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Epidemiology and Public Health Research

Review Article

A hypothetical discussion of the linkage of airborne pollen exposure to COVID-19 outbreak phenomenon, as well as to development of various intractable diseases and cancers

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ABSTRACT

Since 2003, the author has reported in four epidemiological analyses that Kawasaki disease (KD) in infants which has still been considered to be of unknown etiology, is probably a pollen-induced disease (PID) triggered by pollen. In 2018, the author showed in an epidemiological analysis that Takayasu disease, a designated intractable vasculitis syndrome is also a PID. Next, in analyzing the correlation between pollen counts and the number of newly diagnosed cases of various specific intractable diseases, the author has proposed that 40 designated intractable diseases, as well as 24 types of cancer and malignant tumors may be PIDs. The four severe viral infections in the 21st century consist of SARS (2002~2003), pandemic 2009 H1N1, MERS (2012~), and COVID-19 (2019~) due to SARS-COV-2 infection. Having studied for many years the involvement of pollen sensitivity in the background of the development of many intractable diseases, the author has recently come to assume that these viral infections would also be related to pollen exposure in the host population. When I looked into the pollen dispersal situation in Wuhan, the city where SARS-CoV-2 originated, I found that Chinese research reports up to 1989 stated that the number of pollens dispersed in Wuhan was significantly higher than in other Chinese cities. We reported on these topics in our previous report in a predictive manner. The author has already reported the phenomenon that onset of KD which is delayedly induced by pollen exposure is suppressed during influenza epidemics, and at the same time, the number of KD and influenza patients parallelly moved. This report closes up the three-way relationship between pollen exposure and the number of influenza patients as well as KD patients, and further points out the possible involvement of pollen exposure in the SARS-CoV-2 outbreak. The authors hypothesize that the host who has been compromised after a large amount of pollen exposure responded to the coronavirus, which happened to be a slightly different parasite from the conventional one, with an abnormal response similar to the carcinogenesis process, and that the virus made many mistakes in the replication process, resulting in the virulent and highly infectious SARS-CoV-2. In addition, it is expected that SARS-CoV-2 mutants will emerge simultaneously in many countries in the future, when a patient host who has been compromised after pollen exposure in spring becomes infected with SARS-CoV-2 by chance.

Key words: Kawasaki Disease, pollen exposure, intractable diseases, cancers, influenza, COVID-19, SARS-CoV-2, mutant, Wuhan, host and parasite, compromised, ophthalmologist, Parkinson disease, pollen avoidance, Takayasu disease, pollen-induced diseases(PID), influenza epidemics

INTRODUCTION

The COVID-19 pandemic has been going on for over a year. In addition to intractable diseases, cancers, and malignant tumors that are thought to be triggered by pollen exposure, the COVID-19 outbreak phenomenon by SARS-CoV-2 is forcing a further change in the medical concept of disease development. It is not surprising that SARS-CoV-2 variants occur not only by transmission from country to country, but also in parallel in different countries, because there are patients in every country who are compromised by exposure to pollen.

Pollen as the trigger for the onset of Kawasaki disease (KD)

Among the animal and plant kingdoms that make up the existing biological world, what is the fundamental idea in medical treatment of diseases in the animal kingdom, especially in humans, domestic animals, pets, and zoo animals? Can't we make it possible for all living things to live a life of high quality of life (QOL) on a peaceful and safe planet for as long as possible they wish? Will there ever be a day when academic, medical activity and that of economic activity in practice of medicine to confront illnesses will be carried out from a different standpoint or in conjunction with politics toward the above goals?[1]. I would like to leave the discussion and debate from the fundamental, biological perspective of the birth of life to others, and proceed with the practical aspects hereinafter. While some diseases, like injuries and trauma, show visible signs of progress, most diseases occur and progress invisibly. In spite of extensive treatment, the disease often progresses, and in the worst cases, even in this modern age of advanced medical care, people die unexpectedly early, though not as quickly as in the past. In today's world of advanced medical care, the number of diseases with unknown causes has been decreasing. However, diseases with unknown causes have often been considered to be diseases of invisible microbial origin or autoimmune diseases.

A typical case was Kawasaki disease (KD) in infants, which was first reported by a Japanese pediatrician, Tomisaku Kawasaki in 1962 [2], but in 2003, our epidemiological analysis suggested that it may be pollen-induced diseases (PID) [3]. The authors conducted a correlation analysis between the number of patients with KD and pollen counts in Kanagawa Prefecture and Tokyo over a 40-year period from the late 1970s to the late 2010s, and found a significant linkage between them (Figure 1). In addition, KD, which

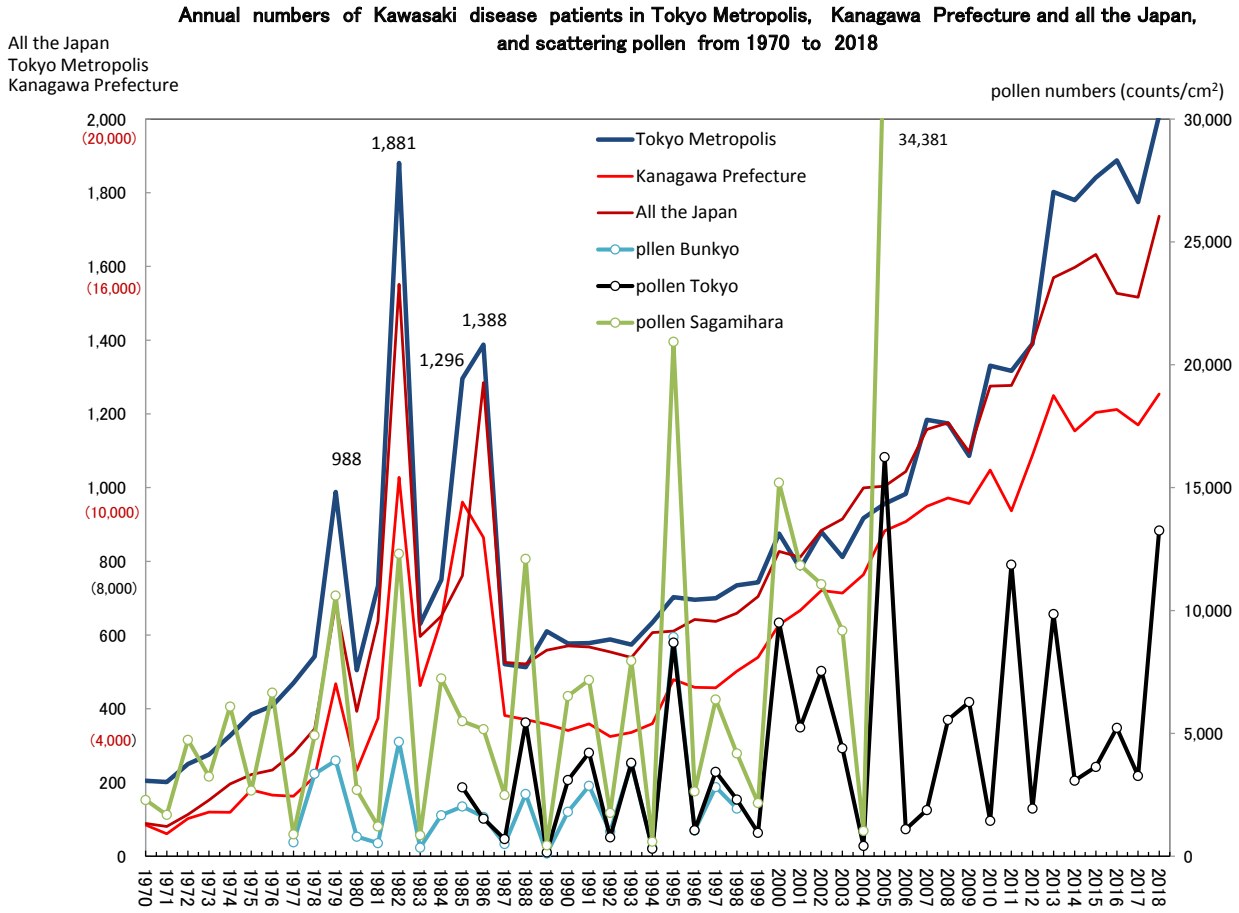

Figure 1. Annual numbers of Kawasaki disease patients in Tokyo Metropolis, Kanagawa Prefecture and all the Japan, and scattering pollen from 1970 to 2018.

is considered to be a pollen-induced delayed-type hypersensitivity reaction disease, has been reported in a total of our four papers [3-6], including a phenomenon in which the onset of the disease is suppressed during the influenza season [6]. In the fourth report among these KD papers [6], there is a graph that also suggests a relationship between the number of influenza patients and the number of pollen dispersed (Figure 2), and would like to mention beforehand how the epidemiological facts which lead to the claims of this opinion article were recognized.

In addition to breathing the air of the outside world and being exposed to sunlight, living creatures in the animal kingdom are after the birth through a life exposed to pollen for more than eight months every year in Japan. This pollen exposure may be recognized as a distant cause of the onset of many designated intractable diseases, cancers, malignancies, and many other diseases, as well as a proximate cause of intractable diseases during the intervening years. Nowadays, as shown by what our four recent epidemiological studies have uncovered [7-10], it is considered impossible to talk about the onset of disease without pollen. In KD, children aged 0 and 1 account for half of the patients with the disease, and it is a typical intractable disease that develops in infants, probably due to their constitutional susceptibility to pollen exposure, while their experience of pollen exposure is extremely short. It should be recognized that our research findings on KD are not only a precursor to the pathogenesis of juvenile intractable diseases such as Juvenile idiopathic arthritis [11], but also a precursor to the pathogenesis of various adult intractable diseases as described below.

Pollen as the trigger for the onset of specific intractable diseases

In June 2018, our epidemiological analysis revealed that Takayasu disease [12], a vasculitis syndrome discovered by a Japanese ophthalmologist, Mikito Takayasu in 1908, may be a second PID found after KD. Pollen can easily enter the body through the eyes, nose, ears, mouth, and skin. Harada disease (Vogt-Koyanagi-Harada disease) was reported by a Japanese ophthalmologist, Einosuke Harada in 1926 [13]. Alfred Vogt and Yoshizo Koyanagi were also Swiss and Japanese ophthalmologists, respectively. At the end of the text in this paper, the author will describe the fifth, a Chinese ophthalmologist who communicated at first the fact of outbreak of COVID-19. The results of our epidemiological analysis over a 40-year period showed that a total of 40 designated intractable diseases are also likely to be PIDs that occur in individuals who have been continuously exposed to pollen and have been compromised [7,8,10] (Figure 3). These include Takayasu disease and other vasculitis syndromes, collagen diseases such as scleroderma, autoimmune or degenerative diseases in the field of neurology such as multiple sclerosis, myasthenia gravis and Parkinson's disease, inflammatory bowel diseases such as ulcerative colitis, interstitial pneumonia, idiopathic dilated cardiomyopathy, and a number of intractable diseases that have been designated as genetic diseases.

Pollen as the trigger for the onset of cancers and malignant tumors

Furthermore, based on our analysis of 24 cancers and malignancies,

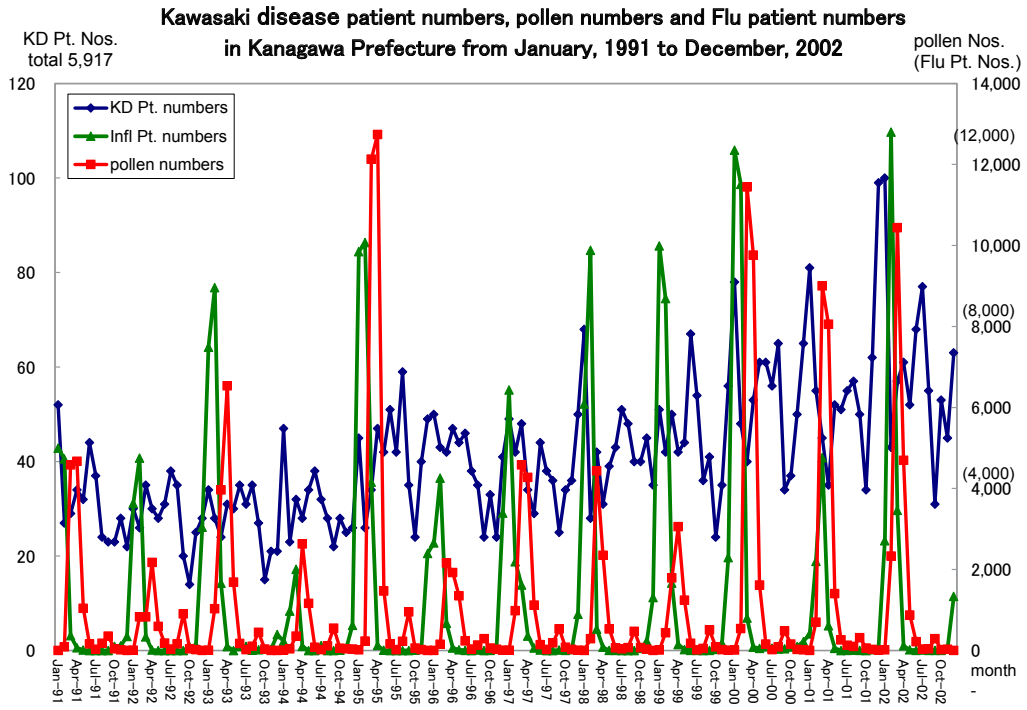

Figure 2. Kawasaki disease patient numbers, pollen numbers and Influenza patient numbers in Kanagawa Prefecture from January,1991 to December, 2002

we have reported since 2019 the epidemiological fact that cancers also develop with pollen as a trigger [9,10] (Figure 3). The authors have found that under conditions where the individual's assumed pollen responsiveness exceeds a threshold, the proximate cause of irritation from high pollen exposure may be the simultaneous development of lung, breast, pancreatic, prostate, and other cancers two or six years later after pollen exposure, or even in the same year [9,10]. Thus, apart from the conventional allergic rhinitis and conjunctivitis (hay fever), does this mean that people of different fractions of the population having constitution with high pollen reactivity are susceptible to designated intractable diseases, cancer and malignant tumors? There is an urgent need for scientists to develop a variety of clinical diagnostic parameters, different from pollen-specific IgE antibodies, to predict and identify the onset of these intractable diseases, which are different from type 1 allergies.

Therefore, nowadays when the epidemiological fact that pollen is one of the triggers for the onset of intractable diseases and cancers has become clear, it can be said that an era of hope for the prevention of designated intractable diseases and cancers has arrived [14,15]. Human beings should recognize that they are faced with the need to establish a lifestyle in which they work hard to avoid daily exposure to pollen that comes into contact with humans for the rest of their lives. In Japan, the number of hay fever patients has continued to increase since 1978, and the custom of wearing masks has been established as a preventive measure. In the midst of the corona scourge, the wearing of not only masks but also goggles and face shields has become common, and as a result, pollen-protective lifestyle habits (including the installation of air purifiers) are being strongly practiced during the annual mass pollen dispersal period in spring and the slight advance dispersal period of cedar pollen from September to November before early spring. In this vein, if the public is encouraged to take new preventive measures against the onset of intractable diseases and cancer and malignant tumors, the number of cases of many diseases may decrease. It is necessary for the community of medicine and medical and healthcare industries as well as pharmaceutical science and pharmaceutical industries to make the knowledge of natural sciences and epidemiological results

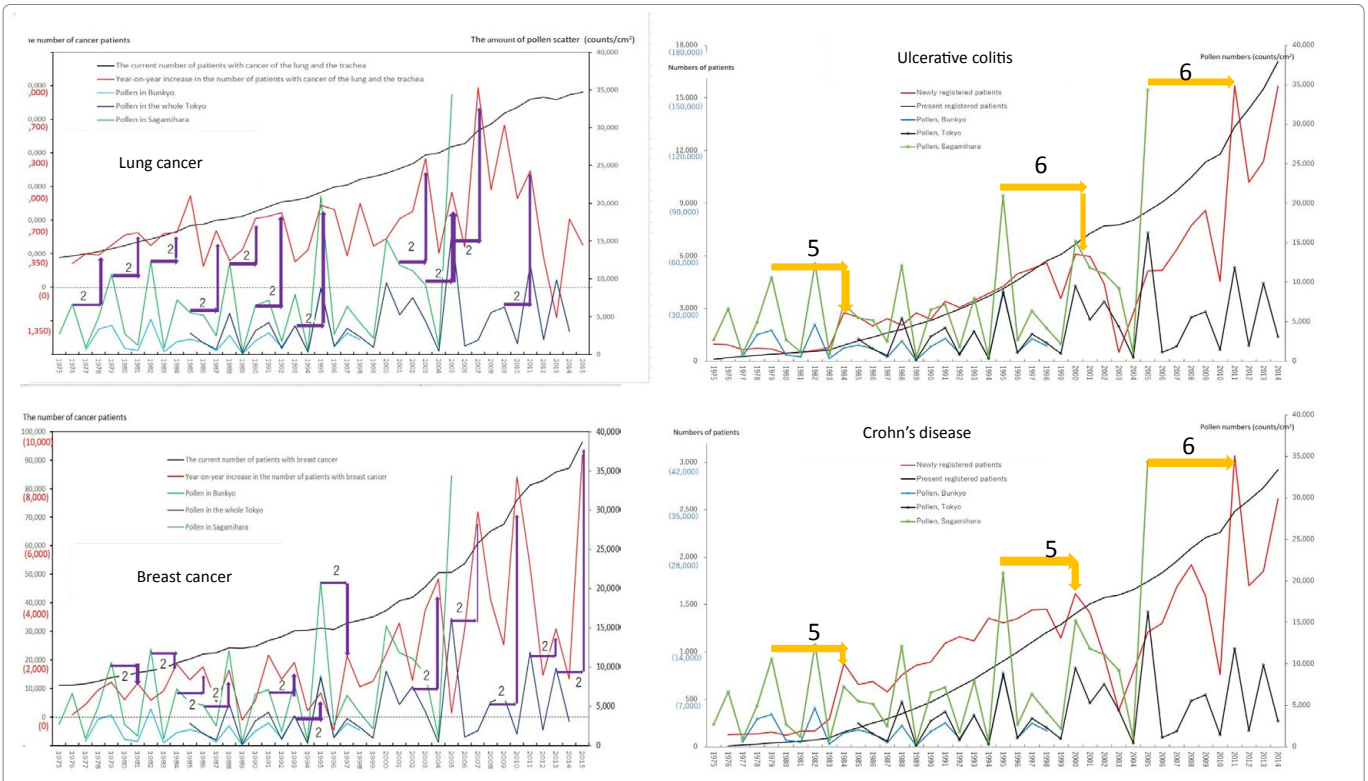

Figure 3. The current number of Japanese males and females (presently registered patients) registered for lung and breast cancer, and ulcerative colitis and Crohn's disease at the year diagnosed, its year-on-year increase (newly registered patients), and the amount of air borne pollen scatter in 3 areas during the period from 1975 to 2015.
The line graphs for lung and breast cancer, and ulcerative colitis and Crohn's disease representing numbers of presently and newly registered patients in each year, as well as the amount of pollen scattered in Bunkyo-City area of Tokyo, the whole Tokyo Metropolitan area and Sagamihara City during the period from 1975 to 2015. Numbers of patients are shown on the left axis whose scales consist of red numbers for newly registered patients and black numbers for presently registered patients. Pollen numbers in counts/cm2 are shown on the right axis. the whole Tokyo Metropolitan area and Sagamihara City during the period from 1975 to 2015. Violet arrows indicate phasic increments of newly registered patients occurring two years after phasic increments of airborne pollen scatter. Orange arrows indicate phasic increments of newly registered patients occurring five or six years after phasic increments of airborne pollen scatter.

concerning the development of such diseases the basis of their research, education and economic activities, and to reflect them in all their policies.

The four severe viral infections in the 21st century and possibility of association between pollen exposure and viral infections

SARS (2002~2003) due to SARS-COV infection, pandemic 2009 H1N1 due to H1N1 pdm 09 type influenza virus infection and MERS (2012~) due to MERS-COV infection caused pandemic, and COVID-19 (2019~) due to SARS-COV-2 infection has been spreading all over the world at present.

Today, epidemiological studies have revealed that pollen seems to act as a trigger in the onset of many intractable diseases and cancers in humans and other living organisms (Figure 3). We have also come to realize that pollen is the mastermind behind the onset of infectious diseases as well. In addition to the 65 diseases already described [10], the author has pointed out that pollen exposure acts as a trigger in patients who develop infectious diseases and contagious infections since the beginning of the reports on KD [16]. For example, mild infections involving summer cold viruses such as hand-foot-and-mouth disease, erythema infectiosum, and aseptic meningitis have been considered to occur because the immune status of the host, which is exposed to large amounts of pollen in the spring, has become susceptible to infection [17]. Furthermore, as mentioned forecasting in our previous perspective article on SARS-CoV-2 we assume that outbreaks of severe viral infections are based on the view that unconventional viruses with enhanced contagiousness and epidemic potential are born when a special biological response, similar to a carcinogenic process, backfires, such as the treatment of infectious viruses as parasites of a host that has been promoted after pollen exposure [18].

Correlation between the number of seasonal influenza patients during 1982 to 2019 and airborne pollen levels

The author hypothesized that the explosive seasonal influenza epidemic in Tokyo in 2008-2009 may have been caused by the late effects of pollen exposure in 2005, the year of the largest pollen dispersal ever in Japan, and by boosting via the pollen exposure effects due to the peak pollen count in 2008-2009 [7,17] (Figures 4 and 5). The incidence of KD, intractable diseases and cancer and malignant tumors was found to distinctly increase during these periods [6-10] (Figures.1 and 3). The explosive outbreak of seasonal influenza in Tokyo in 2008-2009 was followed by the well-known worldwide pandemic of H1N1 which swept across Japan in the latter half of 2009 (Figure.5), and also across Mexico as a new swine flu strain in the early spring of 2009.

As for the recent pandemic caused by the new coronavirus SARS-CoV-2, which has persisted for more than a year [19], the first case of the disease occurred in Wuhan City, China, which was once reported to be the area having the highest number of pollen dispersal [20] (Figure.6). After the countrywide survey of airborne pollen counts was conducted in China during 1985 to 1989, the collaborative study on pollinosis in China has been begun by Japanese and Chinese co-research group consisting of otolaryngologists and epidemiologists

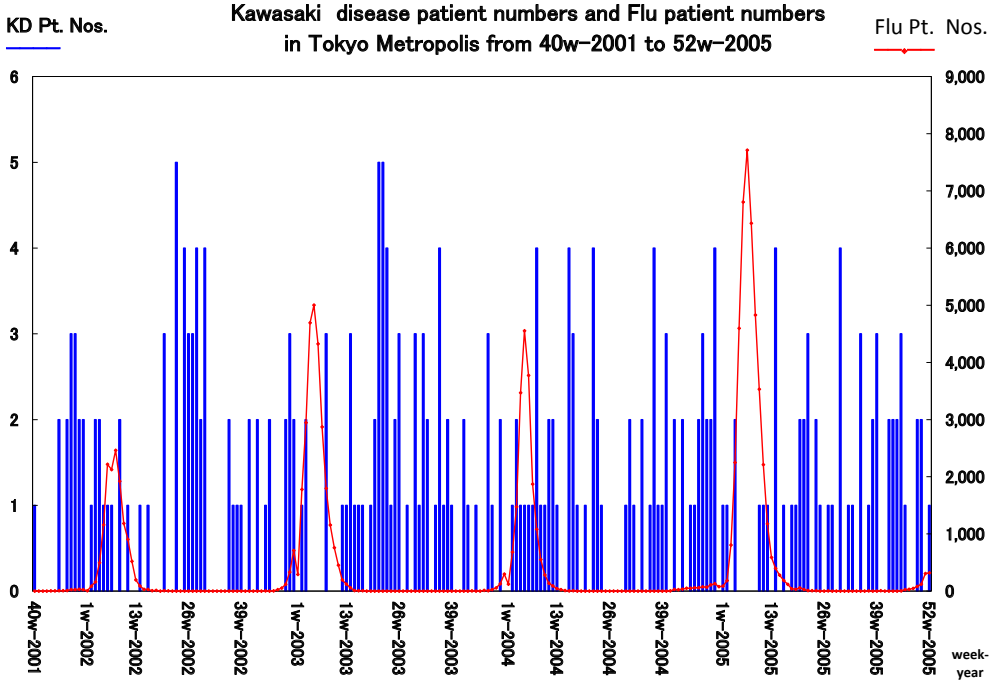

Figure 4. The reported number of Kawasaki disease and influenza patients in Tokyo infectious diseases weekly reports (IDWRs) gathered from 2001 to 2005 Variation from week 40 of 2001 to week 52 of 2005

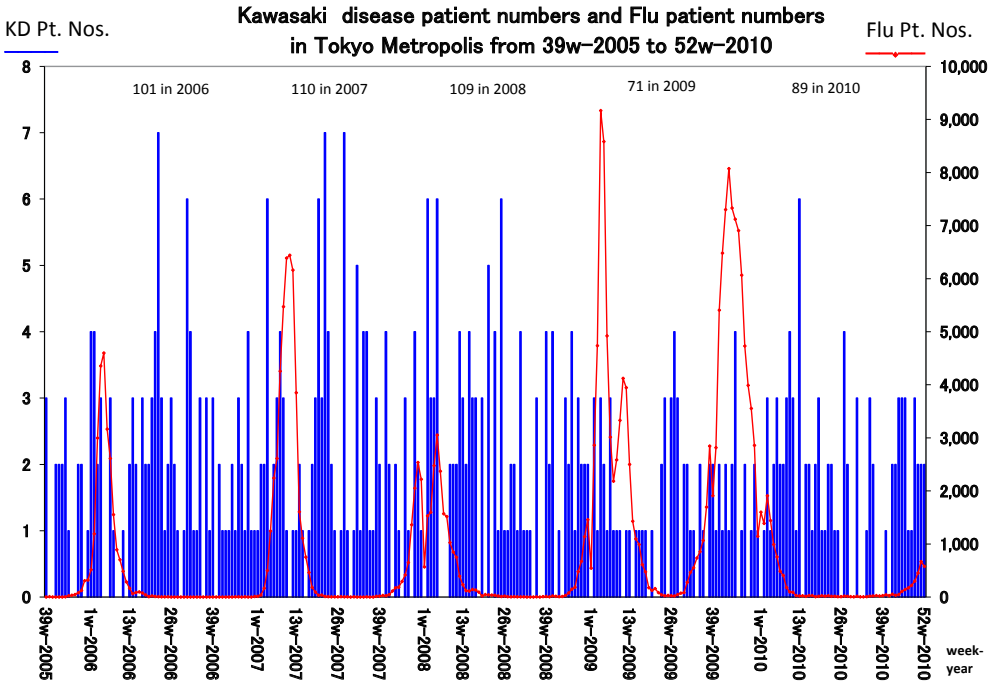

Figure 5. The reported number of Kawasaki disease and influenza patients in Tokyo infectious diseases weekly reports (IDWRs) gathered from 2005 to 2010. Variation from week 39 of 2005 to week 52 of 2010

Region in China	Quantity of cedar pollen per year	Cedar pollen ratio
①Jinan	56	0.40%
②Luck Castle	43	0.68%
③Xuzhou	100	0.97%
④Zhengzhou	4	0.02%
⑤Xi'an	36 (southern suburbs) 149 (city southwest district)	0.44% 1.78%
⑥Nanjing	10 (city west district) 13 (Baixia district)	0.06% 0.11%
⑦Changzhou	46	0.52%
⑧Suzhou	34	0.45%
⑨Wuhan	1551(Wuchang district) 21(Hankou district)	6.56% 0.07%
⑩Hangzhou	4	0.09%
⑪Chengdu	674	11.27%
⑫Fuzhou	15	0.17%
⑬Guiyang	19	0.45%
⑭Kunming	16	0.08%
⑮Nanning	228	3.27%

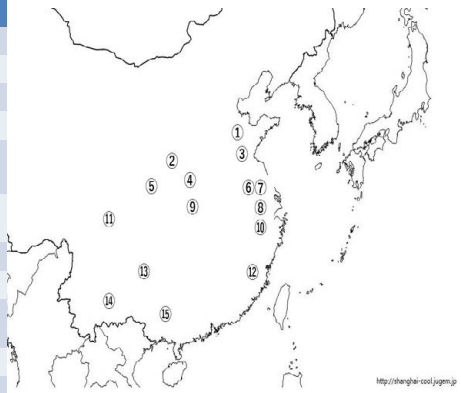

Figure 6. Region in China, quantity of cedar pollen per year, and cedar pollen ratio (left) and distribution map of pollen survey points in People's Republic of China (right). Quoted from partially modified figure 12 of Ref. 21 by kind permission of the author, Prof. Akira Miyoshi.

since 1995. The survey of airborne pollen counts was conducted by them in Wuhan City in 2000 and 2001 [21-24]. In the case of viral infections, pollen exposure may have triggered the host in the animal kingdom to enter a state of compromised immunity, and the different environment provided by the host to the parasite virus may have made the virus virulent and contagious.

Although this is not the story of the subject, it is a fact that the onset of KD is triggered by pollen exposure, and at the same time, that the number of patients decreases due to the suppressive effect of influenza epidemics [6].To complicate matters a bit, the influenza epidemic is also triggered by pollen exposure. Analysis of the data on influenza cases in Kanagawa Prefecture during 1982-2019 shows a remarkably significant correlation between the number of pollen counts and the number of influenza cases in the same year and four years later. Analysis of influenza case data in Tokyo shows also a significant linkage correlation between pollen counts and the

number of influenza cases two and six years later, and a tendency for the p-value to be close to 0.05 between pollen counts and the number of influenza cases in the same year and four years later.

We have newly clarified the epidemiological fact that there is a three-way correlation between pollen counts, the number of KD patients, and the number of influenza cases, although the presentation of the results is in preparation.

In order to clarify whether pollen exposure is one of the triggering factors of the SARS-CoV-2 outbreak, we would like to know the annual trends of pollen counts in Wuhan City and surrounding areas. For the above new strain of swine influenza H1N1, we would like to obtain data from Mexico on the observed pollen count data and influenza patient count data before 2009.

Implication of association of pollen exposure with influenza epidemics to epidemiology of COVID-19

Based on the epidemiological facts that pollen exposure may be a trigger for the development of the broad spectrum of diseases, such as many intractable diseases, cancers and malignant tumors, infectious diseases caused by invisible microorganisms, including influenza and COVID-19, we would like to consider that the medical community is under pressure to change the medical concept of disease, based on the providence of the natural world that all diseases are stimulated and caused by visible pollen produced by the plant world surrounding the animal world.

In the case of the newly introduced SARS-CoV-2, the conventional response of the host to infection with coronaviruses might be altered by compromised states after the large amount of pollen exposure, forcing the host to respond differently. Through these reactions occurring in the host, the parasite coronaviruses are thought to make many replication mistakes and to act wildly during the replication process, resulting in the birth of virulent new viruses. If virus researchers can identify the various facets of host-parasite interactions, they will be able to develop new antiviral drugs that target these interactions.

The biological mechanism of reactivity to pollen, avoidance of disease by protection against pollen, and tolerance to pollen behind the extension of life span

We would like to elucidate the initial response process to pollen exposure, and investigate how the effects are linked to each step of the immunological and allergic processes that have been established in the past. Consideration should be given to perturbing the traditional research scheme. On the flip side, it is imperative that we shift our evaluation criteria and methods, recognizing that the onset of a variety of diseases is influenced by pollen exposure, and that the symptoms of patients who received therapy after the onset of the disease will be affected by further pollen exposure daily [16]. In the field of experimental medicine, we must hasten to conduct research in complex experimental systems to clarify whether adding pollen exposure with or without bioaerosoles as reference to conventional animal systems or adding pollen components with or without bioaerosoles as control to conventional cultured cell systems accelerates biological reactions, thereby promoting inflammatory mechanisms and accelerating the onset of disease. We hope that pollen exposure will be applied to the long-lived Hadaka-deba rat (Naked mole rat) [25] and to the aging-accelerated mouse model SAM, and that the aging-progression parameters will be comprehensively identified one after another. Traditionally, pollen exposure has been viewed as a one-to-one cause-effect relationship, with only hay fever and some asthma disorders being associated with pollen exposure. As the work of otorhinolaryngologists and allergy researchers, they have avoided conducting research that involves exposing animals to pollen or adding pollen to cell experimental systems, so the immunology research paradigm also needs to be restructured and reformed. It is necessary to raise awareness of the need for research to consider that pollen, to varying degrees, has an effect on the basis of all life phenomena.

On the other hand, epidemiological studies are needed to determine whether people with low pollen reactivity and high pollen tolerance have a longer life expectancy, i.e., whether the degree of pollen reactivity might influence the length of life. A comparative study of the effect on longevity of differences in cumulative pollen counts in different regions of Japan, while excluding the effect of other constitutional factors, could be considered. Large-scale, long-term epidemiological studies will also be conducted to see if there is a difference in life expectancy between those who have practiced pollen avoidance and those who have not. The author has already proposed a short-term comparative study of the effect of pollen avoidance on reducing the recurrence rate of KD and the sibling morbidity of KD in infants for a period of at most 5 years [26], although I will leave the proposal to the interest of pediatricians.

As an active countermeasure against pollen, desensitization and desensitization therapy against pollen, so-called allergen immunotherapy, has been used for many years as a treatment for hay fever. First of all, why don't we apply allergen immunotherapy to patients who have received allergen immunotherapy for hay fever treatment and who are already suffering from designated intractable diseases, cancer, or malignant tumors? If good results are obtained, allergen immunotherapy may be applied at an early date to prevent intractable diseases and cancers in the younger generation.

The SARS-CoV-2 outbreak in Wuhan and the subsequent occurrence of pandemic and mutant strains of the virus in multiple countries

Pollen flies in every country where plants exist, and everyone is exposed to pollen right from birth, including in the womb. In the same year or two to six years later, some people will develop cancer and others will develop intractable diseases due to the stimulus of high pollen exposure when their individual pollen responsiveness exceeds the expected threshold. The record number of seasonal influenza cases in Tokyo in 2008-2009 indicated that the onset of some viral diseases might also be a result of the host's biological response to massive pollen exposure in 2005 and in 2008-2009, as

discussed previously. As in the case of the influenza epidemic in Japan, the initial outbreak of COVID-19 in Wuhan City is assumed to be a counter-attack disease caused by the birth of a novel virulent SARS-CoV-2, which is the result of an unusual biological response to an old coronavirus or a slightly unusual SARS-CoV-2 precursor virus that was accidentally transmitted through a compromised host patient with massive pollen exposure. It is an urgent task to disclose or collect data on the annual pollen count in Wuhan City.

In December of 2020 when summer season in the southern hemisphere was coming to an end, there were reports of mutant outbreaks in South Africa and Brazil, and in the earliest cases, the occurrence of mutants was already noted in October. People with allergic tendencies in each country who were exposed to a large amount of pollen in the spring and summer may have developed a different biological mechanism of reaction to the virus in a state of compromised condition, resulting in the creation of a mutated form of SARS-CoV-2 that had already been spreading. Isn't it more reasonable to understand that people in each region produce their own mutations. It is not surprising that Japanese people who have not traveled to the southern hemisphere can produce mutations of the same type as those produced in the southern hemisphere, giving rise to an unconventional effect on the virus due to increased sensitivity to pollen from the small amount of cedar pollen that is dispersed in advance from September to November before next year.

The fact that the mutant species were found in the UK in November and December may be due to the biological response and mechanism of the host, who moved from South Africa to UK, but was also compromised by the pollen dispersal of its own autumn heath and other pollen sources. Based on the epidemiological facts we have discovered, Parkinson's disease has been referred to as a pollen disease[10]. It is interesting to note that Parkinson's disease was first reported in England in the middle of the Industrial Revolution, when air pollutants were probably flying around. The fact suggests the involvement of pollen, which has become more allergenic due to the attachment of air pollutants. There are a large number of human hosts that have been compromised by pollen exposure in any part of the world. It should be recognized that parasite viruses can mutate anywhere in the world within the body cells of a human host, if the host responds abnormally to infection with an unusual coronavirus or SARS-CoV-2. It is still awaiting to be clarified what kind of abnormal response of the virus, depending on the constitution of the host strongly affected by the pollen exposure, can cause the occurrence of the mutant of SARS-CoV-2.

Expectation for collaborative works with Chinese researchers through WHO

An initial outbreak of COVID-19 in Wuhan, China was reported via Chat as an alarm message at the end of December 2019. The alleged informant, Dr. Li Wenliang, was working at the ophthalmological department of the hospital. For example, could it be that a patient who had been coming to the hospital for treatment of Behcet's disease, uveitis, or allergic conjunctivitis and happened to be in a compromised immune state due to the small amount of cedar pollen that flew ahead in the fall? The medical record history (laboratory data, etc.) of the patient who initially contracted the disease is important information, although it is assumed that the new coronavirus might be produced in the person's body after infection with the coronavirus, perhaps around or before November 2019. We would like to obtain as much data as possible on annual and monthly variations in pollen counts in Wuhan and surrounding areas from as far back as possible, and graphically analyze them in comparison with the number of new cases of KD, intractable diseases, cancer, and influenza patients, in order to explore the relationship between pollen counts and SARS-CoV-2 outbreaks.

There are great expectations for collaboration with Chinese researchers.

A fundamental concept of medical education and treatment, that pollen exposure acts as cause of disease development

The outbreak of the COVID-19 pandemic caused by SARS-CoV-2 has reminded us once again, for the first time in 100 years since the Spanish flu, that invisible microbial viruses are a major threat to humanity. On the other hand, it may be a ray of sunshine in the midst of a great disaster for us to be motivated to hastily report an unintended consequence of knowledge that has finally emerged about influenza infections, and to report that the pollen emitted by the plant kingdom, which exists in the background as a counter part of the animal kingdom, contributes greatly to the human race, and is full of good things, may be involved in the development of COVID-19 as well as KD, designated intractable diseases, and cancer and malignant tumors, and to report an unintended consequence of knowledge that has finally emerged about influenza infections.

In Japan, where pollen dispersal begins in early February, there are fears that many compromised hosts will appear that have been exposed to pollen through the summer, and that a variety of mutant species will be born. For the COVID-19 pandemic, where the effects of pollen exposure have not been taken into account at all, we may have to refrain from carelessly optimistic responses.

Reports by researchers other than our own noting the relationship between pollen exposure and corona infection risk

It has recently become clear that researchers other than our own are also taking an interest in the relationship between pollen exposure and corona infection risk. In Spring of 2020, Dr. Athanasios Damialis et al noted that the outbreak of the coronavirus pandemic appeared to coincide the tree pollen season in the northern hemisphere, and collected data on airborne pollen concentrations, weather conditions and SARS-CoV-2 infections, taking into consideration the variation of infection rates from one day to another and the total number of positive tests. In their calculations, the team also included data on population density and the effects of lockdown measures. The 154 researchers analyzed pollen data from 130 stations in 31 countries

on five continents. On March 8, 2021, they published a paper [27] describing the results that increased pollen concentrations correlate with higher SARS-CoV-2 infection rates. When airborne pollen levels were higher, increased SARS-CoV-2 infection rates were determined, by a large-scale study conducted by an international collaborative research team. They stated that that exposure to pollen weakens the natural immunity to respiratory viruses. In that case, it was rhinovirus, instead of SARS-CoV-2. They aimed to assess whether pollen may interfere with antiviral immunity. They combined data from real-life human exposure cohorts, a mouse model and human cell culture to test their hypothesis. In mouse experiments, they observed that the expression of antiviral genes was weakened in airway cells exposed to pollen, making them susceptible to infection [28]. This phenomenon was the same for people without pollen allergies. They found that pollen significantly diminished interferon-λ and pro-inflammatory chemokine responses of airway epithelia to rhinovirus and viral mimics and decreased nuclear translocation of interferon regulatory factors. In mice infected with respiratory syncytial virus, co-exposure to pollen caused attenuated antiviral gene expression and increased pulmonary viral titers. In non-allergic human volunteers, nasal symptoms were positively correlated with airborne birch pollen abundance, and nasal birch pollen challenge led to downregulation of type I and -III interferons in nasal mucosa. In a large patient cohort, numbers of rhinovirus positive cases were correlated with airborne birch pollen concentrations. High pollen concentrations lead to a weaker immune response in airways to viruses that can cause coughs and colds. This is also the case with SARS-CoV-2. They concluded that the ability of pollen to suppress innate antiviral immunity, independent of allergy and suggested that high-risk population groups should avoid extensive outdoor activities when pollen and respiratory virus season coincide. They noted that members of high-risk groups could protect themselves by watching pollen forecasts and wearing dust filter masks.

CONCLUSION

We may be led to have hope for longevity because we are able to recognize the possibility that the trigger for occurrence of many diseases including intractable diseases, cancers, malignant tumors and further viral infectious diseases etc. may be pollens. We expect for advance of research in exploring the first step of molecular and physiological bases and mechanisms concerned with contact of pollen cells and their constituents leading to onset of various diseases. The authors would like to propose that avoiding pollen exposure and using these knowledge and information to medical education and treatment, all the people will reach getting better QOL in daily life.

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CONFLICTS OF INTEREST

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REFERENCES

1. WHO. About WHO. Better health for everyone, everywhere. Available at: https://www.who.int/about
2. Kawasaki T. Non-scarlet fever desquamative syndrome. Chiba Med J. 1962; 38: 279.
3. Awaya A, Sahashi N. The etiology of Kawasaki disease: Does intense release of pollen induce pollinosis in constitutionally allergic adults, while constitutionally allergic infants develop Kawasaki disease? Biomed Pharmacother. 2004; 58: 136-140.
4. Awaya A, Murayama K. Positive correlation between Japanese cedar pollen numbers and the development of Kawasaki Disease. Open Allergy J. 2012; 5: 1-10.
5. Awaya A, Nishimura C. A combination of cross correlation and trend analyses reveals that Kawasaki disease is a pollen-induced delayed-type hyper-sensitivity disease. Int J Environ Res Public Health. 2014; 11: 2628-2641.
6. Awaya A. Suppressive influence of seasonal influenza epidemic on Kawasaki disease onset. Nihon Rinsho Meneki Gakkai Kaishi. 2016; 39: 528-537.
7. Awaya A. Development of many so-called autoimmune diseases including various vasculitis syndromes may be commonly triggered by pollen exposure. Jacobs J Aller Immuno. 2018; 5:26.
8. Awaya A, Kuroiwa Y (2019) A Retrospective study on the relationship between annual airborne pollen levels during four Decades of 1975-2014 and annual occurrence of ulcerative colitis, Crohn's disease, primary biliary cirrhosis, fulminant hepatitis, severe acute pancreatitis, interstitial pneumonia, amyloidosis, based on the National Registry Database of Specific Intractable Diseases in Japan. Arch Epidemiol Public Health 1: 112.
9. Awaya A, Kuroiwa Y. The Relationship between Annual Airborne Pollen Levels and Occurrence of All Cancers, and Lung, Stomach, Colorectal, Pancreatic and Breast Cancers: A Retrospective Study from the National Registry Database of Cancer Incidence in Japan, 1975-2015. Int J Environ Res Public Health. 2020; 17: 3950.
10. Awaya A, Kuroiwa Y. Forty Specific Intractable Diseases and 24 Types of Cancer and Malignancies as Well as Kawasaki Disease May be Triggered by Pollen. Arch Environ Sci Environ Toxicol. 2020; 3: 130.
11. Juvenile idiopathic arthritis. Brochure downloaded from HP of Japan Intractable Diseases Research Foundation. Available at: http://www.nanbyou.or.jp/entry/141.
12. Takayasu disease. Brochure downloaded from HP of Japan Intractable Diseases Research Foundation. Available at: http://www.nanbyou.or.jp/entry/141.
13. Vogt–Koyanagi–Harada disease. Available at: https://en.wikipedia.org/wiki/Vogt-Koyanagi-Harada_disease.
14. Awaya A. An era of hope for the prevention of designated intractable diseases has arrived. Rares blog. 2020. Available at: https://raresnet.com/blog-9/. (Accessed August 1, 2020). (In Japanese).

15. Awaya A. An era of hope for the prevention of cancer and malignant tumors has arrived. (YAKUJI NIPPO (Pharmaceutical News). Available at: https://www.yakuji.co.jp.

16. Awaya A. Urgent matter of launch of demonstrative research on the presence of not so few of Pollen-Induced Diseases -As the start point beginning from the finding that the trigger of Kawasaki disease may be pollen-The allergy in Practice 2004. 24(5):378-379, 2004. (In Japanese).

17. Awaya A. Proposal for construction of test and evaluation method in basic research and clinical study of medicines considering the effect of pollen exposure. Res Drug Interact. 2020; 44: 1-8.

18. Awaya A, Kuroiwa Y. Outbreak of a new coronavirus (SARS-CoV-2) infection and pollen exposure. Arch Community Med Public Health. 2021; 7(1): 012-016.

19. Copiello S, Grillenzoni C. The spread of 2019-nCoV in China was primarily driven by population density. Comment on "Association between short-term exposure to air pollution and COVID-19 infection: Evidence from China" by Zhu et al. Sci Total Environ. 2020; 744:141028.

20. The Executive Board of NSAAPC: A National Survey of Airborne and Allergenic Pollen in China. Beijing Press, Beijing, 1991.

21. Miyoshi A, Peng JR, Chen JZ, et al. Field work on nasal allergy II. Otologia Fukuoka. 1998; 44: 644-666.

22. Shi HB, Cheng L, Enomoto T, Takahashi Y, Sahashi N, Shirakawa T, et al. Recent Advances in Pollen Survey and Pollinosis Research in China. Jpn J Palynol. 2002; 48: 109-127.

23. Sanbe T, Miyoshi A, Cheng L, Takahashi Y. Incidence of pollinosis of students in Hubei Medical School located in Wuhan City in Hubei in China. Jpn J Allerogol. 2002; 51: 301.

24. Takahashi Y, Cheng L, Xu LJ, Zhang SY, Yang Q, Tao ZZ, et al. Airborne cedar pollen and cypress pollen survey in Wuhan in China. Otologia Fukuoka. 2003; 49: S108-S112.

25. Wikipedia. Hadaka-deba rat (Naked mole rat). Available at: https://en.wikipedia.org/wiki/Naked_mole-rat

26. Awaya A (2017) Pollen-Induced Diseases (PID) No.9; Prevention of Kawasaki disease by pollen avoidance life: Decrease of recurrence cases and family cases are criteria. THE YAKUJI NIPPO (Pharmaceutical News) No.11922. Available at: https://www.yakuji.co.jp. (In Japanese).

27. Damialis A, Gilles S, Sofiev M, Sofieva V, Kolek F, Bayr D, et al. Higher airborne pollen concentrations correlated with increased SARS-COV-2 infection rates, as evidenced from 31 countries across the globe. PNAS. 2021; 118: e2019034118.

28. Gilles S, Blume C, Wimmer M, Damialis A, Meulenbroek L, et al. Pollen exposure weakens innate defense against respiratory viruses. Allergy. 2020; 75: 576-587.

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