since 2018, eight papers have reported that these designated intractable diseases, as well as cancer and malignant tumors, similarly to KD, are triggered by pollen exposure, reaching the starting line of onset,

entering the onset process, and ultimately leading to disease development [13-20].

Furthermore, the author analyzed the correlation between seasonal influenza patient numbers in Tokyo and Kanagawa Prefectures and fluctuations in pollen dispersal levels from 1982 to 2019. During this analysis process, we conducted a monthly correlation analysis between seasonal influenza patient numbers and pollen dispersal levels in Kanagawa Prefecture over the 12-year period from 1991 to 2002 (144 months). This revealed that seasonal influenza, like KD, develops and spreads approximately 10 months after pollen exposure [21].

(4) While the line graph of asthma deaths had shown a steady downward trend since 1950, experts offered only speculative comments regarding the sudden surge in asthma deaths observed in 1995 and its possible connection to seasonal influenza [22]. Experts showed no interest in the fact that asthma deaths remained at a high plateau between 1978 and 1996, fluctuating between increases and decreases, and there appears to have been no thorough discussion or research whatsoever [23]. The author's understanding appears to differ from the academic community's perspective, which only imagined that seasonal influenza epidemics might affect asthma mortality rates without conducting further investigation.

We must focus on the relationship between these two phenomena, as we believe it will provide valuable insights for analyzing asthma pathogenesis.

And with the exception of a temporary increase in asthma deaths in 1999, asthma deaths continued to decline rapidly after 1996 due to the widespread adoption of inhaled steroid therapy [23].

The author graphically represented downloaded data from Japan's Ministry of Health, Labour and Welfare regarding monthly asthma deaths from 1980 to 1999. Using 1995 data as a representative example, observing the monthly trend where death counts were high in May and March, it was understood that pollen exposure's impact on asthma deaths exceeded its impact on seasonal influenza.

In 1995, a large number of individuals at risk of dying from asthma passed away, and since 1996, the number of asthma-related deaths in Japan has been steadily declining. The author wishes to point out the lack of information exchange and sharing between asthma researchers, who have largely ignored the massive pollen dispersal since the 1980s as if it were someone else's problem, and researchers in other medical fields. Such observations still hold profound medical significance as sharp lessons even in today's medical practice.

The information regarding the annual trend in asthma deaths was obtained through observation of the bar graph [24] created by the Ministry of Health, Labour and Welfare. Therefore, we created a new, more effective line graph to observe fluctuations in asthma deaths. We attempted to clarify the environmental factors contributing to asthma deaths through the line graph as shown below.

## Materials & Methods

The yearly data of Asthma death were download from e-Stat General mortality Volume 1 5-12 Trends in deaths and death rates (per 100,000 population) by sex and causes of death: Japan. [https://www.e-stat.go.jp/en/stat-search/files?stat\\_infid=000040206117](https://www.e-stat.go.jp/en/stat-search/files?stat_infid=000040206117)

The monthly data were obtained from below-described

[https://www.e-stat.go.jp/stat-search/files?page=1&layout=data1ist&toukei=00450011&tstat=000001028897&cycle=7&tclass1=000001053058&tclass2=000001053061&tclass3=000001053065&cycle\\_facet=tclass1&tclass4val=0](https://www.e-stat.go.jp/stat-search/files?page=1&layout=data1ist&toukei=00450011&tstat=000001028897&cycle=7&tclass1=000001053058&tclass2=000001053061&tclass3=000001053065&cycle_facet=tclass1&tclass4val=0) The data before 2000 were still printed in papers, so we had to copy and in-put them into Exel files.

The data of Influenza (flu) incidence of Kanagawa Prefecture and Tokyo Metropolis were gathered as described in our previous report in 2021 that “Awaya A, Kuroiwa Y, Yamashita T. Before the dawn of the heyday of the Covid-19 epidemic in winter in place of Influenza, a summary of correlation between pollen exposure, and Kawasaki disease onset and Influenza epidemic from around 1980 [21]. The data of KD incidence of Japan were obtained from data of Nationwide Epidemiological Surveys of Kawasaki Disease in Japan as described in our previous report of Reference 9.

## Results

(A) There was speculative commentary suggesting that seasonal influenza may have influenced the sudden increase in asthma deaths observed in 1995 [22]. The author had long noted a bar graph created by the Ministry of Health, Labour and Welfare showing the declining trend in asthma deaths over the period from 1970 to 2019. The author converted this into a line graph. We created a merged line graph combining this line graph with the previously reported line graph [21] comparing seasonal influenza patient numbers and pollen dispersal counts in Tokyo and Kanagawa Prefectures (Fig. 1).

Asthma deaths showed a declining trend from 1950 to 1963, but a brief period of slight increase in asthma deaths occurred between 1963 and 1968.

Asthma deaths continued to decline from 1968 to 1978, but

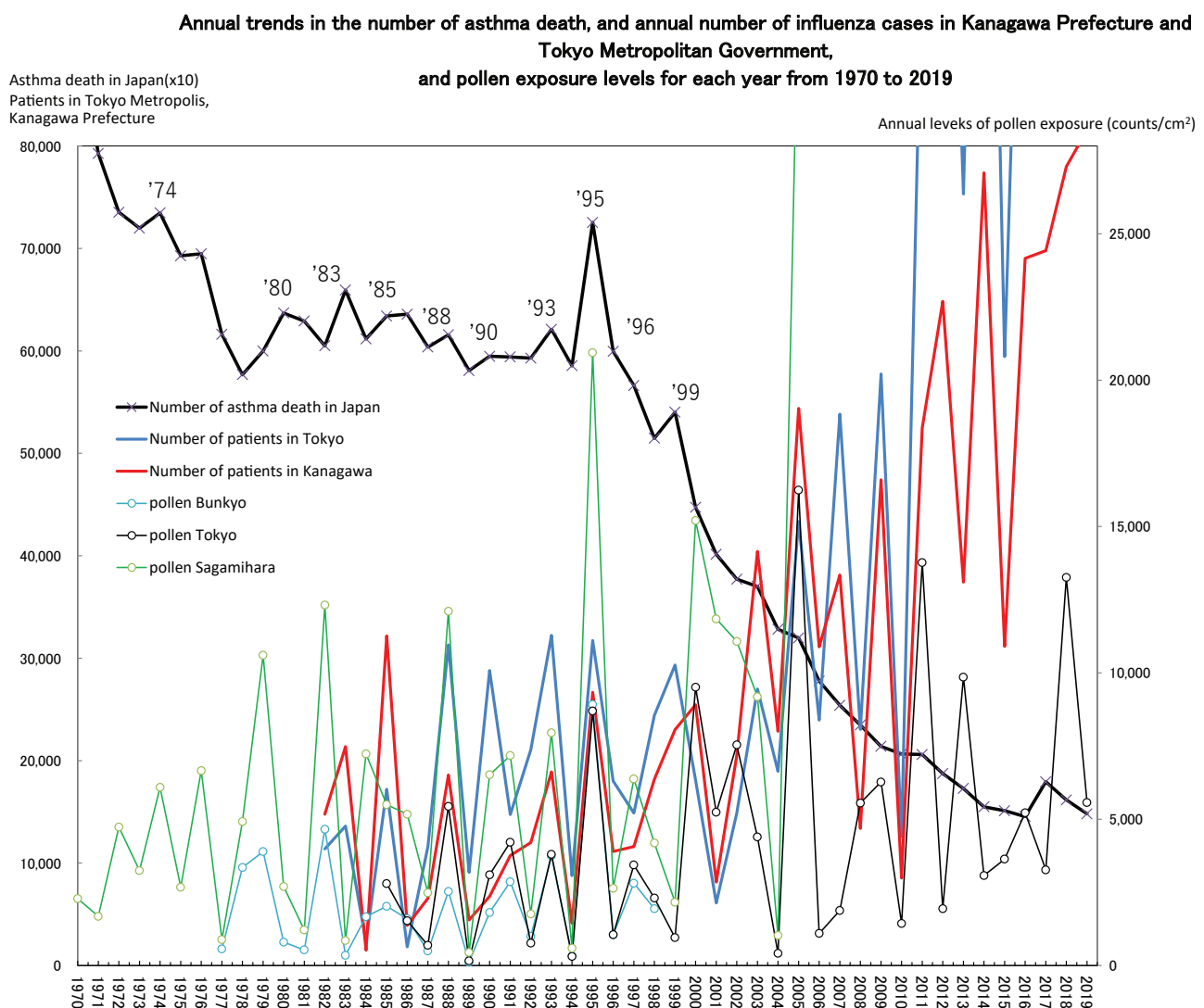


Figure 1. Annual trends in the number of asthma death, and annual number of influenza cases in Kanagawa Prefecture and Tokyo Metropolitan Government, and pollen exposure levels for each year from 1970 to 2019. Vertical axis: left side; number of Asthma death ( $\times 10$ ) and Influenza patients (persons), and right side; annual levels of pollen exposure (counts/cm<sup>2</sup>).

Asthma death graph is placed on a graph showing relation between pollen exposure and incidence of Flu and KD onsets similar to resultant graphs of previous study reported in Ref. 21; Vertical axis: left side; number of and Influenza patients (persons), and right side; annual levels of pollen exposure (counts/cm<sup>2</sup>).

after bottoming out in 1978, they rose slightly until 1980. From then on, asthma deaths fluctuated, increasing and decreasing repeatedly until 1996. We would like to focus on the peaks in asthma deaths recognized in 1983 and 1995, respectively.

The line graph showing the steady decline in asthma deaths since 1950 highlights two particularly notable points: the significant increase in asthma deaths in 1995, and the suppression and stagnation of the downward trend over the preceding 18 years from 1978 to 1996, during which asthma deaths plateaued at a high level. What, then, is the real cause of these two phenomena? The author believes that the true cause of these two phenomena was likely the period mentioned above, when massive pollen dispersal began in Japan and asthma patients exhibited biological reactions to pollen exposure unlike anything they had previously experienced.

Noteworthy are the years 1995 and the three peak years of massive pollen dispersal that occurred between 1978 and 1987. While 1995 did not reach the record pollen count of 2005, it was the year with the highest pollen count on record at that time.

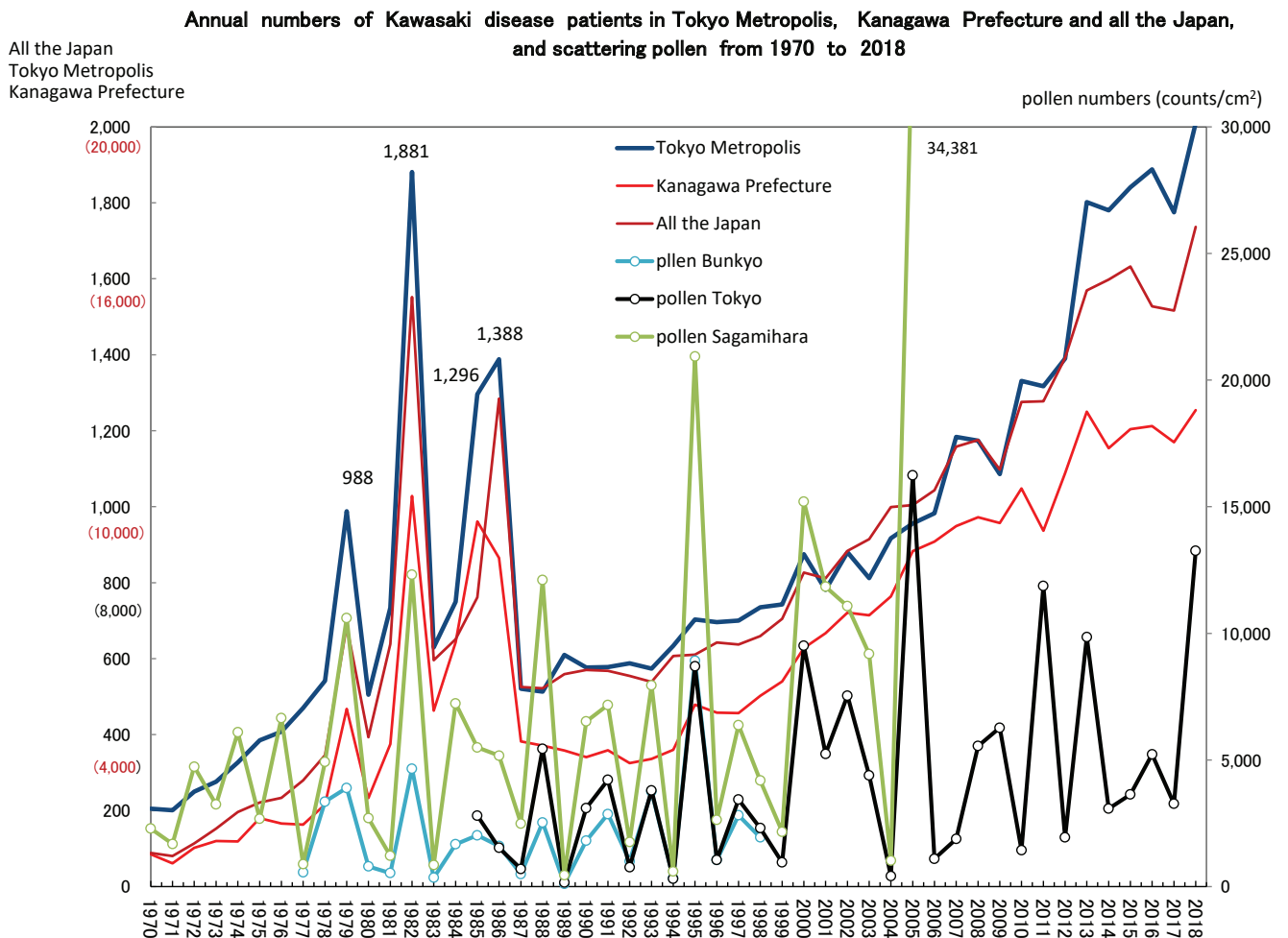
Given the environmental context of that era, the number of asthma-related deaths did not decrease due to pollen exposure, and the number of patients whose asthma became chronic increased as a result of pollen exposure.

It remains unclear what biological reactions were triggered in these chronic asthma patients, who could be considered a precursor group for asthma-related deaths, but their biological dynamics are clearly illustrated in the line graph.

Regarding the dynamics of asthma deaths, we would like to present compelling evidence suggesting that pollen exposure may be responsible for these peculiar fluctuations.

Pollen exposure, even if not the fundamental cause of asthma onset, is undoubtedly a contributing factor, an enabler, or an aggravating factor that shapes the worsening of asthma symptoms.

Fig. 1 shows that despite a significant difference in asthma mortality rates between 1993 and 1995, the number of seasonal influenza patients in Kanagawa Prefecture was nearly identical when comparing these two years (12, Kawasaki Disease Report



**Figure 2.** Annual numbers of Kawasaki disease patients in Tokyo Metropolis, Kanagawa Prefecture and all the Japan, and scattering pollen from 1970 to 2018.

Vertical axis: Left side; number of KD patients of Tokyo, Kanagawa and all the Japan. Black scale is persons for Tokyo and Kanagawa, and red scale is persons for all the Japan. Right side; annual levels of pollen exposure (counts/cm<sup>2</sup>).



No. 4). Furthermore, considering that the incidence of seasonal influenza did not show significant variation over the 12-year period including 1995 (from 1988 to 1999) (12, Fig. 1 and influenza paper), the author is convinced that the pollen count in 1995 had a profoundly significant impact on the increase in asthma deaths observed that year.

A significant proportion of those at risk of dying from asthma, who had been exposed to unprecedented levels of pollen, died one after another in a massive wave throughout 1995, as if clearing out a stockpile.

Therefore, the authors state that the impact of seasonal influenza epidemics on asthma deaths cannot be considered significant.

Looking at the seasonal influenza patient counts in Kanagawa Prefecture and Tokyo in 1983, the year with the second-highest asthma deaths after 1995, the numbers are not particularly high. Therefore, it is assumed that many individuals in the asthma-related death risk group who experienced the highest pollen exposure on record in the previous year, 1982, developed chronic, severe, or critical conditions, leading to a higher number of deaths in 1983 compared to other years.

(B) We reproduce here the previously reported graph comparing the dynamics of KD patient numbers with fluctuations in pollen counts (Fig. 2) and wish to compare it with the graph

of asthma deaths.

Looking at Fig. 2, we can see three distinct peaks in the number of KD patients that perfectly coincide with the peaks in pollen counts observed during 1978-1980, 1982 (the largest on record at the time), and 1984-1986. Subsequently, pollen counts peaked in 1988, 1991, 1993, and 1995. In 1995, which saw the second-highest pollen count on record after the peak in 2005, the number of KD patients showed a renewed sharp increase.

The line graph of KD cases showed three distinct peaks in 1980 and 1983, with consecutive peaks in 1985 and 1986, similar to the patterns described in the first and fourth reports of the KD studies [9,12]. By comparing the line graph of asthma deaths with those line graphs of KD cases (Fig. 1), we observed that asthma deaths also exhibit the same three distinct peaks as KD.

On the other hand, after our first report on KD the author had found three distinct peaks in the number of allergic rhinitis patients during this period in the report by Osaka University's Department of otolaryngology's physician showing their graphical representation of the proportion of such patients among outpatients (Fig. 3, [25]).

It bears repeating that while the sharp increase in asthma deaths in 1995 may have been partially influenced by the seasonal influenza epidemic (Fig. 1), which correlates with pollen dispersal levels, the primary cause can be considered the direct effects of pollen exposure due to the unprecedented mass dispersal of pollen at that time.

Considering the increase in asthma deaths in 1999, although pollen dispersal was low that year, the high pollen dispersal in 2000 suggests that the rise in asthma deaths may have resulted from biological reactions to the early dispersal of cedar pollen occurring from September to December following the intense summer heat of 1999 (Fig. 1).

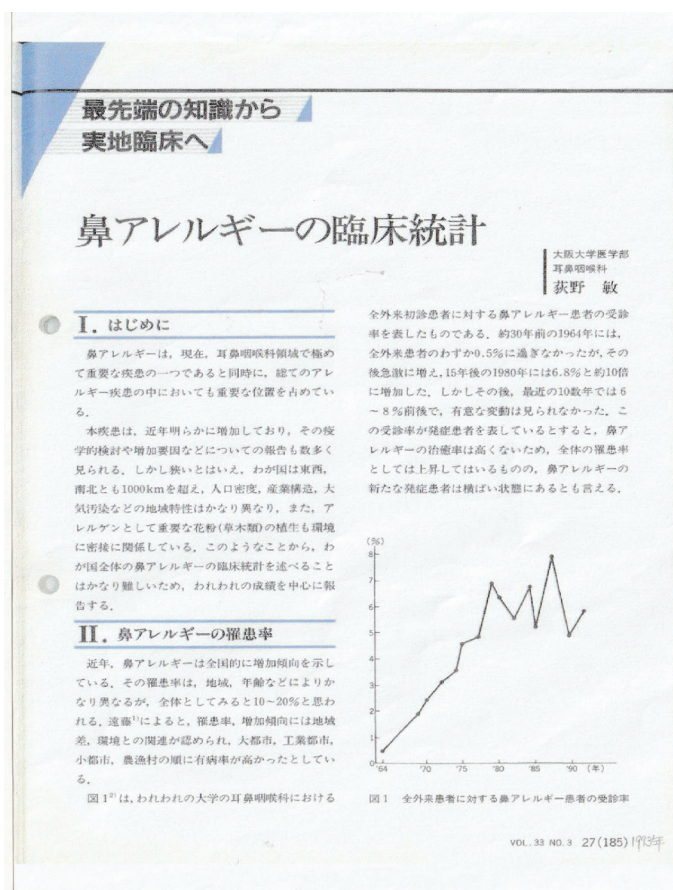
(C) To distinguish and compare the environmental factor of seasonal influenza outbreaks centered on January and February with the environmental factor of pollen exposure most common from February to May—which we argue influences asthma deaths—we retrieved monthly asthma death counts from the Ministry of Health, Labour and Welfare data bank (M&M) since 1970 and plotted them graphically.

Figure 4 plots the number of asthma deaths per month from 1980 to 1989, while Figure 5 plots the number of asthma deaths per month from 1990 to 1999.

Overall, analysis of the period from 1980 to 1989 indicates that asthma deaths are higher in January. In seven of the ten years (1980–1989) covered by the data, the high number of asthma deaths in January began to decrease in February, continuing this downward trend through September before shifting to an upward trend from September to December.

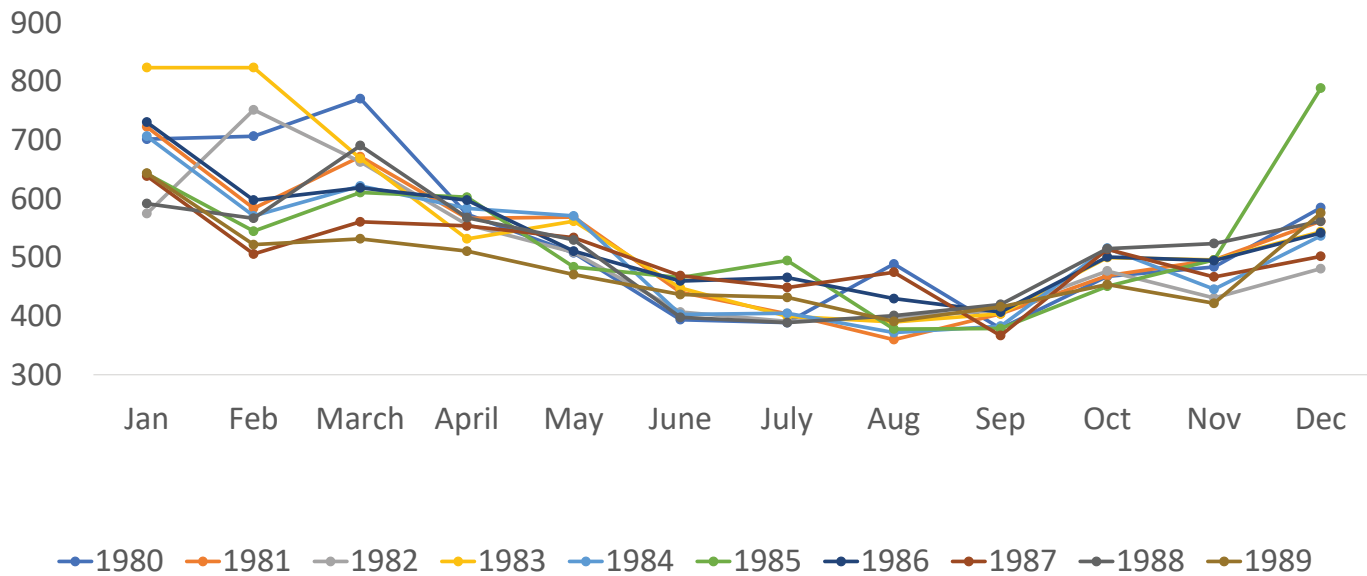
The reason asthma deaths show an increasing trend from September to December, as also seen in the pollen count fluctuation graph in Fig.1 in Ref.11 and Fig.7 in Ref.13, is thought to be due to exposure to pollen during the early dispersal period of cedar pollen from September to December, albeit in small quantities.

Focusing on data from 1983, the year with the highest number of asthma deaths, the highest figures occurred in January and February. In May, there were 562 deaths. In comparison, asthma deaths in 1981 totaled 569, and in 1984, 571, placing them among the highest years.



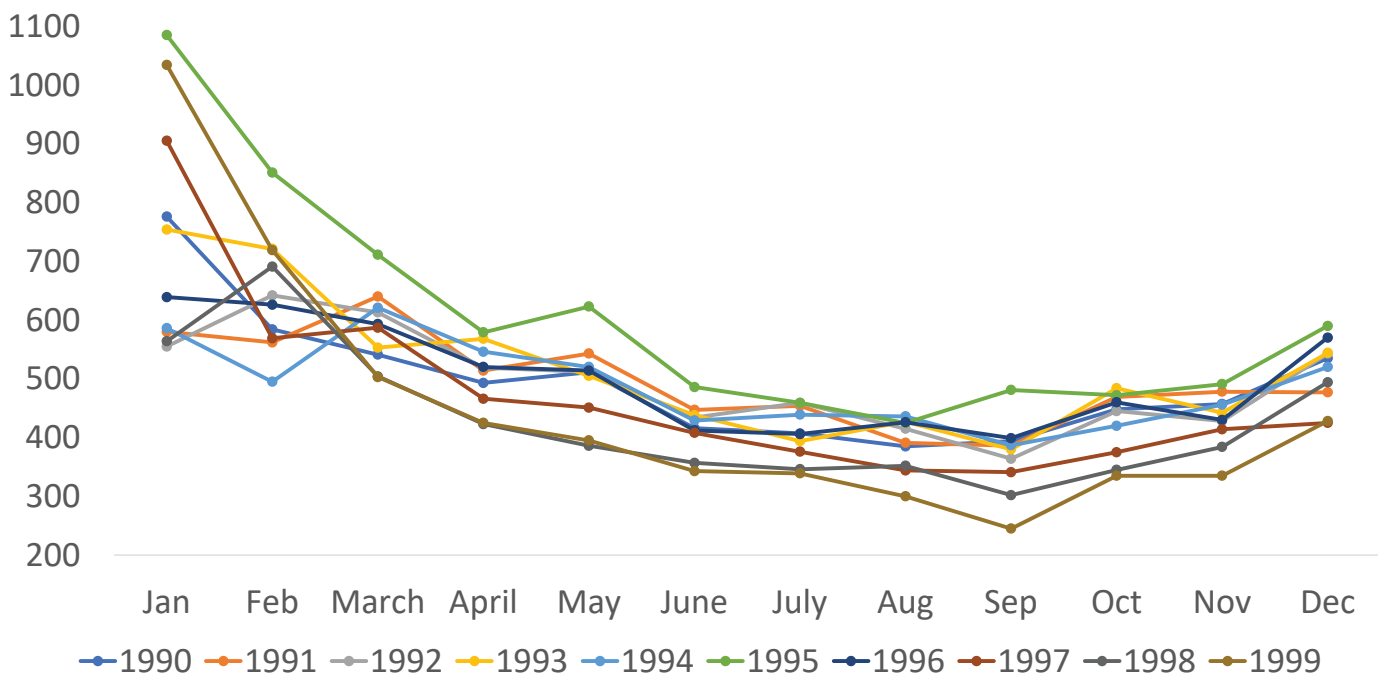
**Figure 3.** Clinical statistics of allergic rhinitis. Consultation rate of allergic rhinitis patients out of outpatients. By Satoshi Ogino, Department of Otorhinolaryngology, The University of Osaka, School of Medicine. *Iyakunomon* Vol 33, No.3,185-190, 1993. Vertical axis: Scale %.

### Monthly numbers of asthma death in Japan from 1980 to 1989



**Figure 4.** Monthly numbers of asthma death in Japan from 1980 to 1989. Vertical axis: number of asthma death persons

### Monthly numbers of asthma death in Japan from 1990 to 1999



**Figure 5.** Monthly numbers of asthma death in Japan from 1990 to 1999. Vertical axis: number of asthma death persons.

The number of asthma deaths in 1980 and 1988 was higher in March than in January and February. The number of asthma deaths in 1982 was higher in February than in January. In 1985, the number of asthma deaths in July and December was higher than in other years.

The period from 1990 to 1999 showed greater variability in asthma deaths in January compared to the period from 1980 to 1989, with five years experiencing a decrease in February. The number of asthma deaths increased in February and March 1992, in March 1994, and in February 1998. The number of asthma deaths in 1991 peaked in March and also increased in May. The number of asthma deaths in 1993 showed an increase in April.

Generally speaking, during the period from 1990 to 1999, similar to the period from 1980 to 1989, asthma deaths peaked in January, followed by a decreasing trend until September, and then shifted to an increasing trend from September to December. The most striking fact that highlighted the extent of pollen exposure's contribution to asthma deaths was the dynamics of asthma deaths in 1995. Specifically, in 1995, asthma deaths were highest throughout the entire year, with clear peaks occurring in May and again in September, months considered to be significantly affected by pollen.

## Discussion

As described in Results (B), it was noted this time that, as shown in Fig. 1-2, during the period from 1978, when massive pollen dispersal began, to 1986, three peaks in the number of high-pollen days, three peaks in asthma deaths, and three peaks in the number of Kawasaki disease (KD) patients each occurred synchronously.

Furthermore, the author had noticed three peaks during the period in the trend graph of number of allergic rhinitis patients reported by a physician of Osaka University's Department of Otolaryngology, as above mentioned in Results (Fig. 3) [25].

If otolaryngologists had shared their experience in managing environmental phenomena involving massive pollen dispersal and their medical expertise in diagnosing and treating pollen-exposed patients with medical societies and physician associations, and if there had been close information exchange and sharing between these departments with healthcare providers and researchers specializing in asthma and Kawasaki disease (KD), the medical community's understanding might have been somewhat different. If physicians had begun focusing on the simultaneous commonality of reactivity and disease onset in response to pollen exposure across three conditions—Kawasaki disease, asthma, and allergic rhinitis—from the late 1980s onward, it is estimated that Japanese healthcare might have taken a slightly different course.

I had the impression that pollen topics scarcely appeared in the Japanese Society of Allergology asthma-related conference reports during the 2000s.

Until the author's 2003 conference report [9] on the correlation between massive pollen dispersal and large-scale patient outbreaks, the prevailing view within the Japanese Society of Kawasaki Disease seemed to be that KD was an idiopathic disorder involving some form of microorganism. However, even since then and up to the present, understanding of KD has remained largely unchanged.

Even if we cannot definitively state that pollen exposure is the trigger for the onset of asthma, it is a fact that it contributes to or promotes the worsening of asthma. The author expects

researchers studying bronchial asthma to clarify how pollen exposure acts as a booster in the causative mechanisms of bronchial asthma. It is more reasonable to understand that the transient increase in asthma deaths in 1995 was not the result of a seasonal influenza epidemic, as had been speculated, but rather caused by unprecedented mass exposure to pollen.

In 2018, both the number of cancer and malignant tumor patients and the number of patients with designated intractable diseases increased [26,27]. While it would not be surprising if asthma deaths also increased in 2018, we believe it is more reasonable to attribute the rise in asthma deaths to the effects of pollen exposure rather than to the impact of flooding. Given that the number of Kawasaki disease cases in Hiroshima Prefecture, which Utsumi et al. included in their epidemiological study, increased in 2018 and 2019, we believe it would be beneficial for them to investigate the relationship between asthma and pollen exposure in Hiroshima Prefecture as well.

The author noted that a characteristic transient increase in asthma deaths occurred in 1995, as shown in the traditional bar graph depicting the annual trends in asthma deaths since 1950. We believed this increase in asthma deaths was likely due to the effects of pollen, which asthma-related academic societies at the time had not taken note of. To determine the cause of asthma deaths, the author shifted strategy from using bar graphs to creating line graphs to represent the dynamic trends in asthma deaths, based on the perspective that a more detailed examination of asthma death data values is necessary.

The number of Takayasu's disease patients has traditionally been shown using bar graphs. However, to observe years with significant fluctuations, it is better to calculate the year-on-year change in patient numbers and display it as a line graph. A line graph clearly shows a significant peak in the incidence of Takayasu's arteritis, Behçet's disease, and Berger's disease during the year 1994, which saw a prolonged period of heavy pollen dispersal. This finding was also reported in our paper published in 2018 [13].

Epidemiological studies comparing and examining the dynamics of various diseases between 2018—a year that also saw heavy pollen dispersal—and 2019, both years preceding the COVID-19 epidemic yet, arriving in Japan from December, 2019, and 2020—a year starting in January and during the COVID-19 pandemic—are also anticipated. Asthma deaths showed a slight increase from 2017 to 2019.

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## Conflicts of Interest

The authors declare that they have no conflicts of interest.

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