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Influence of sulfur dioxide on the respiratory system of Miyakejima adult residents 6 years after returning to the island

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Abstract: Background: Mount Oyama, on the Japanese island of Miyakejima, began erupting in June 2000, necessitating the evacuation of 3,000 island residents. Volcanic gas emissions, primarily consisting of sulfur dioxide (SO_2), gradually decreased and residents returned to the island after the evacuation order was lifted in February 2005. **Objectives:** To assess the exposure-effect and exposure-response relationships between SO_2 exposure and effects on respiratory system in adult Miyakejima residents. **Method:** Health checkups focusing on pulmonary function and respiratory/irritative symptoms were conducted six times every November from 2006 to 2011. The study population comprised 168 subjects who underwent all health checkups. SO_2 concentrations were measured at six fixed monitoring stations in inhabitable areas. **Result:** Based on the annual mean SO_2 concentration, inhabitable areas were classified into three categories; namely, lower (L), higher (H-1), and highest (H-2) areas. Average SO_2 concentrations (ppb) during 3 months prior to each health checkup dropped from 11.3 to 3.29, 32.2 to 13.4 and 75.1 to 12.6 from 2006 to 2010/2011 in L, H-1, and H-2. No significant declines in pulmonary function were observed in all areas. However, prevalence of subjective symptoms such as "Cough," "Irritation and/or pain in throat," "Irritation, runny nose, and/or nasal sniffles," and "Irritation and/or pain in the eyes," dependently increased on SO_2 concentration. Odds ratios were statistically significant at approximately 70 ppb of SO_2 or above. **Conclusion:** Adult residents of Miyakejima island showed no deterioration in pulmonary function at SO_2 levels, but complained of respiratory/irritative symptoms in an SO_2 concentration-dependent manner.
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Introduction

Miyakejima is a volcanic island located 180 km south-southwest of metropolitan Tokyo, with a diameter of 8 km. Historical records show that Mount Oyama, located at the center of the island, has erupted as many as fifteen times since 1085 AD, and approximately every twenty years since 1940. The last eruption began in June 2000, and a pyroclastic flow appeared following a massive eruption in August 2000. This eruption caused large-scale volcanic gas emissions, which are harmful to human health and environmentally destructive, leading to an island-wide evacuation order in September 2000.

Although volcanic gas generally comprises at least 90% water vapor, it also includes deleterious components such as suspended particulate matter (SPM) (Tokyo Metropolitan Government and the Cabinet Office of Japan. 2003), carbon dioxide (CO_2), hydrogen chloride (HCl), hydrogen sulfide (H_2S), and sulfur dioxide (SO_2). A major feature of the most recent Mount Oyama eruption was the high emission of large amounts of SO_2, which reached 80,000 tons/day during the peak period (November 2000)

and continued for a long time. Volcanic gases other than SO_2 are unlikely to have caused the health effects that we have uncovered in this study: CO_2 is not a respiratory irritant, while H_2S has been continuously monitored at five sampling sites in Miyakejima and recorded levels have been low, with a maximum concentration of 2.9 ppm to date (Tokyo Metropolitan Government and the Cabinet Office of Japan. 2003)[1]. Likewise, HCl and SPM were also discharged, but their concentrations have been negligible. In Miyakejima Island, the environmental concentration of HCl itself has not been measured. However, according to the volcanic gas component analysis, it is known to be around one tenth of the sulfur dioxide concentration. Since the complex effect with SO_2 was alarming, the concentration of SPM was observed from November 20, 2002 to February 19, 2003. According to the results, the average concentration of SPM during this period was 13 to 20 $\mu g/m^3$ correlated with SO_2 concentration, and influence by the volcanic gas was observed, although it was at a lower level than the environmental standard. Furthermore, the average concentration in Miyakejima was lower than that in Tokyo (37 $\mu g/m^3$ in 2001). Based on these observations, the possibility of the occurrence of health effects due to the exposure of SPM is extremely low from the observation result this time[1].

In October 2003, the Tokyo Metropolitan Government and Cabinet Office of the Japanese Government jointly established a Scientific Committee for the Assessment of Health Risks and Volcanic Activity on Miyakejima Island (*Miyakejima Gas Kentoukai*) to determine at what point the residents could safely return to the island. The Committee Report, issued in March 2003, determined that both the chronic effects of long-term exposure to SO_2 and acute effects of instantaneous or short-term inhalation of highly concentrated SO_2 must be considered human health impacts. The report specified an yearly average SO_2 concentration of ≤0.04 parts per million (ppm) as a general measure for the avoidance of long-term effects, and also determined that the optimal avoidance of chronic symptoms from repeated respiratory system stimulation would require environmental conditions such that hourly values exceeding 0.1 ppm occur ≤10% of the year.

The report determined that the following safety measures, implemented mainly by the Miyake village government with support from the Tokyo Metropolitan Government and Cabinet Office of the Japanese Government, would be required to minimize health impacts. First, to understand changes in volcanic gases and share accurate information with residents, a system to monitor and observe plume emission conditions, wind speed and wind direction must be implemented. Second, a system for continually monitoring SO_2 concentration and transmitting information via outdoor displays and similar modalities must be established. Third, to prepare for episodes of high SO_2 concentration, evacuation policies such as implementation thresholds, community notification methods, evacuation locations, evacuation procedures, and evacuation cancellation protocols must be developed, as well as public awareness of instructions for evacuations must be created. Fourth, all residents must undergo health checkups prior to returning to the island, and awareness of sensitivity to SO_2 should be promoted among individuals. In addition, after the residents return, early detection of health effects should be performed via annual health checkups (e.g., respiratory tests), and the relationship with the local ambient SO_2 levels should be explored. At last, residents should be educated to promote a sound understanding and awareness of volcanic gases; related phenomena such as earthquakes and acid rain; emergency responses; and health concerns such as skin and eye irritation and exacerbation of respiratory diseases, including asthma.

To help the residents understand that their health could be protected through both a range of government measures and their own actions, the authors advised the village government to advertise risk information regarding health effects and safety measures as clearly as possible, and emphasized the importance of efforts to promote risk communication by utilizing communication opportunities at various stages during fluctuations in SO_2 concentration. Approximately 60 risk communication events were held with the cooperation of the authors (Kikuchi et al. 2006)[2] between April 2003 and March 2004, before the residents returned to the island, in which approximately 1600 residents participated. In July 2004, the village council decided that the evacuation should cease in February 2005, and the village government subsequently began to conduct health checkups in the autumn of 2004. These checkups enabled residents to learn about their respiratory health and to make decisions based on whether they are normosusceptible or hypersusceptible to SO_2. On February 1, 2005, the residents returned to Miyakejima and restarted their lives on the island.

The village government decided to conduct annual health checkups on all residents following their return. As part of this process, we conducted a cohort study in which we analyzed SO_2 concentrations and evaluated the respiratory health status of adults on Miyakejima (age ≥18 years) over a 6-year period after the eruption. Medical checkups were conducted in February 2006 and subsequently every November from 2006 to 2011. Data from February 2006 were excluded from statistical analysis because of the extensive variation in respiratory effects caused by large seasonal fluctuations in SO_2 between November 2005 and February 2006. Here, we focus on the association between SO_2 concentration and respiratory system in adults.

In this study, the village government conducted annual health checkups under the Ordinance of Security for Safety and Health against the Volcanic Gas promulgated

by the Miyake Village Government. In addition, according to Japanese ethical guidelines about epidemiology study, human subjects of investigation conducted based on legal regulation did not need to obtain informed consent. Therefore, we did not obtain informed consent from participant.

Subjects and Methods

Assessment of SO_2 concentrations

The Tokyo Metropolitan Government continuously monitors SO_2 levels using SO_2 monitors (100-AH, Rikenkeiki, Tokyo, Japan, or APSA-360, Horiba, Kyoto, Japan) placed at six stationary sampling points in inhabited areas along the road that encircles the island. Furthermore, 2.46×10^6 measurements are performed at each sampling time point, and average SO_2 levels are determined at 5-minute intervals. Based on these values, we categorized the inhabited areas as follows: Lower SO_2 Area (Area L, including Izu and Kamitsuki districts), Higher SO_2 Area (Area H-1, including Igaya and Tsubota districts), and Highest SO_2 Area (Area H-2, including Ako district). The 5-minute average SO_2 concentrations in each area from November 2006 to November 2011 (prior to the respective health checkups) are shown in Table 1.

Study population

To determine the effects of exposure to volcanic gas and SO_2 on adult Miyakejima residents, residents underwent health checkups prior to returning to the island in the autumn of 2004 and five subsequent health checkups (November 2006, 2007, 2008, 2009, and either November 2010 or 2011). In 2010, as SO_2 concentration decreased, health checkups were conducted only in the Ako district in Area H-2 and Igaya district in H-1, at the discretion of the study group and the village government. In 2011, health checkups were conducted in the remaining areas (Izu and Kamitsuki districts in Area L, and Tsubota district in Area H-1). Health checkups in 2010 and 2011 were counted as a single round of checkups.

Eligible subjects for health checkups were individuals who held a certificate of residence for Miyakejima at the time of each medical checkup. The total number of adult (≥18 years) residents who attended at least one of the health checkups was 3,426. Of these, 168 participated in all six checkups (2004, 2006, 2007, 2008, 2009, and 2010 or 2011). Among these, 80 residents (46 females and 34 males) successfully conducted all five pulmonary function tests (2006, 2007, 2008, 2009, and 2010 or 2011). We used these sets of 168 and 80 residents as our two study populations for analyzing subjective symptoms and pulmonary function tests, respectively. Based on the cross-sectional and follow-up outcomes of each health checkup, a single certified pulmonologist with no knowledge of the subjects' residential area classified all participants as either having or not having bronchiolar hypersusceptibility. The criteria for hypersusceptibility in this study were as follows: (1) asthma or a history of asthma; (2) obstructive pulmonary function; (3) symptoms of whistling and wheezing; and/or (4) deterioration of specific pulmonary symptoms.

Medical examinations

Respiratory symptoms were evaluated using the Japanese version of the self-administered American Thoracic Society-Division of Lung Disease (ATS-DLD) questionnaire (Ferris 1978)[3], with the inclusion of additional questions regarding the life history and annual changes in subjective symptoms. All answers were confirmed by medical doctors and, when necessary, details were obtained from the doctors' interviews. Forced maximum expiratory flow-volume tests (spirometry) were conducted by experienced clinical laboratory technicians using electronic autospirometers (Easy One spirometer; ndd Medical Technologies, Andover, MA, USA). Flow-volume tests (FEV_1 and FVC) were repeated at least three times for each subject, and the results were analyzed according to the criteria recommended by the ATS (Standardization of Spirometry, 1994 Update. 1995)[4]. Predicted values were calculated as percentages using prediction equations developed by the Japanese Respiratory Society (Clinical Pulmonary Functions Committee of The Japanese Respiratory Society. 2001)[5].

Statistical analysis

For continuous variables, mean values were compared using one-way analysis of variance, followed by Dunnett's test. For dichotomous variables, Fisher's exact test was used to determine prevalence rates. The Cochran-Armitage test for trends was used to assess the dose-response trends in prevalence rates and annual variations in Areas L, H-1, and H-2. Prevalence rate ratios were converted to odds ratios after adjusting for age, gender, smoking status, and hypersusceptibility using a logistic regression model. Because there were no SO_2-free areas on Miyakejima Island, we selected Area L in 2008, which had the lowest SO_2 concentration results, as the reference area. If the prevalence of Area L in 2008 was 0%, then the area with the subsequent lowest SO_2 concentration, Area L in 2010 to 2011, was used as a reference. All statistical analyses were performed using SPSS version 19.0 (IBM, Co., Armonk, NY, USA) and Excel 2010 (SP3; Microsoft Corp., Redmond, WA, USA).

Results

Subject characteristics and SO_2 concentrations

Table 1 shows the general characteristics of Miyakejima residents who were examined in the autumn of 2004 and from 2006 to 2011, as well as the 5-minute average

Table 1. Characteristics of study subjects who underwent all six examinations (n=168) and SO_2 concentrations

	Autumn-2004	Nov-2006	Nov-2007	Nov-2008	Nov-2009	Nov-2010 Nov-2011
Male (%)						
Area L	31.4	–	–	–	–	–
Area H-1	42.6	–	–	–	–	–
Area H-2	36.7	–	–	–	–	–
*p**	0.45					
Age (years old: mean±SD)						
Area L	65.8±9.9	–	–	–	–	–
Area H-1	68.9±10.4	–	–	–	–	–
Area H-2	63.8±12.0	–	–	–	–	–
P#	<0.05					
Smoking (%)						
Area L	11.8	11.8	11.8	7.8	9.8	7.8
Area H-1	8.8	8.8	11.8	8.8	8.8	4.4
Area H-2	16.3	16.3	14.3	12.2	12.2	10.2
*p**	0.47	0.47	0.9	0.73	0.83	0.47
Hypersusceptibility (%)						
Area L	–	15.7	15.7	21.6	17.6	19.6
Area H-1	–	19.1	20.6	29.4	20.6	26.5
Area H-2	–	12.2	18.4	16.3	14.3	20.4
*p**	–	0.61	0.79	0.24	0.68	0.61
SO_2 concentration						
Last 12 months						
Mean concentration (ppb)[a]						
Area L		6.64	7.00	2.81	5.20	3.29
Area H-1		31.2	20.7	21.9	18.5	13.4
Area H-2		41.2	39.3	28.0	28.9	12.6
Frequency of 0.1 ppm levels in hourly measurements (%)						
Area L		1.90	1.90	0.90	1.70	0.85
Area H-1		5.50	4.20	4.87	4.03	3.19
Area H-2		7.75	8.50	6.05	6.55	2.98
Last 3 months						
Mean concentration (ppb)[a]						
Area L	–	11.3	4.48	3.13	5.28	3.29
Area H-1	–	32.2	14.2	18.1	18.7	13.4
Area H-2	–	75.1	68.4	45.4	37.7	12.6
Maximum concentration (ppb)[a]						
Area L	–	1580	1160	770	930	390 360
Area H-1	–	7110	3870	2710	4180	2660 2060
Area H-2	–	5090	3790	2650	2670	1420 1880

Area L: Izu, Kamitsuki, and Mimoi districts. Area H-1: Igaya and Tsubota districts. Area H-2: Ako district.
p#: *p* by one-way ANOVA, *p**: *p* by chi-square test, or Fisher's exact test.
[a]: A 5-minute average concentration of SO_2. SD: standard deviation; ppb, parts per billion

SO_2 concentrations during the 3 months prior to each health checkup. No significant differences were observed between the years in terms of the proportions of males or smokers or the rate of sensitivity. The average SO_2 concentration decreased during the study period in all three areas, particularly in Area H-2. Between 2006 and 2010/2011, average SO_2 concentration (ppb) dropped from 11.3 to 3.29, 32.2 to 13.4 and 75.1 to 12.6 in Areas L, H-1, and H-2, respectively. The lowest 5-minute average SO_2 level for the 3 months prior to a health checkup was in Area L

Table 2. Average annual changes (AAC) in pulmonary function test results among residents who underwent all six examinations (n=80) in Area L (n=27), Area H-1 (n=26), and Area H-2 (n=27).

		AAC (mean±SD)	p^*	Autumn-2004	Nov-2006	Nov-2007	Nov-2008	Nov-2009	Nov-2010, 11	$p^\#$
%FVC (%)	Area L	0.34±2.48	Ref	96.7±16.3	106.3±18.5	110.3±17.4	107.7±18.6	112.1±19.6	108.2±18.9	0.80
	Area H-1	–0.06±2.23	0.805	98.2±15.3	101.8±15.4	104.6±14.8	103.9±19.2	104.8±22.5	101.9±18.7	0.95
	Area H-2	–0.22±3.09	0.656	93.2±20.2	97.2±18.7	98.4±18.5	96.0±18.3	99.6±16.6	95.5±18.1	0.92
	p†	0.73		0.56	0.17	<0.05	0.07	0.07	<0.05	
%FEV_1 (%)	Area L	0.28±2.60	Ref	94.4±19.4	104.1±19.9	102.7±19.2	102.7±18.6	105.5±18.0	104.5±22.6	0.98
	Area H-1	0.05±1.82	0.900	93.5±14.3	98.5±16.9	101.7±15.9	101.5±17.9	100.9±19.4	99.4±16.9	0.96
	Area H-2	–0.60±1.99	0.237	89.6±17.9	93.3±18.7	93.4±20.0	88.8±16.4	94.1±17.9	90.0±17.7	0.77
	p†	0.30		0.57	0.11	0.14	<0.01	0.08	<0.05	
FEV_1% (%)	Area L	–0.21±1.39	Ref	96.7±9.5	97.2±8.9	92.2±9.1	94.9±9.8	93.7±10.7	94.8±10.3	0.43
	Area H-1	0.09±1.62	0.707	95.1±8.0	96.0±8.9	96.2±5.5	97.3±7.6	95.9±8.8	96.5±6.5	0.97
	Area H-2	–0.49±1.78	0.756	96.8±12.7	95.6±8.8	94.0±7.3	92.6±11.1	93.5±6.9	93.4±7.5	0.77
	p†	0.42		0.78	0.78	0.15	0.22	0.55	0.39	
PEF (L/s)	Area L	–0.08±0.19	Ref	6.28±2.48	6.44±2.65	6.61±2.52	6.41±2.43	6.69±2.33	6.04±2.52	0.89
	Area H-1	–0.09±0.29	0.975	5.92±2.17	6.07±1.95	6.33±1.78	6.22±1.89	6.09±2.19	5.66±1.98	0.79
	Area H-2	–0.07±0.28	0.989	5.67±2.22	6.04±2.24	6.28±2.17	5.95±2.23	6.24±2.26	5.72±2.30	0.89
	p†	0.95		0.61	0.77	0.84	0.75	0.60	0.81	

p^*: p by Dunnett's test compared to Area L
p†: p by one-way ANOVA among living areas
$p^\#$: p by one-way ANOVA among years (Nov-2006, Nov-2007, Nov-2008, Nov-2009, Nov-2010, 11)
SD, standard deviation; %FVC, percent predicted forced vital capacity; %FEV_1, percent predicted forced expiratory volume in one second; FEV_1%, percent of forced expiratory volume in one second; PEF, peak expiratory flow

in November 2008, with a value of 3.13 ppb; this value was accordingly used as a reference for odds ratio calculations.

Pulmonary function tests

In accordance with the Japanese Respiratory Society and the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria, subjects with extremely reduced lung function at baseline, defined as beyond Phase III (forced expiratory volume in 1 second [FEV_1]/forced vital capacity [FVC] <70%, predicted FEV_1 <50%), were excluded from the initial analysis. Table 2 presents the pulmonary function test results of 80 adults who underwent all five follow-up examinations (2006, 2007, 2008, 2009, and 2010 or 2011). In Area H-2, pulmonary function test results were relatively low, but this was also the case prior to the study period. No significant differences in pulmonary function tests were observed among the three areas, except for %FVC (%) in 2007 and 2010 to 2011 and %FEV_1 (%) in 2008 and 2010 to 2011. Furthermore, there were no significant differences in comparisons over the years. Hypersusceptible subjects also exhibited no deterioration in pulmonary function after a 6-year SO_2 exposure (data not shown).

Table 2 (supplement) compares the ratios of respiratory function tests among 3054 adults by area and year. Evaluation based on pulmonary function tests revealed two significant differences: In %FVC (%) in Area H-1, and in PEF (L/s) in Area H-2. No significant differences in pulmonary function tests were observed in the three areas, except for the %FVC (%), %FEV_1 (%), PEF (L/s) in 2008, and %FVC (%), %FEV_1 (%) in 2010 to 2011.

Subjective symptoms

Tables 3-1, 3-2, and 3-3 compare the ratios of respiratory symptoms and complaints among the 168 people who underwent a total of five health checkups by area and year. The Cochran-Armitage trend evaluation based on an examination year revealed significant dose-dependent trends in the prevalence of reported respiratory symptoms such as "Do you usually havea cough?," "Does your chest ever make a wheezy or whistling sound?," "Cough," "Irritation and/or pain in throat," "Irritation, runny nose, and/or nasal sniffles," and "Irritation and/or pain in the eyes," in Area H-2; likewise, significant dose-dependent trends were observed in "Cough," "Irritation and/or pain in throat," "Irritation and/or pain in the eyes," and "Itchy skin" in Areas L and H-1. In general, as SO_2 concentration decreased, the risk of irritation symptoms also clearly decreased.

Tables 3-1, 3-2, and 3-3 (supplement) compare the ratios of respiratory symptom complaints among all 3,426 adults who underwent health checkups according to area and year. The Cochran-Armitage trend evaluation by area

Table 3-1. Prevalence of subjective symptoms among residents who underwent all five health examinations (n=168) in Area L (n=51), Area H-1 (n=68), and Area H-2 (n=49).

	Nov-2006	Nov-2007	Nov-2008	Nov-2009	Nov-2010, 11	$p^{\#}$
	Prevalence	Prevalence	Prevalence	Prevalence	Prevalence	
Prevalence of respiratory symptoms						
Do you usually have cough?						
Area L	21.6%	21.6%	27.5%	21.6%	23.5%	0.58
Area H-1	17.6%	20.6%	23.5%	13.2%	17.6%	0.31
Area H-2	26.5%	22.4%	18.4%	16.3%	14.3%	<0.05
p†	0.28	0.46	0.86	0.76	0.88	
Do you usually bring up phlegm from your chest?						
Area L	23.5%	27.5%	31.4%	29.4%	17.6%	0.31
Area H-1	23.5%	27.9%	22.1%	22.1%	19.1%	0.18
Area H-2	26.5%	20.4%	18.4%	20.4%	18.4%	0.19
p†	0.36	0.79	0.94	0.86	0.46	
Does your chest ever make a wheezy or whistling sound?						
Area L	11.8%	13.7%	19.6%	13.7%	15.7%	0.69
Area H-1	14.7%	19.1%	19.1%	16.2%	14.7%	0.42
Area H-2	10.2%	18.4%	6.1%	4.1%	4.1%	<0.05
p†	0.59	0.27	0.97	0.93	0.96	
Have you ever suffered an attack of wheezing that has made you feel short of breath?						
Area L	7.8%	9.8%	7.8%	7.8%	5.9%	0.31
Area H-1	16.2%	5.9%	8.8%	10.3%	11.8%	0.35
Area H-2	4.1%	4.1%	6.1%	6.1%	10.2%	0.91
p†	0.72	0.88	0.62	0.62	0.23	

p†: p by Cochran-Armitage trend test among living areas
$p^{\#}$: p by Cochran-Armitage trend test among years

revealed significant differences in the occurrences of "Cough," "Irritation and/or pain in throat," "Irritation, runny nose, and/or nasal sniffles," "Irritation and/or pain in the eyes," "Itchy skin," and "Catching colds" over multiple years (including nonconsecutive years). The Cochran-Armitage trend evaluation according to the year revealed a significant dose-dependent trend in "Irritation and/or pain of throat" in Area L, Area H-1, and Area H-2; likewise, significant dose-dependent trends were observed among all 3,426 adults who underwent "irritation and/or pain in the eye" in Area H-1 and "Catching cold" in Area H-2.

Fig. 1 shows the adjusted (gender, age, smoking status, and hypersusceptibility) odds ratios (ORs) resulting from multiple logistic regression analysis of irritation symptoms with respect to the mean SO_2 level during the 3 months prior to each health checkup. Exposure-response relationships were apparent for the symptoms "Cough," "Irritation and/or pain in throat," "Irritation, runny nose, and/or nasal sniffles," and "Irritation and/or pain in the eyes," and ORs were statistically significant at approximately more than 70 ppb SO_2.

Discussion

Our 6-year follow-up study evaluated the influence of volcanic gas on the health of adults (≥18 years) who returned to Miyakejima Island after evacuation. The results reveal that the prevalence of irritation symptoms correlated strongly with ambient SO_2 concentration. During the 6-year period of SO_2 exposure, no deterioration in pulmonary function was detected in the 46 female or 34 male residents who were examined six times. Therefore, an average SO_2 exposure of 22.1 ppb over a 6-year period may be an acceptable level for both normosusceptible and hypersusceptible adult populations. As compared with the results obtained prior to returning to the island, some spirometric parameters had slightly improved, which is an unusual change from a physiological perspective that we cannot adequately explain. We speculate that this may

Table 3-2. Prevalence of subjective symptoms among residents who underwent all five health examinations (n=168) in Area L (n=51), Area H-1 (n=68), and Area H-2 (n=49).

	Nov-2006	Nov-2007	Nov-2008	Nov-2009	Nov-2010, 11	$p^{\#}$
	Prevalence	Prevalence	Prevalence	Prevalence	Prevalence	
After you returned to the island, did you experience an increase in the frequency of symptoms listed below within 1 year?						
"Cough"						
Area L	9.8%	7.8%	3.9%	3.9%	3.9%	0.07
Area H-1	8.8%	8.8%	2.9%	1.5%	2.9%	<0.05
Area H-2	16.3%	12.2%	6.1%	2.0%	10.2%	<0.05
p†	0.15	0.23	0.29	0.73	0.08	
"Phlegm"						
Area L	11.8%	9.8%	3.9%	5.9%	5.9%	<0.05
Area H-1	10.3%	13.2%	2.9%	1.5%	8.8%	0.07
Area H-2	14.3%	14.3%	6.1%	6.1%	8.2%	0.06
p†	0.35	0.25	0.29	0.48	0.33	
"Wheezy or whistling when breathing"						
Area L	3.9%	2.0%	2.0%	0%	3.9%	0.39
Area H-1	5.9%	2.9%	2.9%	2.9%	0%	<0.05
Area H-2	4.1%	6.1%	2.0%	2.0%	4.1%	0.32
p†	0.48	0.12	0.49	0.22	0.49	
"Irritation and/or pain in throat"						
Area L	17.6%	17.6%	0%	0%	3.9%	<0.01
Area H-1	16.2%	10.3%	1.5%	4.4%	5.9%	<0.01
Area H-2	16.3%	14.3%	4.1%	4.1%	10.2%	<0.05
p†	0.57	0.69	0.06	0.11	0.10	
"Irritation, runny nose, and/or nasal sniffles"						
Area L	9.8%	9.8%	0%	9.8%	2.0%	0.07
Area H-1	14.7%	14.7%	2.9%	1.5%	13.2%	0.07
Area H-2	20.4%	14.3%	8.2%	2.0%	10.2%	<0.05
p†	0.07	0.25	<0.05	0.97	0.07	

p†: p by Cochran-Armitage trend test among living areas
$p^{\#}$: p by Cochran-Armitage trend test among years

have resulted from (1) the environmental change from the small and uncomfortable urban apartment complex where evacuees lived during the 4-year evacuation period; (2) improved physical capacity resulting from moderate agricultural activity; and/or (3) improvements in the subjects' spirometry skills.

The results of the 80 residents who underwent all six examinations and resided in Area H-2, which had a higher regional SO_2 concentration, revealed a decrease in %FVC (%) as compared to the results prior to returning to the island. This observation is similar to the results of analyses stratified by smoking habit, gender, and sensitivity. Although some influence of regional characteristics is present, these observations cannot be explained only by regional differences, and unidentified confounding factor/s may be present. During the 1983 eruption, or long before the 2000 eruption, it is conceivable that Area H-2 might have also experienced dust exposure or harmful effects from exposure to gases such as SO_2, particularly in the Ako district, which was affected by lava flow.

Short-term exposure to high concentrations, rather than to average concentrations, might contribute to the symptoms of irritation. The significantly higher prevalence of nasal irritation observed in Areas H-1 and H-2 in November 2006 might have been due to the higher maximum 5-minute concentrations in these places at that time. Consistent with this notion, Ishigami et al. (2008)[6] conducted an hour-based follow-up study of 611 healthy volunteers who visited Miyakejima Island to provide support to residents and stayed on the island for up to 15 days between February and July 2005. The hourly incidence of irritation symptoms indicated clear exposure-response relationships, as hourly average SO_2 concentrations of above 10 ppb increased the rates of symptoms such as throat irritation and cough.

In the present study, we found that the prevalence of ir-

Table 3-3. Prevalence of subjective symptoms among residents who underwent all five health examinations (n=168) in Area L (n=51), Area H-1 (n=68), and Area H-2 (n=49).

	Nov-2006	Nov-2007	Nov-2008	Nov-2009	Nov-2010, 11	$p^{\#}$
	Prevalence	Prevalence	Prevalence	Prevalence	Prevalence	
After you returned to the island, did you experience an increase in the frequency of symptoms listed below within 1 year?						
"Irritation and/or pain in the eyes"						
Area L	29.4%	13.7%	0.0%	3.9%	9.8%	<0.01
Area H-1	22.1%	19.1%	2.9%	4.4%	14.7%	<0.05
Area H-2	30.6%	24.5%	2.0%	4.1%	14.3%	<0.01
p†	0.45	0.09	0.22	0.48	0.25	
"Itchy skin"						
Area L	11.8%	9.8%	2.0%	3.9%	3.9%	<0.05
Area H-1	10.3%	11.8%	5.9%	1.5%	5.9%	<0.05
Area H-2	14.3%	4.1%	0.0%	0%	8.2%	0.05
p†	0.31	0.84	0.71	0.93	0.19	
"Catching cold"						
Area L	11.8%	9.8%	3.9%	13.7%	2.0%	0.10
Area H-1	10.3%	8.8%	11.8%	10.3%	2.9%	0.11
Area H-2	10.2%	6.1%	8.2%	18.4%	10.2%	0.81
p†	0.60	0.75	0.22	0.25	<0.05	

p†: p by Cochran-Armitage trend test among living areas
$p^{\#}$: p by Cochran-Armitage trend test among years

ritation symptoms using the questionnaire correlated strongly with ambient SO_2 concentration. In contrast, three other studies have reported clinical responses to volcanic gas exposure. Based on a 10-year follow up observation in the Azores, Portugal, Amaral *et al.* (2007)[7] reported a relationship between exposure to volcanic gases and the incidence of chronic bronchitis recorded at local health centers. Relative risks of chronic bronchitis in males and females exposed to volcanic gases were 3.99 (95%CI; 2.98-5.35) and 10.74 (6.55-17.34), respectively, as compared to those living in volcanically inactive areas. Mean SO_2 concentrations measured by diffusion tubes placed in a residential area for a 2-week sampling period were 10 ppb (Baxter PJ et al. 1999)[8]. Likewise, Mannino et al. (1996)[9] and Michaud et al. (2004)[10] analyzed emergency department visits and Kilauea Volcano fog-related air quality in Hilo, Hawaii, and concluded that asthma/COPD had consistent, positive associations with air quality. The air quality data means from February 21, 1997 to May 31, 2001 were 1.97 ppb (range; 0.0-108.5) for SO_2 and 1.91 μg/m^3 (0.0-56.6) for PM_1. These reports indicate that SO_2 is a major causal component of chronic bronchitis in volcanically active areas. In contrast, we observed that only irritation symptoms increased in the 6 years post-eruption. Because chronic bronchitis and SO_2 exposure duration differed between our present and these three previous studies, it is difficult to compare exposure-response relationships between SO_2 concentrations.

Iwasawa et al. (2009)[11] found that SO_2 exposure-related respiratory symptoms that were subjectively reported had increased among adult Miyakejima residents two years after returning to the island. The population in that study comprised 823 Miyake adult residents who participated in the 2006 health examination. The mean SO_2 concentration from February 2005 to November 2006 was 31 ppb. The study area was divided into four areas according to SO_2 concentration; namely, Areas L, H-1, H-2, and H-3, with average SO_2 concentrations of 19, 26, 32, and 45 ppb, respectively. The study subjects exhibited no deterioration in lung function. The prevalence of cough and phlegm among all participants was significantly higher in 2006 than in 2004, and the age-, gender- and smoking-adjusted odds ratios of cough and phlegm were 1.75 (95% confidence interval: 1.33-2.30) and 1.44 (1.12-1.87). The prevalence of chronic bronchitis-like symptoms among normosusceptible subjects in 2006 was 4.1%, which was significantly higher than the rate of 2.1% in 2004 ($p=0.035$). As compared to Area L, the frequencies of phlegm and nasal irritation were significantly increased in Areas H-2 and H-3. These results seem to be generally consistent with our present findings.

Iwasawa et al. (2015)[12] found clear dose-response relationships in child Miyakejima residents. The study subjects included residents aged between 6 and 18 years who were enrolled in a Miyake elementary, middle, or high school at the time of each medical checkup. Applying a logistic regression model, age-, gender-, and hypersusceptibility-adjusted prevalence odds ratios to the refer-

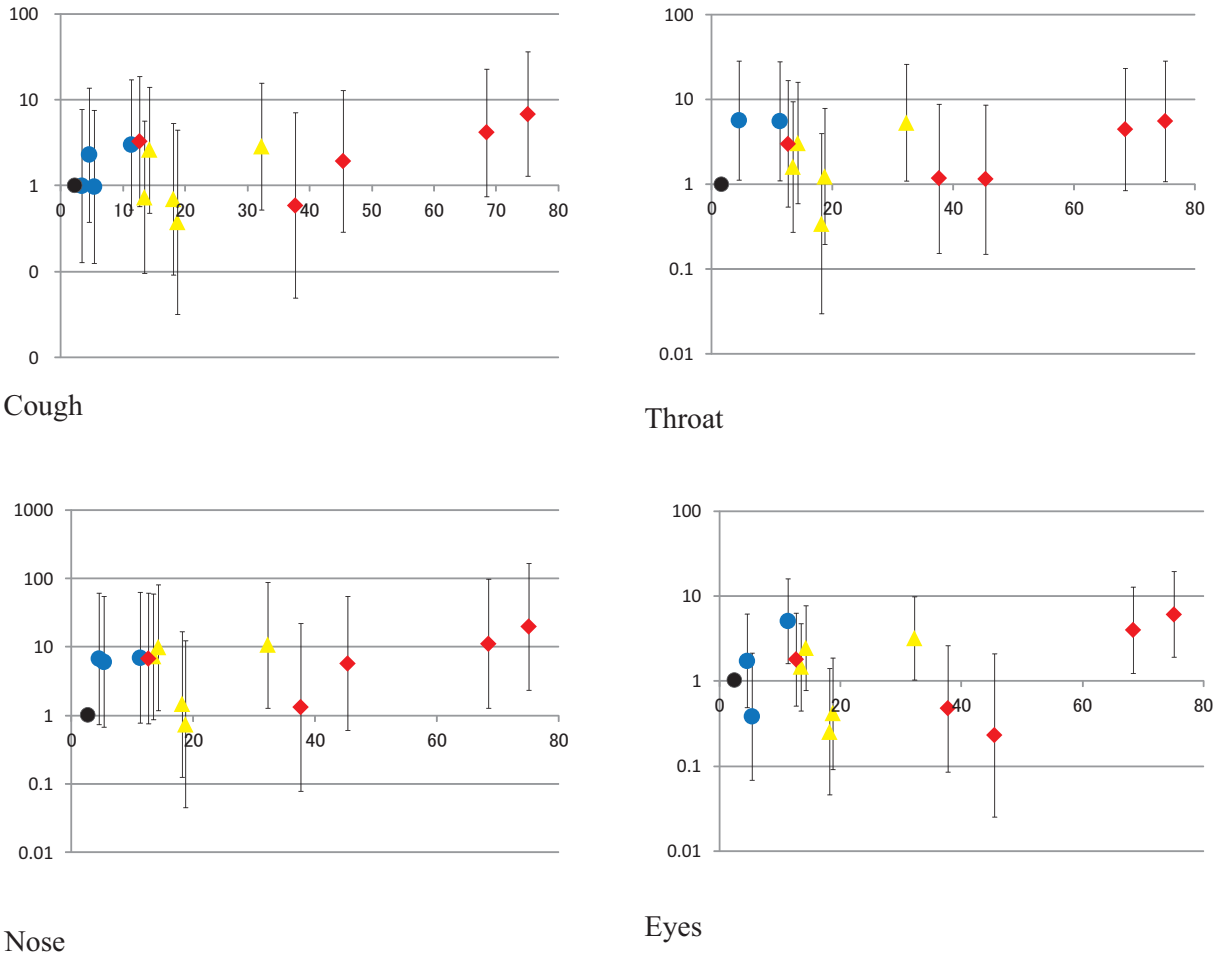

Fig. 1. Odds ratios adjusted for age, gender, smoking status, and hypersusceptibility and 95% confidence intervals of symptoms according to the mean SO_2 concentration during the 3 months prior to the health examination
Odds ratios adjusted for age, gender, smoking status, and hypersusceptiveness and 95% confidence intervals. Black dots indicate reference values (see text). Blue circles represent Area L. Yellow triangles represent Area H-1. Red diamonds represent Area H-2. Vertical bars indicate the 95% confidence intervals of the odds ratios. Data include residents who underwent all five health checkups (n=168).

ence population showed clear exposure-dependent increases in some irritative symptoms such as "Irritation and/or pain in throat" and "in eyes," and approximately 30 ppb seemed to be the threshold concentration. This result seems to be generally consistent with our present findings and a child is more sensitive in some irritative symptoms than an adult.

Our study has several advantages over other studies that investigated SO_2 exposure. The observed health effects could be considered specific to volcanic SO_2, as the potential health effects of other pollutants, including volcanic hydrogen sulfide and particles, and traffic-related pollutants, such as volatile organic compounds (VOCs) and fine particles, have been negligibly low in Miyakejima. In addition, this was a closed cohort study. Our study also has several limitations. First, because no areas of Miyakejima Island were unexposed, we defined the next-to-lowest exposed area as the reference area. We note that the observed dose-response relationships might have been underestimated because an unexposed area would be expected to have a lower prevalence of irritation symptoms relative to our reference area. Second, our study population was classified according to a residential area, rather than SO_2 exposure. This may have introduced errors; for example, subjects would have been exposed to completely different concentrations at their workplaces. Exposure was not personally monitored but instead was approximated from environmental concentrations at the nearest monitoring station. Third, we did not adjust for every possible disease, such as dry eye and atopic dermatitis.

In conclusion, on Miyakejima Island, we observed minor health effects on the respiratory system and irritation symptoms from a 6-year period of exposure to a mean SO_2 concentration of 22.1 ppb. We also observed clear dose-response relationships and determined an apparent

threshold concentration of approximately 70 ppb. Since these results may be indicative of the early stages of longer-term problems, it is necessary to re-evaluate subjects in future.

Conflict of interest: None of the authors has any conflict of interest to disclose.

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Table 2 (supplement). Pulmonary function test results of all examined residents

	Nov-2006 n=771	Nov-2007 n=709	Nov-2008 n=644	Nov-2009 n=569	Nov-2010, 11 n=361	$p^{\#}$
%FVC (%)						
Area L	99.3±17.2	100.8±18.3	101.8±19.2	103.1±17.5	102.6±17.1	0.18
Area H-1	97.4±15.9	101.1±17.3	99.7±17.0	102.0±19.5	98.4±17.2	<0.05
Area H-2	96.6±17.0	98.3±14.8	95.7±19.2	99.2±16.9	95.2±17.0	0.15
p†	0.17	0.13	<0.01	0.09	<0.01	
%FEV_1 (%)						
Area L	94.6±18.9	95.4±19.8	95.8±20.3	96.9±19.0	98.8±19.9	0.34
Area H-1	93.3±17.6	96.0±23.4	95.8±18.6	96.6±21.4	93.8±19.0	0.32
Area H-2	90.7±17.4	93.4±16.8	90.6±20.1	92.8±18.5	90.5±17.7	0.34
p†	0.06	0.31	<0.01	0.07	<0.01	
FEV_1% (%)						
Area L	77.2±8.7	76.5±8.9	76.1±9.9	75.8±8.8	77.5±8.5	0.37
Area H-1	77.4±8.6	76.3±11.8	78.2±8.9	76.1±8.8	76.6±7.9	0.11
Area H-2	76.2±9.3	77.3±7.9	77.0±10.4	76.2±8.9	77.1±8.1	0.63
p†	0.29	0.52	0.08	0.90	0.67	
PEF (L/s)						
Area L	6.12±2.32	6.67±2.36	6.28±2.30	6.57±2.45	6.36±2.32	0.08
Area H-1	6.02±2.19	6.38±2.23	6.48±2.25	6.28±2.21	6.03±2.12	0.09
Area H-2	5.67±2.17	6.45±2.16	6.14±2.20	6.36±2.35	6.18±2.11	<0.01
p†	0.07	0.36	<0.05	0.46	0.47	

p†: p by one-way ANOVA among living Areas

$p^{\#}$: p by one-way ANOVA among years (Nov-2006, Nov-2007, Nov-2008, Nov-2009, Nov-2010, 11)

SD, standard deviation; %FVC, percent predicted forced vital capacity; %FEV_1, percent predicted forced expiratory volume in one second; FEV_1%, percent of forced expiratory volume in one second; PEF, peak expiratory flow

Table 3-1 (supplement). Prevalence of subjective symptoms among all examined residents

	Nov-2006		Nov-2007		Nov-2008		Nov-2009		Nov-2010, 11		$p^{\#}$
	N	Prevalence	N	Prevalence	N	Prevalence	N	Prevalence	N	Prevalence	
Prevalence of respiratory symptoms											
Do you usually have cough?											
Area L (n=297)	75	25.3%	59	23.2%	54	24.1%	56	25.1%	30	22.9%	0.54
Area H-1 (n=290)	61	21.0%	57	20.2%	52	19.6%	38	18.4%	27	16.8%	0.83
Area H-2 (n=235)	76	32.3%	71	25.9%	58	23.8%	43	20.1%	29	24.8%	0.05
p†		<0.05		<0.05		0.42		0.90		0.38	
Do you usually bring up phlegm from your chest?											
Area L (n=297)	76	25.6%	66	26.0%	55	24.4%	55	24.8%	27	20.6%	0.99
Area H-1 (n=290)	77	26.6%	65	23.1%	63	23.8%	52	25.1%	31	19.4%	0.53
Area H-2 (n=235)	76	32.3%	71	25.9%	58	23.8%	51	23.9%	26	22.2%	0.14
p†		<0.05		0.50		0.57		0.58		0.38	
Does your chest ever make a wheezy or whistling sound?											
Area L (n=297)	41	13.8%	34	13.4%	38	16.8%	26	11.8%	17	13.0%	0.62
Area H-1 (n=290)	42	14.5%	47	16.6%	35	13.2%	35	16.9%	23	14.2%	0.74
Area H-2 (n=235)	38	16.2%	42	15.3%	40	16.4%	26	12.2%	19	16.4%	0.73
p†		0.23		0.27		0.22		0.45		0.23	
Have you ever suffered an attack of wheezing that has made you feel short of breath?											
Area L (n=297)	22	7.4%	21	8.3%	20	8.9%	17	7.7%	7	5.3%	0.79
Area H-1 (n=290)	27	9.3%	26	9.2%	22	8.3%	22	10.8%	15	9.3%	0.93
Area H-2 (n=234)	25	10.7%	34	12.4%	24	9.8%	20	9.4%	21	17.9%	0.15
p†		0.09		0.05		0.35		0.26		<0.01	

p†: p by Cochran-Armitage trend test among living Areas
$p^{\#}$: p by Cochran-Armitage trend test among years

Table 3-2 (supplement). Prevalence of subjective symptoms among all examined residents

	Nov-2006		Nov-2007		Nov-2008		Nov-2009		Nov-2010, 11		$p^{\#}$
	N	Prevalence	N	Prevalence	N	Prevalence	N	Prevalence	N	Prevalence	
After you returned to the island, did you experience an increase in the frequency of symptoms listed below within 1 year?											
"Cough"											
Area L (n=294)	43	14.6%	31	12.3%	24	10.7%	26	11.8%	10	7.6%	0.31
Area H-1 (n=289)	45	15.6%	33	11.7%	24	9.1%	16	7.7%	15	9.4%	<0.05
Area H-2 (n=235)	44	18.7%	47	17.2%	33	13.5%	28	13.1%	19	16.2%	0.41
p†		0.11		<0.05		0.15		0.34		<0.05	
"Phlegm"											
Area L (n=296)	32	10.8%	28	11.0%	23	10.2%	19	8.5%	12	9.2%	0.89
Area H-1 (n=289)	45	15.6%	38	13.4%	35	13.3%	21	10.1%	15	9.5%	0.29
Area H-2 (n=235)	39	16.6%	41	15.0%	25	10.2%	24	11.3%	13	11.1%	0.19
p†		<0.05		0.09		0.51		0.16		0.31	
"Wheezy or whistling when breathing"											
Area L (n=295)	15	5.1%	8	3.1%	8	3.6%	7	3.2%	3	2.3%	0.60
Area H-1 (n=289)	18	6.2%	15	5.3%	14	5.3%	11	5.3%	5	3.2%	0.75
Area H-2 (n=235)	13	5.5%	12	4.4%	15	6.1%	11	5.2%	7	6.0%	0.92
p†		0.40		0.25		0.10		0.15		0.06	
"Irritation and/or pain in throat"											
Area L (n=295)	46	15.6%	37	14.6%	17	7.6%	21	9.5%	11	8.5%	<0.05
Area H-1 (n=290)	47	16.2%	36	12.7%	32	12.1%	22	10.7%	16	10.2%	0.30
Area H-2 (n=233)	49	21.0%	48	17.6%	40	16.4%	27	12.8%	23	20.4%	0.19
p†		0.05		0.16		<0.01		0.13		<0.01	
"Irritation, runny nose, and/or nasal sniffles"											
Area L (n=295)	41	13.9%	36	14.2%	16	7.1%	24	10.8%	13	9.9%	0.09
Area H-1 (n=288)	58	20.1%	44	15.6%	38	14.3%	31	15.0%	19	12.1%	0.19
Area H-2 (n=235)	50	21.3%	55	20.1%	53	21.7%	30	14.2%	21	18.1%	0.25
p†		<0.05		<0.05		<0.01		0.15		<0.05	

p†: p by Cochran-Armitage trend test among living Areas
$p^{\#}$: p by Cochran-Armitage trend test among years

Table 3-3 (supplement). Prevalence of subjective symptoms among all examined residents

	Nov-2006		Nov-2007		Nov-2008		Nov-2009		Nov-2010, 11		$p^{\#}$
	N	Prevalence	N	Prevalence	N	Prevalence	N	Prevalence	N	Prevalence	
After you returned to the island, did you experience an increase in the frequency of symptoms listed below within 1 year?											
"Irritation and/or pain in the eyes"											
Area L (n=296)	63	21.3%	45	17.7%	33	14.7%	38	17.1%	18	13.6%	0.24
Area H-1 (n=290)	68	23.4%	49	17.4%	36	13.6%	33	15.9%	21	13.4%	<0.05
Area H-2 (n=235)	62	26.4%	65	23.7%	54	22.1%	40	19.0%	26	22.4%	0.45
p†		0.08		<0.05		<0.05		0.31		<0.05	
"Itchy skin"											
Area L (n=295)	35	11.9%	26	10.3%	10	4.4%	19	8.6%	11	8.3%	0.05
Area H-1 (n=289)	31	10.7%	37	13.1%	31	11.7%	23	11.1%	14	8.8%	0.73
Area H-2 (n=234)	38	16.2%	36	13.2%	38	15.6%	25	11.9%	21	17.9%	0.49
p†		0.08		0.16		<0.01		0.13		<0.05	
"Catching cold"											
Area L (n=290)	21	7.2%	21	8.3%	12	5.4%	6	2.8%	4	3.1%	0.06
Area H-1 (n=287)	26	9.1%	24	8.6%	20	7.5%	12	5.9%	7	4.6%	0.40
Area H-2 (n=234)	19	8.1%	28	10.3%	30	12.3%	10	4.7%	14	12.1%	<0.05
p†		0.34		0.21		<0.01		0.17		<0.01	
Hypersusceptibility											
Area L (n=297)	40	13.5%	27	10.6%	42	18.7%	33	14.8%	18	13.6%	0.09
Area H-1 (n=290)	46	15.9%	48	17.0%	53	20.0%	36	17.4%	32	19.8%	0.43
Area H-2 (n=235)	42	17.9%	46	16.8%	52	21.4%	42	19.7%	29	24.8%	0.71
p†		0.08		<0.05		0.23		0.09		<0.05	

p†: p by Cochran-Armitage trend test among living Areas
$p^{\#}$: p by Cochran-Armitage trend test among years