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Remembering the footsteps of five distinguished ophthalmologists during the COVID-19 pandemic(epidemic)

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Abstract

We have reported that 40 specific intractable diseases and 24 types of cancer and malignancies as well as Kawasaki disease may be triggered by pollen in our previous papers. Further, we reported in 2021 two articles regarding relation of outbreak of Influenza and COVID-19, and pollen exposure. In this paper, five distinguished ophthalmologists will be considered and described. Mikito Takayasu was the first person to report the discovery of Takayasu's arteritis, one of the vasculitis syndromes, which may be a pollen-induced disease as well as Kawasaki disease. Next, Einosuke Harada, Alfred Vogt and Yoshizo Koyanagi are considered and described as the reporters of Vogt-Koyanagi-Harada disease. The fifth ophthalmologist is Li Wenliang who was the first person in the world to report the outbreak of SARS-COV-2 infection. Many people are still unaware of the fact that exposure to pollen can lead to many diseases. The author hopes that those who are involved in medical care will consider the scientific facts, keep their eyes open, and use this knowledge in their daily activities, although clear proof in experimental medicine is craved.

Keywords: Kawasaki Disease, Pollen Exposure, Pollen-Induced Diseases(PID), Pollen Avoidance, Cancers, Influenza, COVID-19, SARS-CoV-2, Mutant, Compromised Host and Parasite, Wuhan, Parkinson Disease, Takayasu Disease, Intractable Diseases

Since February, pollen dispersal has begun in Japan. As of late March, the pollen has shifted from cedar pollen to cypress pollen. Dr. Yozo Saito (1932), Japanese otolaryngologist was the first person in the world to report cedar pollinosis in 1963. The year 1962, when Dr. Tomisaku Kawasaki (1925-2020), Japanese pediatrician reported Kawasaki disease (KD), was the time of Japan's rapid economic growth. It was the period when the automobile society arrived in Japan and mass emissions of air pollutants began to occur in the 1960s. Air pollutants may have an adjuvant effect on the allergenicity of pollen.The situation for the outbreaks of cedar pollinosis and KD in Japan seems similar to the simultaneous outbreaks of hay fever and Parkinson's disease during the industrial revolution in UK in the early 19th century. KD in infants is diagnosed when five or more of the following six symptoms are present: fever, redness of the ocular conjunctiva, bright red lips and strawberry-like tongue, red rash, swollen hands and feet, and swollen lymph nodes in the neck. Since 2003, I have argued that KD is probably a pollen-induced disease with a different concept from hay fever [1-4]. As shown in Figure 1, triphasic outbreaks of KD coincided with three upward peaks of pollen scatter (1978-79, 1982, and 1984-86). In the history of forestry in Japan, cedar trees were rapidly cut on a large scale in the 1940s-50s,because of military and industrial needs during and after the World War II. Then, Japanese government strongly promoted a forestation project in the 1950s-60s and cedar trees were rapidly planted in the entire Japanese land. In the 1970s-80s, namely 20 years after the period of cedar afforestation, the cedar trees gradually reached an age having a high pollen producing capacity. This is the background reason for the fact that cedar pollen release started to increase around the period of (1978-79) and continued to increase until 1986. In June 2018, the author recognized that Takayasu's arteritis (TAK), one of the vasculitis syndromes as well as KD, may be a pollen-induced disease. TAK was reported by Mikito Takayasu

(1860-1938), Japanese ophthalmologist, in 1903. TAK causes inflammatory wall thickening of the aorta and its major branches, pulmonary arteries, and coronary arteries, resulting in stenosis. Stenotic or occluded artery and aneurysms are its pathological features. TAK is more common in young women and is also called pulseless disease. In December 2018, the author reported the results of an analysis based on 40 years of patient statistics from the Intractable Disease Information Center, including Behçet's disease, systemic lupus erythematosus, sarcoidosis, and along with other designated intractable diseases [5]. In 1926, Einosuke Harada (1892-1946), Japanese ophthalmologist published his original work on Harada's disease (HD), that was later united into the name Vogt-Koyanagi-Harada disease. Alfred Vogt (1879-1943) and Yoshizo Koyanagi (1880-1954) were Swiss and Japanese ophthalmologists, respectively. HD is an autoimmune disease in which the melanin pigmented cells are destroyed by lymphocytes. Its symptoms appear in the uvea, hair, skin, ears, and meninges. People who develop HD have a genetic predisposition to it.

Starting in the summer of 2019, the author proceeded with a 40-year statistical analysis of the number of cancer patients and pollen counts based on the cancer incidence data published by the National Cancer Center. The author clearly recognized the fact that pollen exposure is also involved in the development of cancer. In December 2019 [6] and June [7] and December 2020 [8], the author reported that 40 intractable diseases such as Parkinson's disease and ulcerative colitis, and 24 cancers and malignancies would be triggered by pollen exposure, similar to KD [1-4]. Pollen enters the body through the eyes, nose, ears, mouth, and skin, and causes a variety of diseases. Organisms in the animal kingdom are innately exposed to pollen from the plant kingdom for their entire lives (about 8 months per year in Japan). It is assumed that pollen exposure is a distant cause of disease onset in humans, and that in years when pollen exposure or pollen reactivity exceeds the threshold for each person, pollen exposure becomes a trigger (proximate cause) for the onset of diseases, such as KD, designated intractable diseases, cancer, and malignant tumors.

In 2016, the author noticed the effects of pollen exposure extending to infectious diseases, and a linkage between the number of influenza cases and pollen counts, when the author reported that onset of KD is suppressed during influenza epidemics [4]. In December 2019, Dr. Li Wenliang (1985-2020), Chinese ophthalmologist received an internal diagnostic report of a suspected SARS patient at Wuhan Central Hospital. The outbreak was later confirmed not to be SARS, but SARS-CoV-2. He was the first person in the world to report the outbreak of SARS-COV-2 infection, and raised awareness of COVID-19 infections in Wuhan. He later contracted COVID-19 and died from the disease in February 2020, at age 33. The reason why SARS-CoV-2 infection occurred in Wuhan is assumed to be related to the fact that the pollen count in Wuhan was by far the highest of all Chinese cities in a survey conducted in the late 1980s [9,10]. In January 2021, the authors published the first report [11] on the relationship between SARS-CoV-2 infection and pollen exposure. Based on the fact that there is a correlation between the dynamics of the number of influenza cases and pollen counts in Kanagawa and Tokyo from 1982 to 2019, the second report [12] assuming a relationship between the SARS-CoV-2 outbreak and pollen exposure was also published in May. Viruses mutate repeatedly in the bodies of host animals such as humans. People with allergic constitutions who have been exposed to pollen for a long time and are in extremely poor health become immunocompromised and easily infected by coronavirus, causing an unprecedented biological response. The responding virus may have made many mistakes in the replication process, resulting in a new coronavirus. This is similar to the way that pollen exposure is the proximate cause of various types of cancer in humans [7,8]. Recently, other researchers are also taking an interest in the relationship between pollen exposure and corona infection risk.The international collaborative research team in 31countries on five continents described in PNAS the results that increased pollen concentrations correlate with higher SARS-CoV-2 infection rates [13]. Gilles S, et al combined data from real-life human exposure cohorts, a mouse model and human cell culture, and concluded that exposure to pollen weakens the natural immunity to respiratory viruses [14]. In mouse experiments, they observed that the expression of antiviral genes was weakened in airway cells exposed to pollen. Members of high-risk groups could protect themselves by watching pollen forecasts and wearing dust filter masks.

Many people are still unaware of the fact that exposure to pollen is linked to many diseases. The author hopes that those who are involved in medical care will think about the scientific facts, keep their eyes open, and use this knowledge in their daily activities. Clear proof in experimental medicine is craved. Finally, we dedicate this paper to five distinguished ophthalmologists (Takayasu, Harada, Vogt, Koyanag and Li, with respect for their medical contributions to the discovery of TAK, HD, and COVID-19, which are assumed to be related to pollen exposure.

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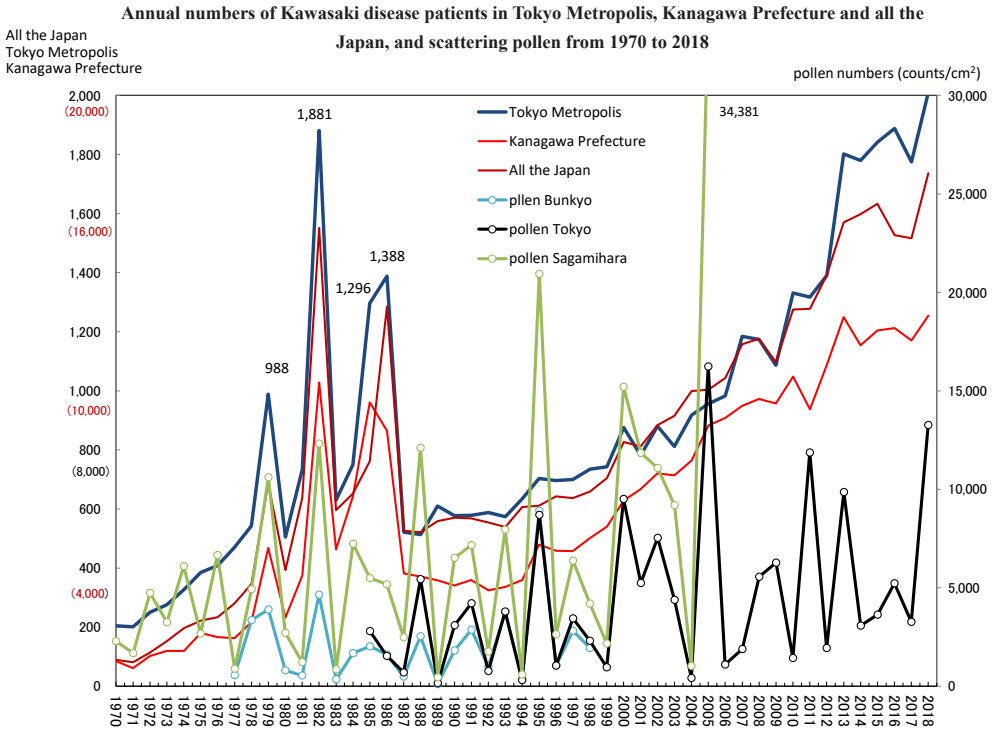

Figure 1: Annual numbers of Kawasaki disease patients in Tokyo Metropolis, Kanagawa Prefecture, and all the Japan, and scattering pollen from 1970 to 2018.

The line graphs for Kawasaki Disease represent numbers of newly diagnosed patients in Tokyo Metropolis (dark blue), in Kanagawa Prefecture (red) and in all Japan (dark red) measured in each year, as well as the amount of airborne pollen levels during the period from 1975 to 2014, in Bunkyo City of Tokyo (light blue), measured and reported by Dr. Yozo Saito as described in the text, in Tokyo Metropolis (black), and in Sagamihara City of Kanagawa Prefecture (green). During the decade of 1977-87, outbreaks of Kawasaki disease showed triphasic peaks of their occurrence (1978-79, 1982, 1984-86) with the highest peak in 1982, which coincided with triphasic upward peaks of airborne pollen release.

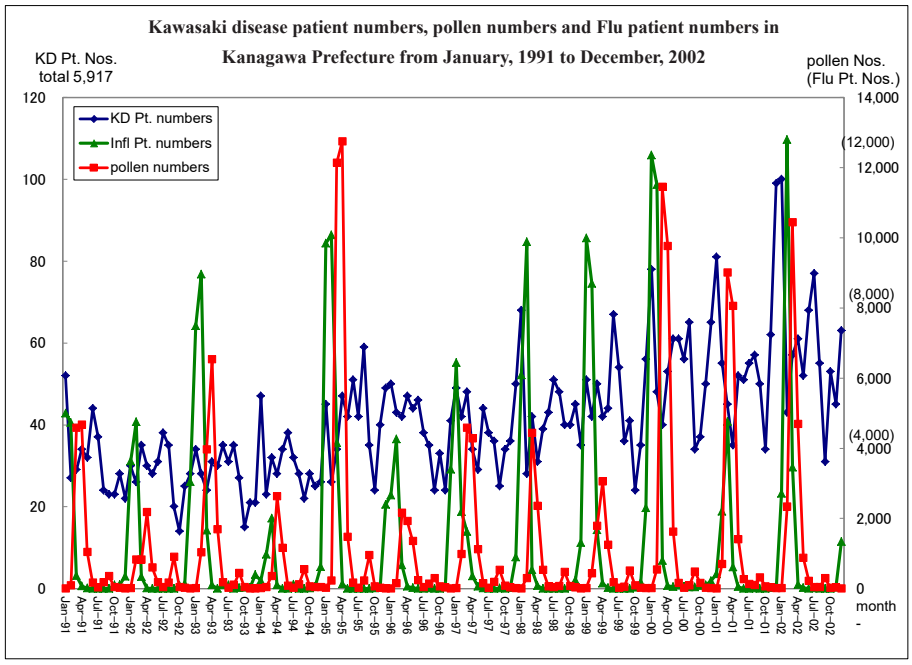

Figure 2: Kawasaki disease (KD) patient numbers, pollen numbers and Influenza patient numbers in Kanagawa Prefecture from January 1991 to December, 2002.

The onset of KD is triggered by pollen exposure, and the number of KD patients decreases during the period of seasonal influenza epidemics. On the other hand, the number of influenza patients is in conjunction with the number of pollen numbers [4] (Figure 2).

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%

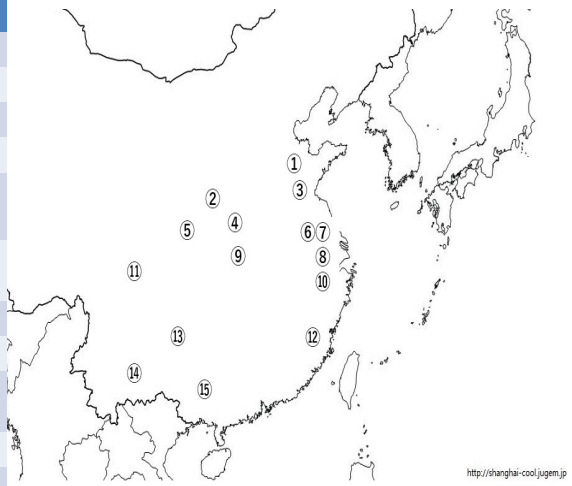

Figure 3: Region in China, quantity of cedar pollen per year, and cedar pollen ratio (left) and distribution map of pollen survey points in People's Republic of China (right).

Some parts of figure 12 of Ref. 10 (which was cited and originated from Ref. 9) are quoted with modifications by kind permission of Prof. Akira Miyoshi, who is Japanese otolaryngologist and afterward in 2000-2001 conducted a survey of airborne and allergenic pollen in Wuhan with his Japanese and Chinese colleagues.

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