

Opinion Article

40 Specific Intractable Diseases and 24 Types of Cancer and Malignancies as Well as Kawasaki Disease May be Triggered by Pollen

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Abstract

This article was written to draw attention of readers to our studies in Japan which revealed that airborne pollen levels were correlated with the development of Kawasaki disease, as well as a number of specific intractable diseases and cancers and malignant tumors. The number of newly registered patients in the patient-registry year “x” was significantly correlated with annual airborne pollen levels, measured in the same year as “x”, for idiopathic dilated cardiomyopathy, periarteritis nodosa and multiple sclerosis, with pollen levels measured 2 years prior to “x”, for lung, breast, skin, pancreatic, and kidney cancers, and with pollen levels measured 6 years prior to “x”, for Crohn’s disease, ulcerative colitis, myasthenia gravis, multiple sclerosis, Moyamoya disease, periarteritis nodosa, Granulomatosis with polyangiitis, pemphigus, and oropharyngeal, oesophageal, prostatic, bladder, uterus, and kidney cancers. When the initial phase of the disease onset is triggered by pollen exposure, the pollen cells are supposed to enter the steps of cellular senescence or degradation. It might cause the condition of the patient who has not become ill yet. At the point when pollen exposure exceeds an individual's threshold, some people go through the process of specific intractable diseases and others go through the process of cancer development. Elucidation of the cellular response sites and processes after pollen exposure may give people hope for the prevention of specific intractable diseases and cancers, and advance to longevity. Thus, we have invited you to discuss in this opinion article the basic cross-section of life phenomena and disease pathogenesis. We hope that this article will make the public aware of the fact that one of etiological causes of a number of chronic diseases is likely to be the pollen to which humans are all destined to be exposed since birth. We expect that the onset of these diseases might be suppressed by a daily lifestyle of avoiding pollen.

Keywords: Pollen disease; Kawasaki disease; Specific intractable diseases; Idiopathic dilated cardiomyopathy; Multiple sclerosis; Kidney cancer; Skin cancer; Oropharyngeal cancer; Oesophageal cancer; Prostatic cancer; Bladder cancer; Uterus cancer

The Pollen Cells of the Plant Kingdom as an Environmental Cause of Human Diseases

This opinion was written to draw attention of readers to the epidemiological fact that the pollen cells of the plant kingdom seem to cause chronic diseases, such as Specific Intractable Diseases (SIDs), cancers and malignancies in the human beings.

Since ancient times, there have been experiences that illnesses are influenced by natural phenomena and tend to occur at the turn of the seasons. In addition to the seasonal changes in natural phenomena such as air temperatures and the amount of sunlight induced by weather like rain, snow, and wind, we will discuss in this paper that scattered pollen from the plant kingdom is also an influencing agent. In the process of developing any disease, besides environmental factors of weather and natural origin, foreign substances such as microorganisms, plant and animal components act as environmental stresses on the human body, and the immune response system is counteractively activated in the body, resulting in an inflammatory mechanism, which has been widely circulated

by the efforts of our predecessors in life sciences [1-3]. Among foreign substances that cause diseases in humans, microorganisms present various symptoms in both acute and chronic diseases.

Our epidemiological studies however revealed that pollen which is different from microorganisms is correlated with the development of Kawasaki Disease (KD), as well as a number of SIDs and cancers and malignant tumors. Humans and mammals living on earth and the animal kingdom receive oxygen, nutritional energy and water, from their partners in the plant kingdom, and benefit immensely in food, clothing, and shelter, and they are essential and full of good things. However, it has become an epidemiological fact that pollen produced by plant life activities may be an inducer of numerous diseases such as KD, SIDs, cancer and malignant tumors in people [4-10]. We have learned from epidemiological data related to pollen exposure, the important portion of human biology is based on the relationship between humans and plants.

Pollen Exposure and Kawasaki Disease

The use of knowledge in the field of pollen type 1 allergy has been applied for many years to the treatment and prevention of rhinitis/conjunctivitis (hay fever) [11,12] and asthma. KD had been considered to have no known cause. However, since 2003, a new disease research paradigm has been proposed for KD, as a Pollen-Induced Disease (PID), which is probably induced by type 4 allergy to pollen exposure [3-6]. We feel that honour was made a little by finding as Japanese people the relation of cedar pollen to KD which has been reported for the first time in our country (Japan) [13], where later, a large amount of release of cedar pollen has been peculiarly found. The following is a brief review of the unique disease incidence in KD and environmental circumstances in Japan over 40 years ago that led to these epidemiological findings. As shown in Figure 1, three outbreaks of epidemic-like KD (the first discovered in 1961) [13] in the spring of 1979, 1982, and 1984-86 were a major debating problem in the paediatric field at the time [4,7]. Many exploratory studies have failed to determine the cause of KD, and the idea that the disease is probably caused by some microbial agent has not yet been dispelled even today. We would like to hear records and testimony from the medical community at the time of this rapid increase in the number of children with KD, whether information was shared with other medical societies, such as those belonging to internal medicine that treated related vasculitis syndromes and those belonging to otolaryngology, where the number of patients with rhinitis similarly showed rapid increase, and whether there was any discussion among frontline doctors.

The author wrote in 2002, "Relation between resistance or sensitivity to hay fever and many or absent moles" [14]. We reported at the Japanese Society for Immunology the finding that the formation ability of moles is a phenotypic predisposition for resistance to allergic diseases such as hay fever. Awaya observed the skin condition of an infant who had developed KD twice, and his parents, and realized that KD was probably also an allergic

disease. The number of patients with KD and the changes in the number of pollen dispersed in eight locations across the country were graphed, and the number of pollen dispersed from the late 1970s to the late 1980s was rapidly increasing, with 1982 being the largest pollen year ever at that time [4,7]. We found that these three pollen peaks coincide with the KD peaks, and reported that pollen may be the trigger of KD at the 23rd Annual Meeting of the Japanese Society of KD in September 2003, based on the correlation graphs plotting data until 2003. The pollen count continued to increase from 1995, 2000-2003, to 2005 (the largest ever), 2011, and 2013, because the industry believes that large scale plantations of cedar and cypress trees were promoted in the post-war era, and then logging of the trees has been avoided by being pushed by imports. This uniquely situation in Japanese forest industry may have led to a large outbreak of KD. The author performed a regression analysis of the number of KD incidence and pollen count [5], cross-correlation analysis [6], trend analysis with exponential equations [6], and ANOVA-multiple analysis with influenza pandemic [7]. Accordingly, four reports have been published in succession, including the report that KD, which is thought to be a PID causing delayed-type hypersensitivity reactions, is suppressed during the influenza pandemic period. In addition, Awaya have published introductory articles on PID in the YAKUJI NIPPO (Pharmaceutical News), The Science News, and MERIC.

Pollen Exposure and Specific Intractable Diseases

In the meantime, Awaya had begun to graph weekly the targeted reporting disease registry reported by the Tokyo Metropolitan Infectious Disease Surveillance Center [15] and noticed that the number of patients with hand-foot-and-mouth disease, erythema infectiosum, aseptic meningitis, etc. was increasing in conjunction with the increase in the number of airborne pollen. Meanwhile, Awaya finally noticed that the Japan Intractable Diseases Research Foundation under the jurisdiction of the Ministry of Health, Labour and Welfare (MHLW) has a homepage for reporting the number of patients with SIDs [16]. He thought that Takayasu disease, which is a vasculitis syndrome discovered like KD in Japan, was probably caused by pollen exposure, so in June 2018, he started to graph the dynamics of the number of patients with Takayasu disease and the annual variation of pollen counts. The graph created by the MHLW showed a bar graph of the current number of registered patients [17], but he made a line graph of the number of patients compared to the previous year, and found a remarkable and unprecedented peak in 1984 (Figure 1). He also pointed out that women in the reserve group for vasculitis syndrome who did not have KD, which is more common in the male to female ratio of disease onset, as infants, may have developed Takayasu disease, which is particularly more common in the female to male ratio of disease onset, as adults. The number of patients with Behcet's disease, Buerger's disease, other vasculitis syndromes, and collagen diseases such as systemic lupus erythematosus, which have closely resembled or similar annual patterns of onset, were also graphed.

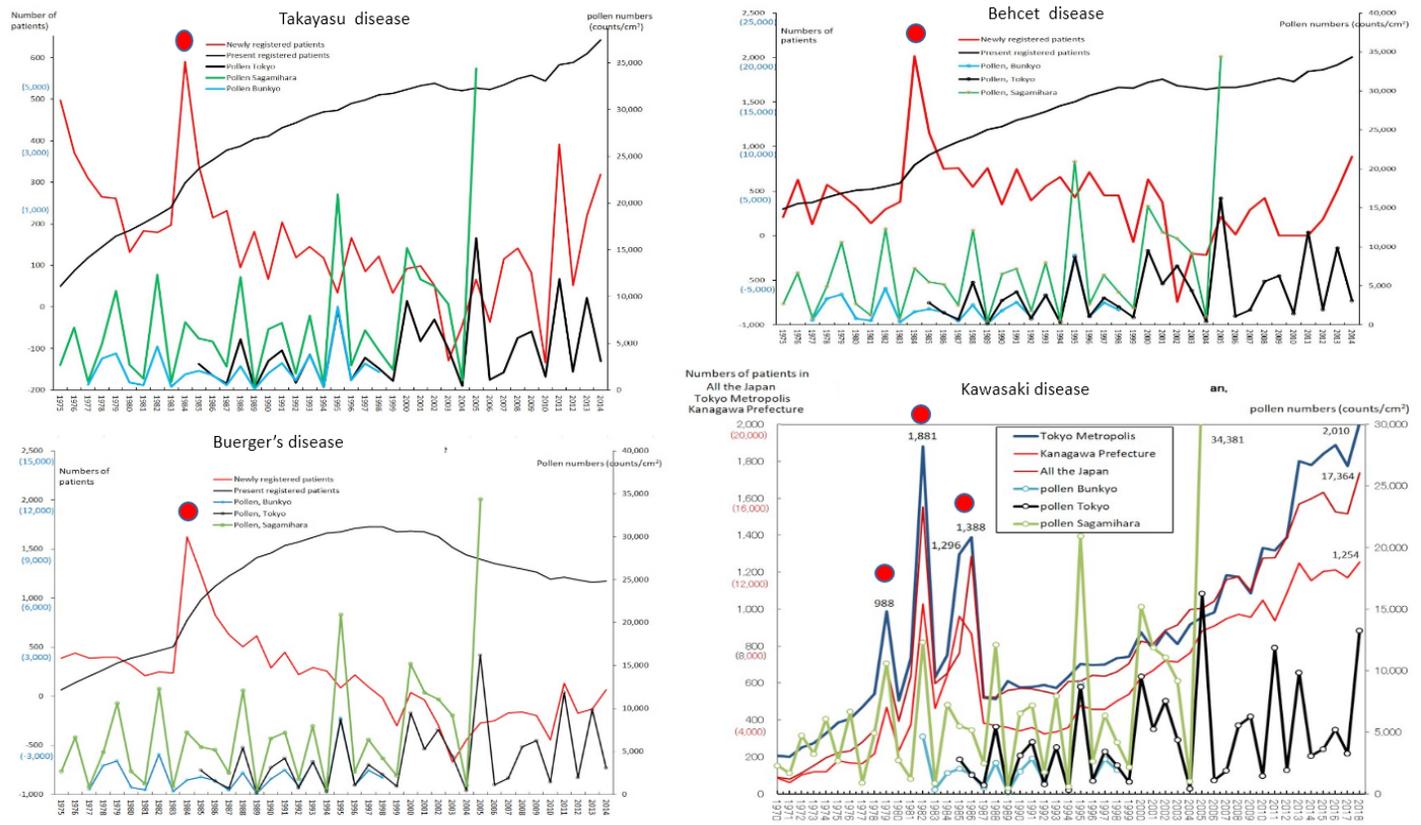


Figure 1: Total number of Japanese males and females registered for four kinds of vasculitis diseases; Takayasu disease (upper left), Buerger's disease (lower left), Behcet disease (upper right), and Kawasaki disease (lower right) at the year diagnosed, its year-on-year increase, and the amount of air borne pollen scatter in 3 areas during the period from 1975 to 2014. The black and red line graphs for these vasculitis diseases representing numbers of presently and newly registered patients respectively in each year, as well as the amount of pollen scattered in Bunkyo-City, Metropolitan Tokyo and Sagami City during the period from 1975 to 2014. Numbers of patients are shown on the left axis whose scales consist of numbers for newly registered patients and numbers in parentheses for presently registered patients. Pollen numbers in counts/cm² are shown on the right axis. As shown by red circles, the notable fact was that outbreaks of newly registered patients were noted in 1984 for any of Takayasu disease, Buerger's disease, and Behcet disease, and in 1979, 1982, and 1984-86 for Kawasaki disease.

It was found that the increase in the number of patients was linked to the increase in the number pollen counts during the 40 years to 2014. Thus, these findings of 11 species of SIDs were reported in December 2018 as the first report of SIDs, while the trends in the number of patients with other SIDs were graphed and analyzed one after another. Along the way, we found a periodic linkage with pollen counts in total 40 major diseases including neuromuscular SIDs such as Parkinson's disease, multiple sclerosis and myasthenia gravis, Inflammatory Bowel Diseases (IBDs) such as ulcerative colitis and Crohn's disease, interstitial pneumonia, idiopathic dilated cardiomyopathy and bone diseases. We first focused on IBDs, which have a large number of patients, and then other SIDs designated by the gastrointestinal system, and

published a second report in December 2019. Some of the findings, including a significant association of IBDs with pollen counts 6 years before the onset of the disease, are shown in Figure 2. We could prove statistically significant correlations with Bonferroni Correction between the number of newly registered patients in the patient-registry year "x" and annual airborne pollen levels in Tokyo and/or Sagami City, measured in the same year as "x", for the 4 SIDs (idiopathic dilated cardiomyopathy, periarteritis nodosa, Parkinson's disease and multiple sclerosis), and measured 6 years prior to "x", for the 9 SIDs (Crohn's disease, ulcerative colitis, scleroderma, myasthenia gravis, multiple sclerosis, Moyamoya disease, periarteritis nodosa, Granulomatosis with polyangiitis (Wegener granulomatosis), and pemphigus).

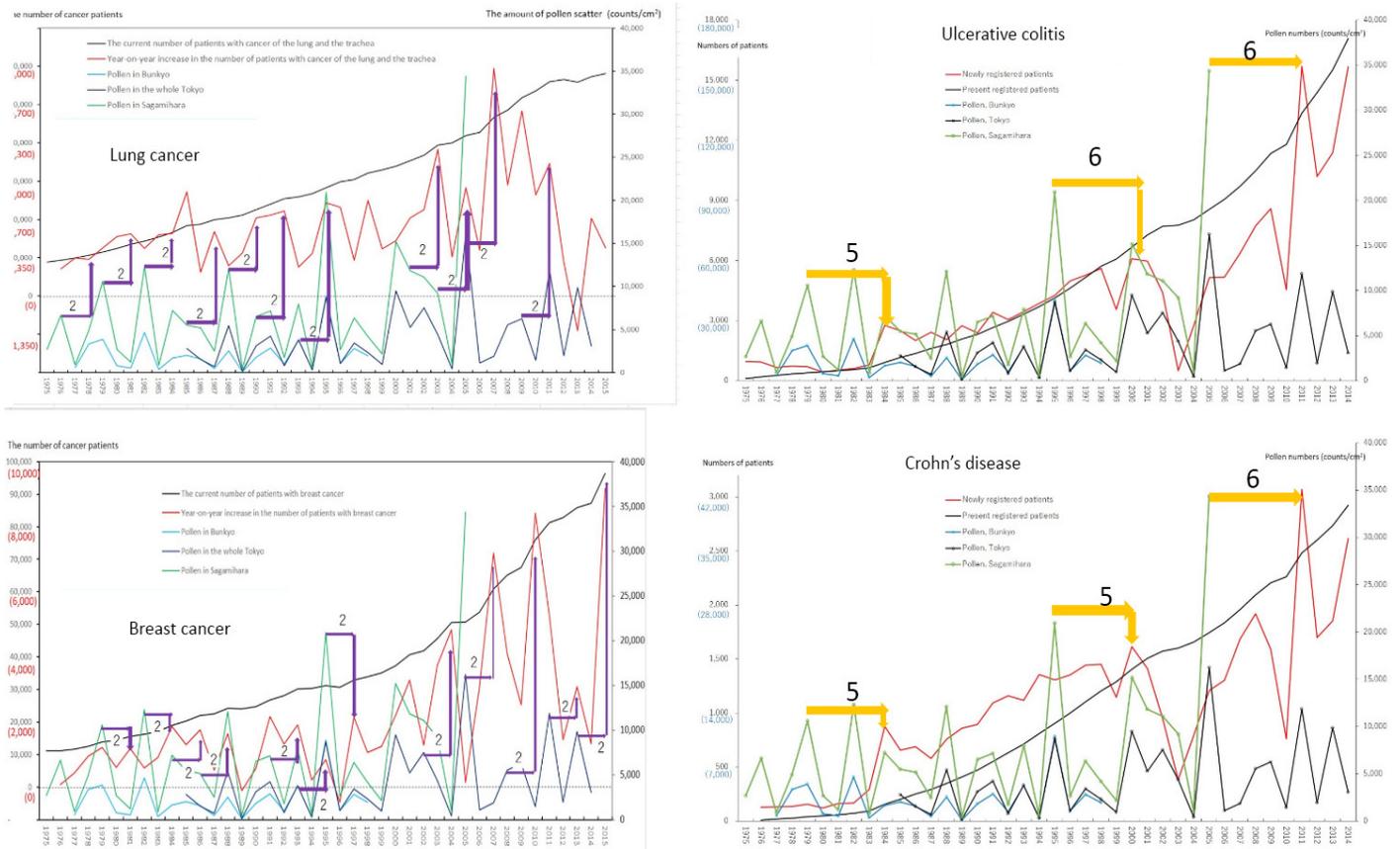


Figure 2: Total number of Japanese males and females registered for lung cancer (upper left), breast cancer (lower left), ulcerative colitis (upper right), and Crohn’s disease (lower right) at the year diagnosed, its year-on-year increase, and the amount of air borne pollen scatter in 3 areas during the period from 1975 to 2015. The black and red line graphs for these vasculitis diseases representing numbers of presently and newly registered patients respectively in each year, as well as the amount of pollen scattered in Bunkyo-City, Metropolitan Tokyo and Sagami-hara City during the period from 1975 to 2015. Numbers of patients are shown on the left axis whose scales consist of numbers for newly registered patients and numbers in parentheses for presently registered patients. Pollen numbers in counts/cm² are shown on the right axis. Violet or orange arrows indicate phasic increments of newly registered patients occurring 2 or 5~6 years after phasic increments of airborne pollen scatter, respectively.

Pollen Exposure and Cancer and Malignant Tumors

All of the SIDs examined in this way, as well as KD, were subjected to pollen. Given the fact that pollen exposure is involved and the commonality of life events, we began graphing the annual incidence figures from the National Cancer Center registry data [18,19] in the summer of 2019, with the expectation that the incidence of another incurable cancer or malignancy would also be largely triggered by pollen exposure. In doing so, we made an annual comparison of the number of cancer patients compared to the previous year and pollen counts, as well as the number of SIDs. Finally, the epidemiological fact that pollen will be the trigger for both SIDs and cancer and malignant tumors as well as KD has been discovered in Japan between 2018 and 2020, ahead of other countries [8-10].

Correlation analysis between the 24 cancers including all cancers combined, and pollen counts, confirmed the epidemiological fact that the first peaks of the year-to-year incidence spikes appeared simultaneously in 1978-1979 and 1985-1986, and that from around 1990 onward, the year-to-year comparisons for each cancer continued to increase synchronously with the increase in pollen counts, in peak and 1-2 year lagged years of pollen counts, until 2015. We then submitted the results of the first cancer paper. Figure 2 showed a correlation between cancer onset and pollen counts two years before the onset of cancer in lung and breast cancer. We further proved statistically significant correlations with Bonferroni Correction between the number of newly registered patients in the patient-registry year “x” and annual airborne pollen levels in Tokyo and/or Sagami-hara

City, measured 2 years prior to “x”, for the following 5 cancers; lung cancer, breast cancer, skin cancer, pancreatic cancer, and kidney cancer, and measured 6 years prior to “x”, for the following 6 cancers; oropharyngeal cancer, oesophageal cancer, prostatic cancer, bladder cancer, uterus cancer, and kidney cancer.

The paper was finally published in June 2020, after a similar process of being rejected on the doorstep of peer review for each of the previous paper submissions, perhaps because of its unconventional content. Some of the data are shown in Figure 2. We are working on a series of reports that will continue to show the epidemiological facts of numerous PIDs, each cancer, malignancy, and SIDs, which, like KD, will likely be triggered by pollen exposure. Common to 65 SIDs and cancers and malignant tumors, the dynamics of the number of patients and pollen dispersal began to increase in parallel from 1978-1986, and continued to rise steadily until 2015. This epidemiological fact suggests that human diseases are distantly related to pollen in the plant kingdom, and numerous diseases are inevitably led to the development process.

The Mystery in the Initial Phase of Common Cellular Responses Induced by Pollen

We have been interested for many years, in the relationship between pollen exposure and the onset of human diseases. We feel that it is important to gaze at and to elucidate the initial phase of common cellular responses induced by pollen. When human bodies are exposed to pollen, the pollen as the environmental stress, may facilitate intra-cellular processing and cellular responses. The environmental stress of pollen exposure must be a common trigger for the development of diseases and highlights the real and essential issues of life phenomena, and the early response of living cells in earlier period of pollen exposure should be elucidated. When the initial phase of the disease onset is triggered by pollen exposure, the pollen cells act on organs, tissues, and cells in the human body, and are supposed to enter the steps of cellular senescence or cellular degradation [20,21]. It might cause the condition of the patient who has not become ill yet, and then induces the progression process to the onset of multiple individual diseases. At the point when pollen exposure exceeds an individual’s threshold, the pollen exposure triggers the initial process of developing a number of SIDs and cancers and malignancies. That is, concurrently, some people go through the process of SIDs and others go through the process of cancer development.

Our hypothesis is that plant pollen acts as a priming agent that starts with a blow to human organs, tissues and cells and leads to the development of various human diseases. We believe that it is essential to focus our investigating efforts on these early stages of disease development dynamics, especially those that are still unknown. It is our hope that life science researchers will give priority and wisdom to investigating the initial processes of biological responses to pollen exposure that are common to all people, and to conceptualize and construct the basic concepts of

life phenomena. Elucidation of the cellular response sites and processes after pollen exposure may give people hope for the prevention of SIDs and cancers, and advance to longevity. Thus, we have invited you to discuss the basic cross-section of life phenomena and disease pathogenesis.

Significance of Pollen Avoidance for Public Health in “With Corona” Era

Some people wear parasols even in winter to avoid ultraviolet and infrared rays, but in the wake of the Covid-19 pandemic, the wearing of masks, goggles, and face shields for protection against infection has become commonplace, not only in Japan, but throughout the world. This, of course, means that pollen avoidance is also practiced in parallel, which may prevent the worsening, progression, or recurrence of symptoms of chronic PIDs [22]. This hypothesis is reminiscent of the proposition “Are longevity people with less susceptibility to disease a group of people with lower response to pollen exposure”? At this time of dispersion of first, small amounts of cedar pollen, September-November, if people suffering from SIDs seem to feel relief of symptoms through the habit of wearing masks, it may give people empirical confidence that the daily habit of pollen avoidance is effective in preventing the contraction and development of diseases, which might alleviate their fears about future health maintenance and give them hope for the future.

As for cancer and SIDs, if we continue our pollen-avoiding habits from the early days of life and make constant efforts to prevent them, we can give hope to the nation and humanity that we can live a long and healthy life until we contract microbial infections, have an accident, or pass away due to old age, which would be a bright spot in the midst of the corona crisis. We hope that this hypothesis will be proven in future through experimental medical research and other means. It is also recommended that patients with cancer or SIDs who are currently undergoing treatment or who have undergone treatment for cancer or SIDs wear masks and goggles, remove pollen from dried bedding, and remove pollen from rooms by using an air purifier, etc., not only in the spring when there is a large amount of airborne pollen, but also during the first small amount of cedar pollen from September to November. This is because we have seen possible worsening or recurrence of symptoms in people with various diseases even during this summer and winter transition.

Conclusions

Our medical care is biologically based on the existence of disease, but also is socio-economically influenced by the activities of the people who are engaged in administrative and economic activities. The authors believe that such a principal fact of the development of diseases should be reflected in public policies and in actual educational and economic activities of the medical and the pharmaceutical communities, which are aimed at the prevention

and treatment of diseases and the maintenance of health in the daily life of the people. All humans breathe the air and are exposed to pollen from the eyes, nose, ears, and skin for more or less 6-7 months a year for life. We will have to work together to make the public aware of the epidemiological fact that one of etiological causes of a number of chronic diseases is likely to be the pollen to which humans are all destined to be exposed since birth. We expect that the onset of a number of chronic diseases might be suppressed by a daily lifestyle of avoiding pollen.

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