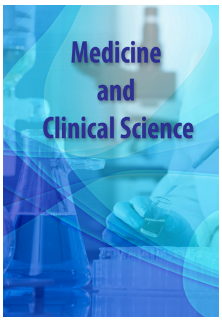
Medicine & Clinical Science

Original Article



Relationship Between Annual Airborne Pollen Levels And Occurrence Of Thyroid, Skin, Esophagus, Kidney And Ovary Cancers, And Leukemia, Multiple Myeloma And All Cancers: A Retrospective Study Based On The National Registry Database Of Cancer Incidence In Japan, 1975–2015

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thyroid, skin, esophagus, kidney, ovary, leukemia, multiple myeloma, cancers, malignancies, all cancers, Kawasaki disease, intractable diseases, pollen levels, pollen exposure, pollen-induced diseases, Tokyo Metropolitan, Sagamihara City of Kanagawa Prefecture, Fukushima, 2013, Chernobyl,1990, Three Mile Island, 1980.

Abbreviations

SIDs: specific intractable diseases; KD: Kawasaki disease; PIDs: pollen-induced diseases; present RPs: presently registered patients; newly RPs: newly registered patients; AP: airborne pollen; PL: pollen levels; PE: pollen exposure

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Abstract

Background: In Japan, pollen counts increased between 1977 and 1987, including three peaks (1978-1980, 1982, 1984-1986) coinciding with Kawasaki disease (KD) outbreaks. Epidemiological findings have been gradually accumulated that KD and related specific intractable diseases and further cancers may be correlated to pollen exposure (PE).

Methods and results: To elucidate the effects of PE on occurrence of thyroid, skin, esophagus, kidney and ovary cancers, and leukemia, multiple myeloma and all cancers, we evaluated the annual onsets of malignant tumors in relation to pollen counts using data from a national database.

Increased rates of these cancers were observed during pollen counts increasing period between 1977 and 1987. Significant correlations were observed between the annual number of newly registered patients (nRPs) and the annual pollen levels (PL) measured with a lag of 2 years for skin and kidney cancers, 4 years for thyroid cancer, 6 years for skin, esophagus cancers, leukemia and multiple myeloma, 8 years for thyroid cancer, and 2,3 and 6 years for all cancers. Peaks of number of thyroid cancer in 2013, 1990 and 1980 are discussed about as compared with other cancers regarding effect of radioactive pollutants occurred from three nuclear plant accidents.

Conclusion: Data suggest newly that the cumulative effects of PE within 2,3,4,6,8 years prior to diagnosis might possibly trigger incidence of eight cancers and malignant tumors.

Introduction

The type of organ affected by cancer or malignancy is naturally different for each patient. If a parent develops stomach or colon cancer, the child may develop cancer in the same organ or in another organ. We are interested in how often patients with ulcerative colitis later develop colorectal cancer and how often they develop cancer of other organs or do not develop cancer. What might account for the selectivity regarding the outcome of these patients with ulcerative colitis? What is the rate of thyroid cancer in people with thyroid diseases such as Graves' disease, Hashimoto's disease, iodine deficiency, and goiter? What kind of people get thyroid cancer? What are the characteristics of people who get thyroid cancer? Is there anything known that is defined at the genetic level in people who get thyroid cancer? It is understood that people exposed to radioactive iodine I-131 have a high probability of developing thyroid cancer in the thyroid gland, which is the organ that produces iodine-containing hormones. When cancer develops in

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more than one organ in a patient, it may be due to metastasis of the cancer, or it may be due to multiple cancers. If a patient is cured of cancer in one organ, what is the frequency of cancer occurring later in another organ? [1,2]. As for statistical data on the number of cancer patients in Japan, we can approach to and look at the Excel data tables of the form gathered up published by the National Cancer Center up to 2015 [3,4].

We would like to know the causes of the various cancer-related phenomena described above. What are the triggers when cancer develops and what are the possibilities regarding the mechanism by which cancer develops are described below. The following description is based on the academic findings from the research results the author has followed. In four papers [5-8], the authors reported the findings that pollen may be a trigger for the development of Kawasaki disease (KD), which accounts for 50% of all cases in children aged 0 and 1 year, and that KD may be Pollen-Induced Diseases (PID) [9]. Finally, in 2018, the author began to examine 40 designated incurable diseases, starting with Takayasu disease, the same vasculitis syndrome as KD, using national registry data from the Center for Research on Intractable Diseases in Japan [10]. In the course of the study, the author compared the annual current number of cases of each disease from 1974 to 2014, as well as the change in the number of cases compared to the previous year (number of newly registered cases) with the change in pollen exposure, and plotted these data in graphs. The author further conducted a statistical correlation analysis and found a statistically significant correlation between the number of newly registered affected patients and pollen exposure, and continues to report that various designated incurable diseases may also be PID [11-13]. The fact that the designated intractable diseases as PIDs are caused by various disease processes in various organs, tissues, and cells in each person led us to consider the possibility that cancer and malignant tumors, in which cell division in various organs continues to increase, may also be PIDs, given the common nature of the life phenomenon. The author statistically analyzed the number of patients with 24 types of cancer and malignant tumors from the National Cancer Center's (NCC's) registry data from 1985 to 2015, employing the same research methodology as used for the analysis of KD and designated incurable diseases. We have already reported these findings in two previous papers [14,15], so for us, this is the third reported paper on the correlation between cancer development and pollen exposure. In two previous papers on lung, breast, pancreatic, stomach, and colorectal cancer and on cancer as a whole, the author compared the change in the number of cases compared to the previous year (number of newly registered cases) with the change in pollen exposure, and plotted these data in graphs. The author further conducted a statistical correlation analysis and have already found a statistically significant correlation between the number of newly registered affected patients and pollen exposure. Lung, breast, and pancreatic cancers were shown to be significantly more likely to develop two years after pollen exposure [14,15].

In this paper, we report the number of newly enrolled patients with thyroid, skin, esophagus, kidney and ovary cancers, leukemia, multiple myeloma, and all cancers. The results of the analysis are described in comparison with pollen exposure. During the 40-year period (1985-2015) in which the authors reviewed statistical data, humanity experienced three nuclear accidents: the Three Mile Island nuclear accident in 1979, the Chernobyl nuclear accident in 1986, and the Fukushima Daiichi nuclear accident in 2011 [16]. In the years following the Chernobyl accident, it was reported that the number of children with thyroid cancer was higher than before the nuclear accident [17]. The author is interested in whether there are any reports on how much radioactive material was dispersed into the air during these nuclear accidents, what was the exposure dose in each country and region, and what effect the nuclear accidents have had on the number of cancer and malignant tumors other than thyroid cancer. The author observed the dynamics of the number of cases of thyroid cancer and cancers occurring in organs other than the thyroid gland. We noticed the possibility of effect of nuclear accidents on cancer onset in the graphs made by our work, and thus point it out and add some discussion of the relationship with the nuclear accident, in addition to the correlation with pollen exposure.

Materials and methods

Since 1958, the governmental authority in Japan, the NCC, has been gathering cancer incidence data by registering patients and releasing the data to the public [3,4]. The data shows the number of presently registered patients (RPs) in each present calendar year. In this study, we initially imported the number of presently RPs into the Excel tables. We then calculated the number of newly RPs in each year based on the annual number of presently RPs in some year and that in its previous year for all cancers and for each of 23 types of cancers or malignant tumors. The work was performed in accordance with the ethical principles for medical research outlined in the Declaration of Helsinki in 1964 and its subsequent revisions (https://www.wms.net/). Data on airborne pollen (AP) release was provided by Dr. Yozo Saito, Dr. Hiroshi Yasueda and Professor Norio Sahashi [5]. Dr. Saito gathered AP data based on the research unit in the Tokyo Medical and Dental University Graduate School of Medicine, Bunkyo-City, Tokyo [5], while Dr. Yasueda surveyed AP data based on the research unit in the National Hospital Organization, Sagamihara National Hospital, Sagamihara, Kanagawa [5–15]. As he ended his service of information transfer in 2006, no data has been obtained since then. The AP data in the Tokyo Metropolis collected from 12 research sites was donated by Mr. Hiroshi Kaneko. The AP data was downloaded after administrative information disclosures from the Tokyo Metropolitan Institute of Public Health website [18].

In the present study, data of numbers of patients with cancers and malignancies in all the Japan were imported into tables in Microsoft Excel. This data was used to create figures of line graphs for each cancers. These figures represent annual numbers of presently RPs as well as newly RPs, and the scattered pollen counts in three areas in Japan (the Bunkyo-City area of Tokyo, the whole area of Tokyo Metropolitan, and Sagamihara City in Kanagawa).

A correlation analysis was performed for each cancer and malignancy, to evaluate the association between the annual number of newly RPs in each patient-registry year “x” during 1975–2015, and the annual amount of AP levels in Tokyo and Sagamihara, measured in the same year as the patient-registry data. A correlation shift analysis was also performed between the annual number of newly RPs in each patient-registry year “x” between 1975 and 2015 and the annual AP levels in both cities measured “α” years prior to the patient-registry year“x”(“α”=1~20). Correlation coefficients and p values were calculated using the Excel function PEARSON via the method described in the brochure http://imnstir.blogspot.com/2014/04/p.htm. A statistically significant positive correlation was defined as $p<0.05$. Marginally significant associations that indicated a possible positive tendency ($0.05\leq p\leq 0.10$) were also reported for reference.

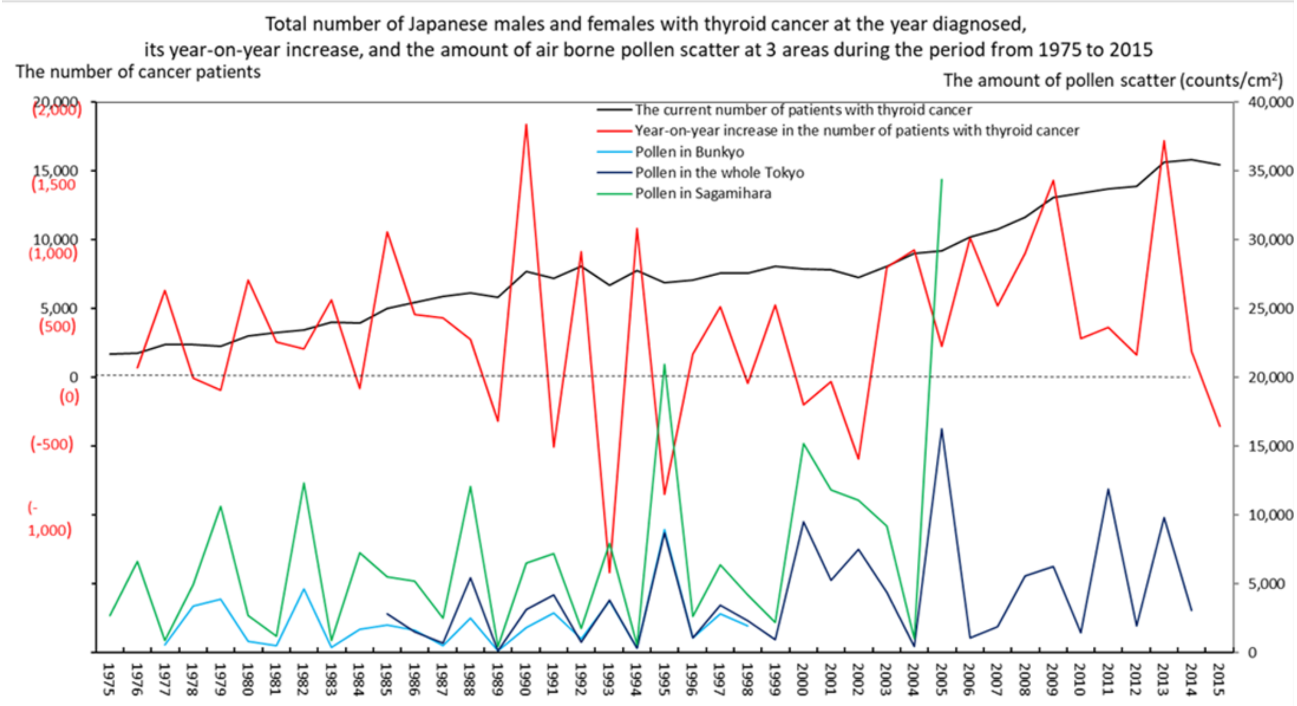

Figure 1. *Total number of Japanese males and females for thyroid cancer at the year diagnosed, its year-on-year increase, and the amount of air borne pollen scatter in 3 areas during the period from 1975 to 2015. The line graphs for all cancers representing numbers of presently and newly registered 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.*

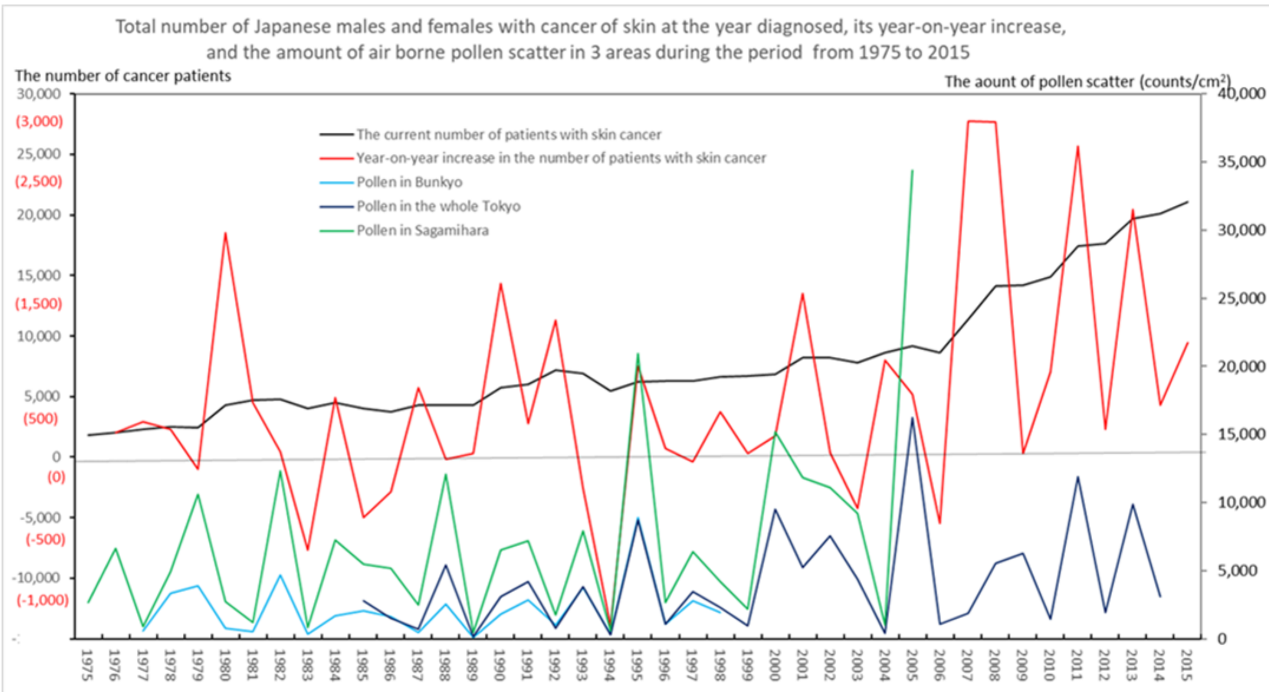

Figure 2. *Total number of Japanese males and females for skin cancer at the year diagnosed, its year-on-year increase, and the amount of air borne pollen scatter in 3 areas during the period from 1975 to 2015. Following explanation is the same as in Figure 1, so to be seen there.*

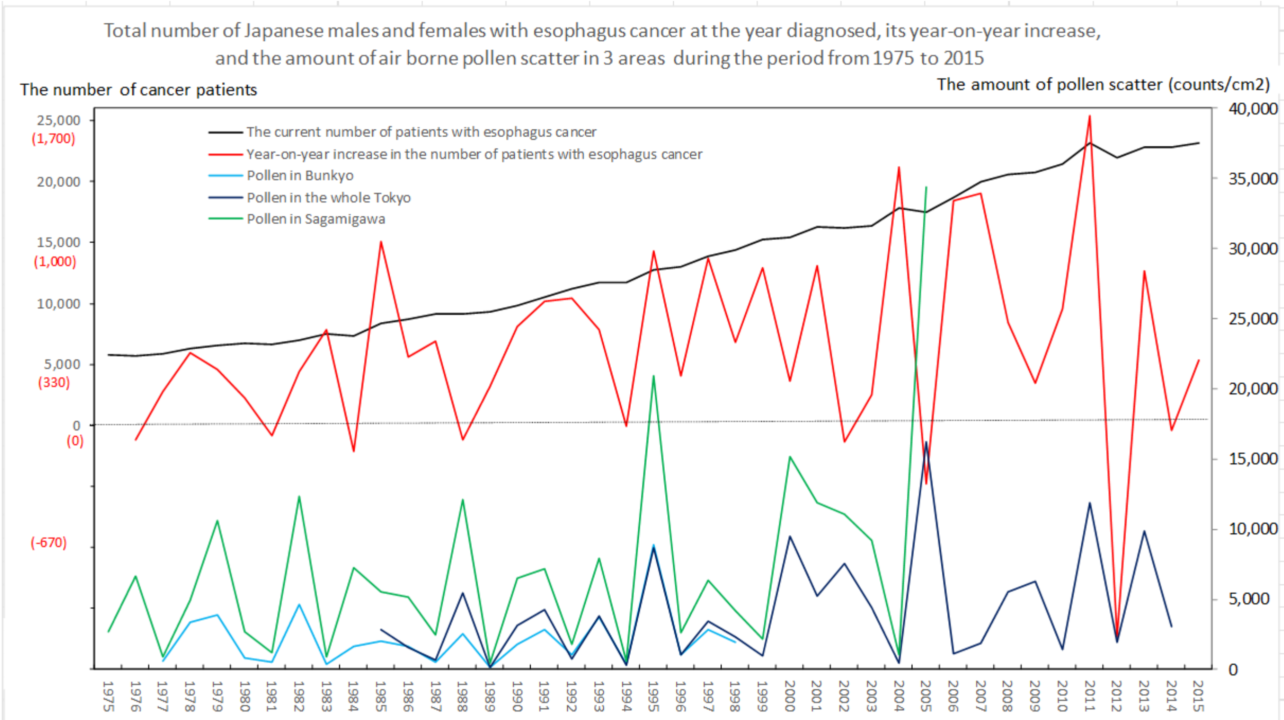

Figure 3. *Total number of Japanese males and females for esophagus cancer at the year diagnosed, its year-on-year increase, and the amount of air borne pollen scatter in 3 areas during the period from 1975 to 2015. Following explanation is the same as in Figure 1, so to be seen there.*

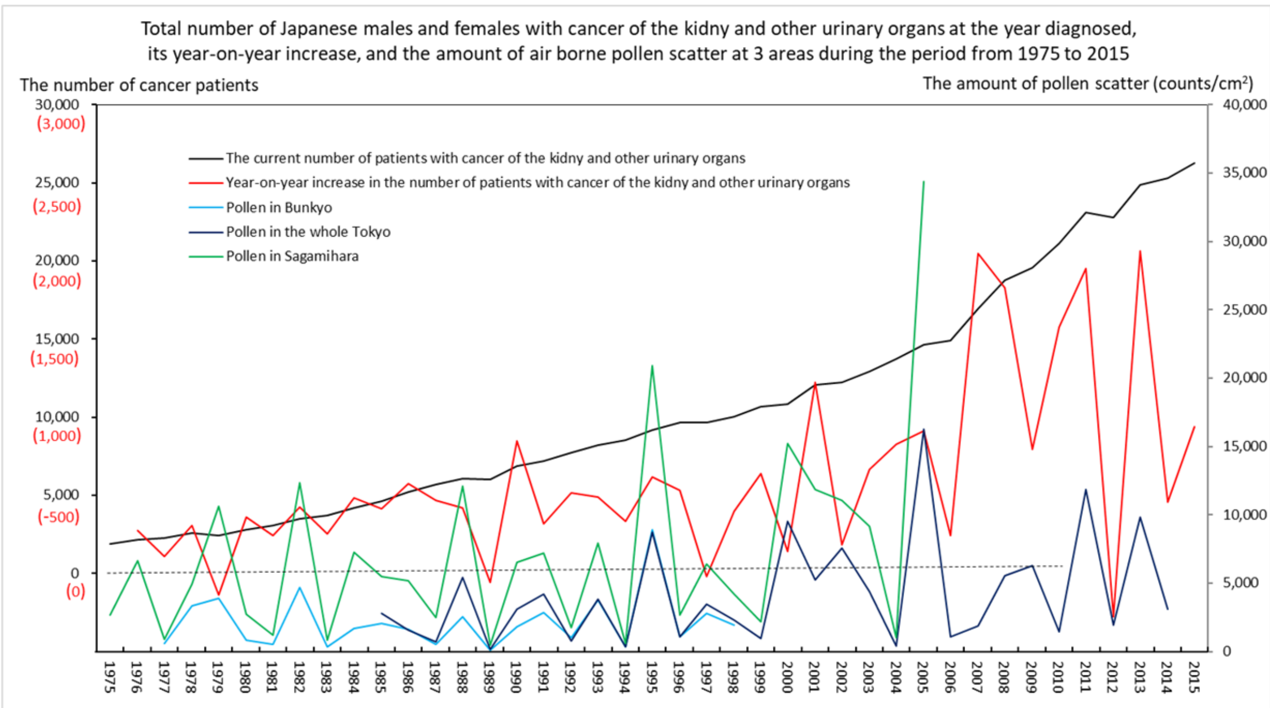

Figure 4. *Total number of Japanese males and females for kidney cancer at the year diagnosed, its year-on-year increase, and the amount of air borne pollen scatter in 3 areas during the period from 1975 to 2015. Following explanation is the same as in Figure 1, so to be seen there.*

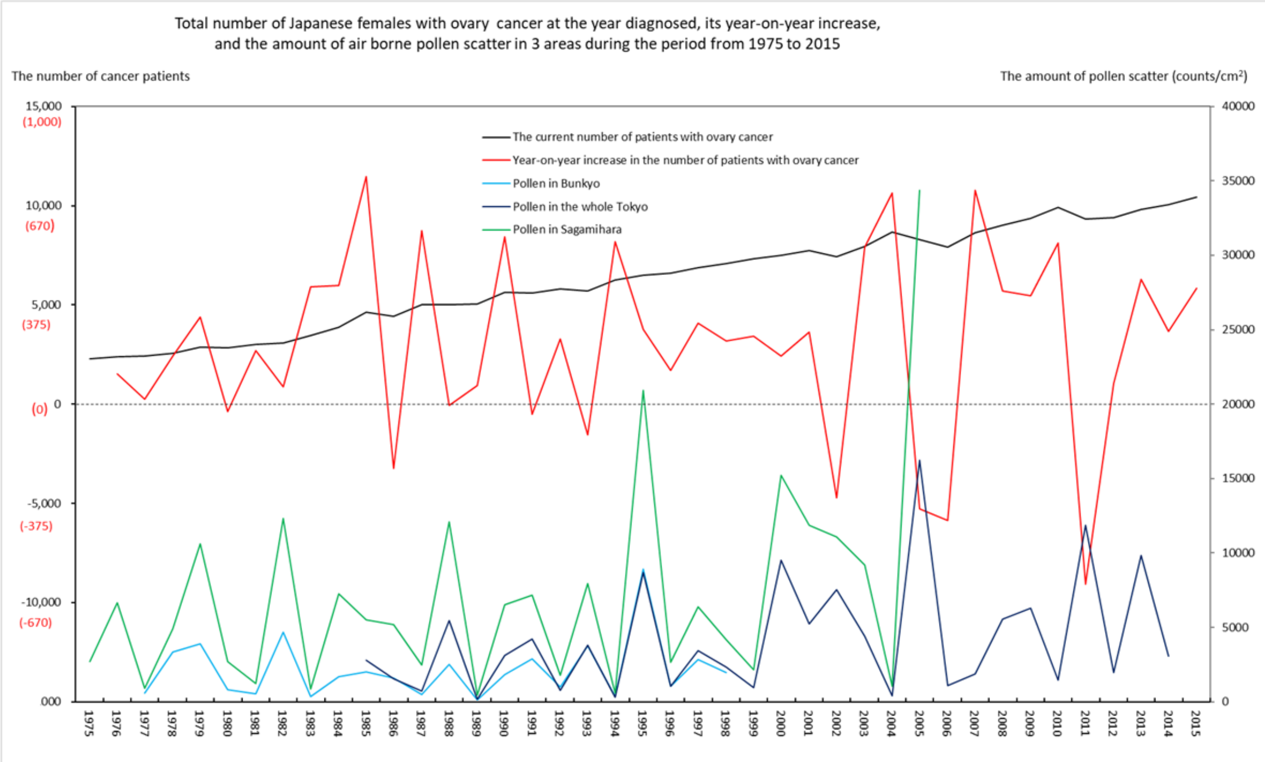

Figure 5. *Total number of Japanese males and females for ovary cancer at the year diagnosed, its year-on-year increase, and the amount of air borne pollen scatter in 3 areas during the period from 1975 to 2015. Following explanation is the same as in Figure 1, so to be seen there.*

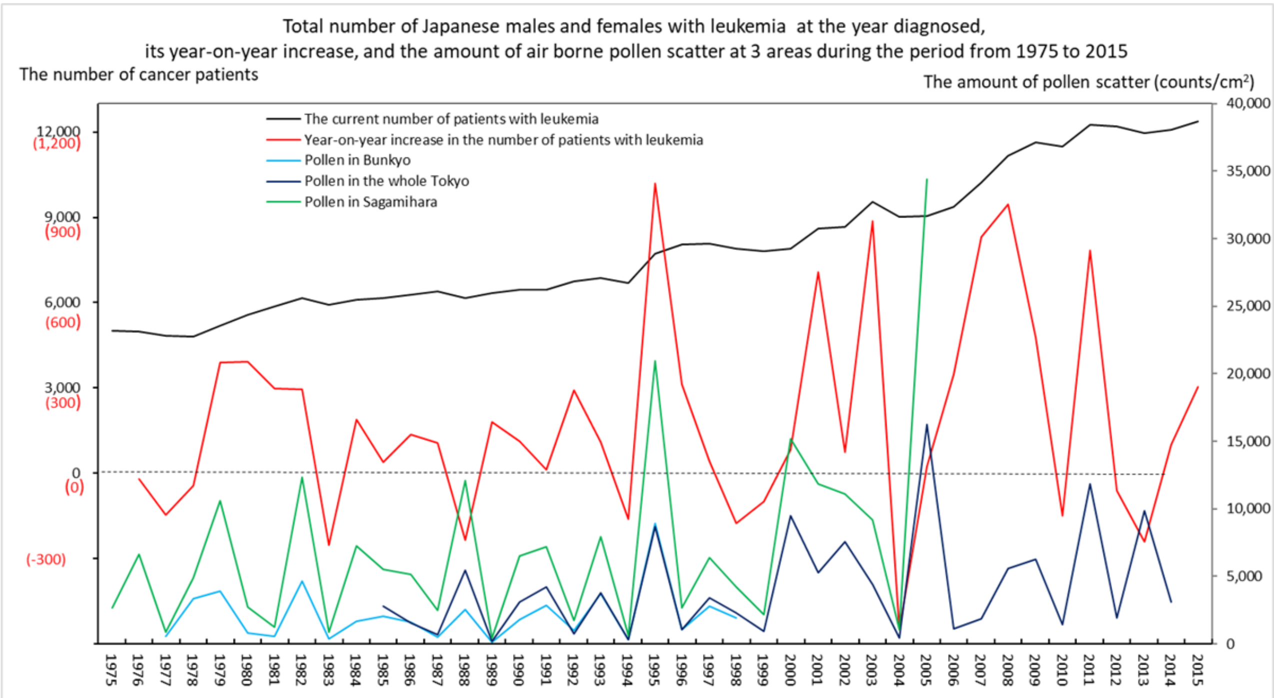

Figure 6. *Total number of Japanese males and females for leukemia at the year diagnosed, its year-on-year increase, and the amount of air borne pollen scatter in 3 areas during the period from 1975 to 2015. Following explanation is the same as in Figure 1, so to be seen there.*

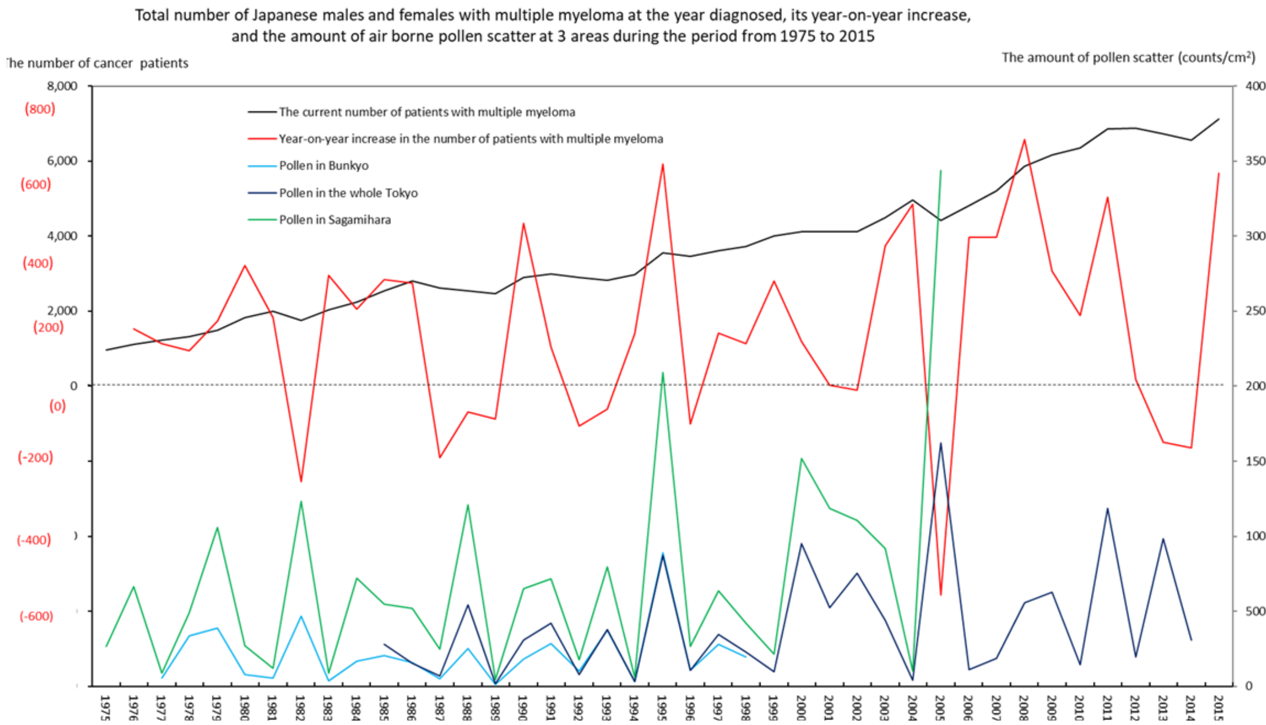

Figure 7. *Total number of Japanese males and females for multiple myeloma at the year diagnosed, its year-on-year increase, and the amount of air borne pollen scatter in 3 areas during the period from 1975 to 2015. Following explanation is the same as in Figure 1, so to be seen there.*

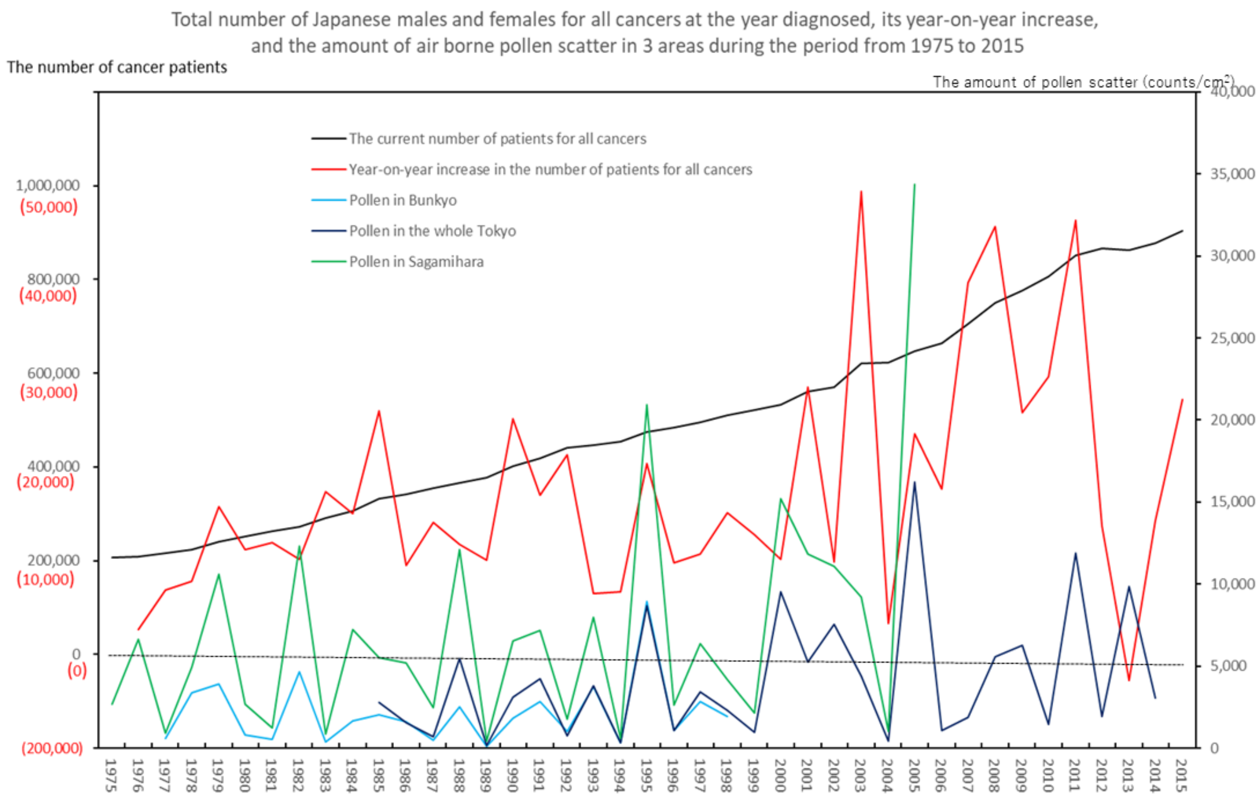

Figure 8. *Total number of Japanese males and females for all cancers at the year diagnosed, its year-on-year increase, and the amount of air borne pollen scatter in 3 areas during the period from 1975 to 2015. Following explanation is the same as in Figure 1, so to be seen there.*

Results

Occurrence of upward peaks in the line graphs of the annual number of newly RPs for eight cancers and malignant tumors in relation to the annual levels of AP scatter

The five line graphs in our figures for eight cancers and malignant tumors consist of two line graphs visualizing the annual patient-registry data for presently RPs and newly RPs, and three line graphs visualizing the annual amount of AP scatter measured in three geographical areas. As shown in our line graphs (Figures 1-8), the amount of cedar pollen scatter in both Sagamihara City and Bunkyo-City started to increase during 1977-87, showing three distinct peaks (1978-80, 1982, 1984-86). Fundamentally, steady phasic increases in annual numbers of both presently and newly RPs concurrent with a consecutive series of 13 upward AP peaks (1978-80, 1982, 1984-86, 1988, 1990-91, 1993, 1995, 1997-98, 2000-03, 2005, 2008-09, 2011 and 2013) were observed for eight cancers and malignancies (Table1), in the same way as already reported in our previous articles on specific intractable diseases or cancers [10-15]. Below described findings suggest that the occurrence of each malignancy appeared to start simultaneously and to increase concurrently with pollen scatter in Japan from the latter half of the 1970s until the early 2010s.

A graph was created simultaneously plotting the number of patient (both presently and newly RPs) cases of thyroid cancer and the number of pollen dispersal for the period 1985-2015 (Figure 1). For the purpose of examining whether the Fukushima Daiichi nuclear power plant accident that occurred on March 11, 2011 affected the number of thyroid cancer cases, we took a closer look at the graph and at a glance found that the number of newly RPs (new cases) in 2013 was 1,723, a significant increase. The increase in the number of new thyroid cancer cases in 2013 appears to be due to the effects of other factors in addition to the effects of pollen exposure in 2008, 2011, and 2013. In 1990, when the number of new thyroid cancer cases was higher than in 2013 (1,839 persons), we felt it necessary to examine whether there was an additional effect of factors related to the April 26, 1986 Chernobyl nuclear accident in addition to the effect of pollen exposure in 1986, 1988 and 1990. We therefore sought to determine among 24 cancers and malignancies in registry data whether cancers other than thyroid cancer were responsible for the observed increase in new cases in 2013 and 1990. Skin cancer (Figure 2), esophageal cancer (Figure 3), cancers of kidney and other urinary organs (kidney cancer, Figure 4), and ovarian cancer (Figure 5) showed a peak increase in new cases in 2013, as did thyroid cancer, while the number of new-onset cases in leukemia (Figure 6), multiple myeloma (Figure 7), and total number of cancer cases (Figure 8) did not show a peak increase in 2013. In addition to the massive pollen exposure in 1978-79, the study also examined what effect the radiological material from the Three Mile Island nuclear power plant accident in 1979 had on cancer incidence in Japan in the most recent year, 1980.

The relationship between transition of peaks of the number of pollen dispersal and change of peaks of the number of cancer cases is shown in Table 1.The number of new cases of thyroid cancer in 2011 and 2012 was low despite the fact that Tokyo pollen exposure was the second highest in history in 2011. The number of new cases of thyroid cancer in 2013 was high at 1,723, adding to the impact of the 2013 pollen count (Figure 1). On the other hand, there were fewer new cases of cancer overall in 2013 (Figure 8). Interaction of effect of pollen exposure and that of the Fukushima nuclear accident supposed to have had an impact on the number of new cases of thyroid cancer between 2011-2013, is as a peculiar case examined in Discussion Increased pollen exposure was seen in 1984-1986, 1988, and 1990, whereas the number of new cases of thyroid cancer increased significantly from -316 in 1989 to 1839 in 1990. In addition, the peak in the number of new cases of all cancers overall was seen in 1990. As a factor other than pollen exposure, we assume the possibility that airborne substances from the 1986 Chernobyl nuclear power plant accident may have affected Japanese people in the thyroid cancer patient reserve group.

Corresponding to the peak in pollen exposure in 1978-79, there was no increase in the number of thyroid cancer cases, and in reversal the pretty distinguished increase in new cases in 1980 was found 707, which imagines the effect of materials those were said to contain extremely few radioactive iodine [16] flying from the Three Miles Island nuclear accident in 1979.The number of new cases of all cancers in 1980 was smaller than in 1979 (Figure 8).

Second, the number 1,851 of new cases of skin cancer in 1980 markedly increased from -100 in 1979 (Figure 2). Although there was a peak in pollen exposure in 1988 and 1990 the number of new cases 1,432 of skin cancer in 1990 was considerably larger than the number of new cases of skin cancer in 1984, 1987, and 1992. Is it therefore possible that the Chernobyl nuclear power plant accident in 1986 may have influenced the increase in new skin cancer cases in 1990? Although there were increases in pollen exposure in 2005, 2007-8, 2011, and 2013, the peaks in 2011 (2,566) and 2013 (2,045) in the increase in new cases of skin cancer are as remarkable as in 2007 (2,772) and in 2008 (2,765). For all cancer patients, the increase in new cases was observed in 2011, but not in 2013. It is also important for cancer experts to consider whether the Fukushima Daiichi nuclear power plant accident could have had any impact on the increase in skin cancer in 2011 and 2013.

Next, the peak number of new cases of esophageal cancer (1,692 in 2011, -1,154 in 2012, and 847 in 2013) clearly responds to the fluctuating peak in pollen exposure (Figure 3). However, the number of new cases of esophageal cancer in 2011-2013 has increased and decreased unusually rapidly, the Fukushima Daiichi nuclear power plant accident in 2011 could have had any impact on the increase in esophageal cancer in 2011 and 2013.

The increase and decrease in the number of new cases of kidney cancer responded well to fluctuations in pollen exposure (Figure 4), but looking at the years since 2000, the number of cases has increased and decreased dramatically in 2007-2008 (2,050 and 1,826), 2010-2011 (1,575 and 1,952), 2012 (-279), and 2013 (2,062), and the overall number of kidney cancer cases continued to increase through 2015. Before 2000, the increase in the number of new cases of kidney cancer were rapid in 1980 (361) and in 1990 (850) in comparison to other near years. Is the kidney an organ that is susceptible to radiation substances in addition to pollen exposure?

The increase and decrease in the number of new cases of ovary cancer responded well to fluctuations in pollen exposure (Figure 5), but looking at the years since 2000, the number of cases has increased and decreased dramatically in 2002-2005, 2006-2008, 2009-2011(a biggest decrease-604 was seen in 2011), and 2012-2014, and the overall number of ovary cancer cases continued to

Table 1. *Peaks of occurrence of cancers in Japan between 1975 to 2015*

Figure. No	1	2	3	4	5	6	7	8
Years of pollen peaks and next years cancers	thyroid cancer	skin cancer	esophagus cancer	kidney cancer	ovary cancer	leukemia	multiple myeloma	all cancers
1978-79, 1980	○̲	○̲	○	○	○	○	○̲	○
1982, 1983	○		○	○	○	○̲	○̲	○̲
1984~6,1987	○	○	○	○	○̲	○	○̲	○
1988, 1989			○	○		○̲		
1990-91, 1992	○̲	○	○	○	○	○	○	○
1993, 1994	○̲		○	○̲	○̲		○̲	
1995, 1996	○̲	○	○	○̲		○	○	○
1997-98-99	○̲	○	○	○	○		○	○
2000~03-04	○̲	○	○	○	○	○	○	○
2005, 2006	○̲	○	○̲	○		○	○̲	○
2008~09	○	○		○	○	○	○	○
2011, 2012		○	○	○	○̲	○	○	○
2013, 2014	○	○	○	○	○			

The relationship between transition of peaks of the number of pollen dispersal and change of peaks of the number of cancer cases is shown.

increase through 2015. Is the ovary an organ that is susceptible to radiation substances in addition to pollen exposure?

The number of new cases of leukemia (Figure 6) showed a marked increase peak in 1995, in 2001, in 2003 and in 2007-2008, a suppressed increase in 2009-2010, and an increase in 2011, followed by a suppressed increase in 2012-2013. The number of new cases of leukemia showed relatively small increases in 1979-1982, 1984-1987, and 1989-1992.

Regarding the number of new cases of multiple myeloma (Figure 7), the increase peaked in 2006-2008 and 2011, but the increase was suppressed in 2012-2014. The number of new cases of multiple myeloma reached a peak of 321 new cases in 1979-1981, then showed a controlled increase from 1987 to 1989, but suddenly peaked at 434 in 1990.

The number of new cases of all cancers (Figure 8) showed relatively small peaks of increase in 1979-1981, 1983-1985, 1986-1989, 1990-1992, 1995, and 1996-2000, followed by large peaks of increase in 2001-2003, 2005-2008, and 2011, but the increase was suppressed in 2012-2013. For the total number of patients affected by all cancers, the number has increased steadily from 1975 to 2015. The number of presently RPs cases in 2015 was 903,914.

Statistical relationships between the number of newly RPs in each patient-registry year and AP levels measured in the same year or prior to the patient-registry year

We examined the statistical correlations between the annual number of newly registered in each patient-registry year "x" ("x"=1975–2015) for eight cancers and malignancies and the corresponding annual AP levels in Tokyo and Sagamihara, measured in the same year as the patient-registry data "x" as well as measured with a lag of "α" years before the patient-registry year "x" ("α"=1–20). Statistically significant positive correlations were indicated by p values <0.05(shown in red in Table 2), and marginal associations were indicated by p values between 0.05 and 0.100. Reference data of associations with p values slightly greater than p=0.10 are also indicated. Only p values in "α=0-8" are shown which were gotten by this calculation in this Table 2.

Our results showed statistically significant correlations between [the number of newly RPs in the patient-registry year "x" abbreviated as Nos in "x" below in this column)] and the amount of AP exposure measured in Tokyo, 2 years prior to the patient-registry year "x" for skin and kidney cancer. Similarly, significant correlations were shown for skin and kidney cancer and all cancers between Nos in "x" and AP exposure measured in Sagamihara, 2 years prior to the patient-registry year "x". In Sagamihara, we found significant correlations for thyroid cancer between Nos in "x" and AP exposure measured, 4 years prior to the patient-registry year "x", and significant correlations for all cancers between Nos in "x" and AP exposure measured, 3 years prior to the patient-registry year "x".

We also found significant correlations for esophagus cancer, leukemia, multiple myeloma and all cancers between Nos in "x" and AP exposure measured in Tokyo, "α"= 6 years prior to the patient-registry year "x". Similarly, significant correlations were shown for skin and esophagus cancers, leukemia, and all cancers between Nos in "x" and the AP exposure measured in

Table 2. *Statistical relationships between the number of newly RPs in each patient-registry year and AP levels measured in the same year or prior to the patient-registry year*

α		Thyroid cancer	Skin cancer	Esophagus cancer	Kidney cancer	Ovary cancer	Leukemia	Multiple myeloma	All cancers
0	T		0.094565		0.077332				
	S				0.098859		0.082625		0.10372
1	T								
	S			0.080948					
2	T		0.009816	0.068307	0.004956	0.165371			
	S		0.002224		0.001076	0.160358	0.135942		0.045788
3	T								0.086997
	S				0.076101				0.015467
4	T	0.089362							
	S	0.020461							
5	T				0.155884				
	S				0.080824				
6	T	0.202035	0.079275	0.020599			0.02283	0.041209	0.010018
	S	0.121567	0.027279	0.004273			0.028324	0.112757	0.004353
7	T								
	S								
8	T	0.012398	0.100042						
	S	0.004803	0.041375						

The statistical correlations were examined between the annual number of newly registered in each patient-registry year “x” (“x”=1975–2015) for eight cancers and malignancies and the corresponding annual AP levels in Tokyo and Sagamihara, measured in the same year as the patient-registry data “x” as well as measured with a lag of “α” years before the patient-registry year “x” (“α”=1–20). Statistically significant positive correlations were indicated by p values <0.05, and marginal associations were indicated by p values between 0.05 and 0.100. Reference data of associations with p values slightly greater than p=0.10 are also indicated. Only p values in “α=0-8” are shown.

Sagamihara, “α”=6 years prior to the patient-registry year “x”. Further, regarding thyroid cancer significant correlations were shown between Nos in “x” and the AP exposure measured in both Tokyo and Sagamihara, and also as to skin cancer, significant correlations were shown to be measured in Sagamihara, “α”= 8 years prior to the patient-registry year “x”.

There were many positive tendencies observed for thyroid cancer (“α”=4), for skin cancer (“α” = 0,2,6,8,13 and 16), for esophagus cancer (“α”=1,2,11 and 16) , for kidney cancer (“α”=0,3 and 5), for leukemia (“α”=0), for multiple myeloma (“α”=16), and for all cancers (“α”=0 and 3) as in part shown in Table 2, which may be part of a pattern of a general correlation between triggering of pollen exposure and occurrence of cancers and malignancies.

Discussion

Because of so far accumulated data, we hypothesized that 65 diseases such as KD, 40 designated intractable diseases and 24 cancers and malignancies might belong to the class of PIDs, or "pollen diseases". The starting point for many disease onset is when pollen exposure in a given year exceeds an individual's threshold for pollen reactivity. The time from the starting line to the onset of disease is assumed to vary depending on the disease, with some diseases developing immediately in the same year as the starting line, some developing within 1-2 years, and others taking 3-6 or 8 years to develop. Factors that determine the number of years required for the biological process from the starting point to disease onset in an individual may depend on the individual's genetic predisposition or on disease-specific pathogenic factors. A clinical-epidemiological analysis of these issues is awaited.

In our two previous papers we reported on the correlation of pollen exposure with the development of lung, breast, and pancreatic cancers. This paper is a report of an extension of those studies. We have demonstrated in this paper that, as in the case of thyroid cancer, skin cancer, esophageal cancer, kidney cancer, ovary cancer, leukemia, and multiple myeloma among cancers and malignancies, in the year when the individual's cumulative pollen reactivity due to pollen exposure exceeds a threshold, the individual reaches a starting point for the process toward cancer and that the development of cancer is diagnosed two to eight years thereafter. In this paper, we have examined the dynamics of the number of patients with thyroid cancer among cancers and malignant tumors from 2011 to 2013, and we have noted that, unlike the dynamics of the number of patients with other cancers, the dynamics of the number of thyroid cancer patients cannot be explained only by the correspondence to the number of pollen dispersal. While the increase in the number of thyroid cancer patients in 2011 was controlled despite the second largest pollen dispersal year ever recorded in Tokyo, a sharp increase in the number of thyroid cancer patients was observed in 2013. The author thought that this increase in 2013 might be a result of the Fukushima Daiichi nuclear power plant accident in 2011. A search of the literature reveals that the number of thyroid cancer cases in Japan began to increase sharply in 2013 [19].

With regard to the suppression of the increase in thyroid cancer in 2011-12, we believe that the radionuclides may have suppressed the pollen reactivity of the host. And the sharp increase in thyroid cancer cases in 2013 is likely due to the development of thyroid cancer in people who are highly sensitive to radioactive materials. The discussion of the percentage contribution of the two factors, pollen exposure and radioactive material exposure, to the development of thyroid cancer is a difficult question. As for the peak of thyroid cancer cases in 1990, literature reports suggest a possible link to the 1986 Chernobyl nuclear power plant accident [16]. The relatively small peak in thyroid cancer cases in 1980 is not necessarily related to the Three Mile Island nuclear power plant accident in 1979, but we will leave this to the judgment of experts. The author thought that the dynamics of skin cancer cases in 2013 and 1990 may be the result of the Fukushima Daiichi nuclear power plant accident in 2011 and the Chernobyl nuclear power plant accident in 1986, respectively. Our impression is that the large peak in the number of skin cancer patients in 1980 cannot be attributed to pollen exposure alone.

The data obtained from our study of the association of pollen exposure with the development of 24 cancers and malignancies clearly demonstrate a correlation between the dynamics of patient populations and the involvement of pollen exposure over the entire 40-year period, and we will continue to report on this topic in future issues. On the other hand, after the study of the dynamics of the number of patients with cancer and malignant tumors in this study, the question arose as to whether the nuclear power plant accident may also have had an effect, and it became necessary to consider the intervention of other factors besides pollen exposure in the dynamics of cancer and malignant tumors. It will be necessary to examine in the future whether exposure to radioactive materials has an effect on the dynamics of the incidence of various designated intractable diseases that are not cancer or malignant tumors.

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 [15,20]. 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.

If our findings are confirmed in further prospective studies, patients with cancers and malignancies should be recommended to avoid pollen exposure as much as possible for the purpose of preventing the aggravation of symptoms or recurrences, as well as the co-occurrence of other diseases. Pollen-avoidance prophylactic measures include the precaution of wearing safety masks, goggles, and transparent shields during pollen peaks from the early postnatal period, and of installing air cleaners in homes, particularly during seasons with large amounts of pollen release in spring and with small amount of forerunning pollen release of cedar pollen in September to November before next spring. These measures may help avoid or delay the first onset of cancers and malignancies, including those in young infants who have a potential risk of developing immune-mediated diseases.

To prevent the development of cancer and malignant tumors, especially to delay the age of onset in people with cancer families, it is important to reduce cumulative pollen reactivity and extend the time to onset by reducing annual pollen exposure. For this reason, it will be necessary to maintain the above-mentioned lifestyle of wearing masks throughout the year, and to install pollen-cutters. In addition, we suggest that the application of pollen allergen immunotherapy to reduce pollen reactivity at the level of practical medical care and careful tasting of pollen-containing health foods might be attempted [21].

In Japan, it has been reported daily in the mass media that more than 200,000 new cases of infection by BA5, a subtype of Omicron mutant, have been reported every day as a result of the COVID-19 pandemic. We have been predicting that COVID-19 pandemic will transit to a seasonal corona during this winter's epidemic [22], but what will actually happen is, of course, unknown. We examined how pollen exposure affected seasonal influenza prevalence from 1982 to 2019 and reported that a correlation exists between the two [22]. Based on a report around 1990 that Wuhan City had by far the highest pollen count among Chinese cities, we reported in our three papers [23-25] in the first half of 2021 the argument that pollen exposure may lie behind the new SARS-CoV-2 outbreak in Wuhan City.

The number of total KD cases reported till 27th week was halved in 2022 compared to those in 2021 in Tokyo [26]. Various possibilities have been raised as to whether this phenomenon is the effect of pollen avoidance, bythe daily wearing of masks and goggles to prevent corona infection, or the suppression of KD directly by SARS-CoV-2 in place of previous seasonal influenza virus till December, 2019 [22]. Although the 2020 KD national survey results report a 35% reduction of incidence compared to 2019, it is estimated that increased SARS-CoV-2 (Omicron mutant) infection more strongly suppressed KD incidence [26].

We assume that the suppression of the pathogenesis mechanism of KD that induces interferon is due to subclinical infection of flu [8,9], but the possibility that a similar mechanism in subclinical infection of SARS-CoV-2 might also be examined [26].

KD is considered to be a model that precociously and pioneeringly manifests various pathological conditions of designated intractable diseases [10-13]. The annual incidence reports for designated incurable diseases for the period April 2019 to March 2022, and those for cancer of 2019, 2020 and 2021 would be the data to refer to.

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Conflict of interest

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