

### Ⅲ. 研究成果の刊行に関する一覧表

雑誌

発表者氏名	論文タイトル名	発表誌名	巻号	ページ	出版年
Fukutomi Y, Taniguchi M, Nakamura H, Akiyama K	Epidemiological link between wheat allergy and exposure to hydrolyzed wheat protein in facial soap	Allergy	69(10)	1405-1411	2014
清水薫子, 今野哲, 木村孔一, 荻 喬博, 谷口菜津子, 清水健一, 伊佐田朗, 服部健史, 檜澤伸之, 谷口正実, 赤澤 晃, 西村正治	北海道上士幌町における成人喘息, アレルギー性鼻炎有病率の検討—2006年, 2011年の比較—	Japanese Journal of Allergology	63(7)	928-937	2014
Sasaki M, Yoshida K, Adachi Y, Furukawa M, Itazawa T, Odajima H, Saito H, Akasawa A.	Factors associated with asthma control in children: finding from a national Web-based survey.	Pediatr Allergy.	25	804-809	2014
Yoshida K, Adachi Y, Sasaki M, Furukawa M, Itazawa T, Hashimoto K, Odajima H, Akasawa A.	Time-dependent variation in the responses to the web-based ISAAC questionnaire.	Ann Allergy Asthma Immunol.	113	539-543	2014
Yoshida K, Adachi Y, Sasaki M, Furukawa M, Itazawa T, Hashimoto K, Odajima H, Akasawa A.	Test-retest reliability of the International Study of Asthma and Allergies in Childhood questionnaire for a web-based survey.	Ann Allergy Asthma Immunol.	112	181-182	2014

## IV. 研究成果の刊行物・別刷

## Epidemiological link between wheat allergy and exposure to hydrolyzed wheat protein in facial soap

Y. Fukutomi<sup>1</sup>, M. Taniguchi<sup>1</sup>, H. Nakamura<sup>2</sup> & K. Akiyama<sup>1</sup>

<sup>1</sup>Clinical Research Center for Allergy and Rheumatology, Sagamihara National Hospital, Sagamihara, Kanagawa; <sup>2</sup>Department of Environmental and Preventive Medicine, Graduate School of Medical Science, Kanazawa University, Kanazawa, Ishikawa, Japan

**To cite this article:** Fukutomi Y, Taniguchi M, Nakamura H, Akiyama K. Epidemiological link between wheat allergy and exposure to hydrolyzed wheat protein in facial soap. *Allergy* 2014; **69**: 1405–1411.

### Keywords

adult food allergy; hydrolyzed wheat protein; protein hydrolysates; risk factors; wheat allergy.

### Correspondence

Yuma Fukutomi, MD, PhD, Clinical Research Center for Allergy and Rheumatology, Sagamihara National Hospital, 18-1 Sakuradai, Minami-ku, Sagamihara, Kanagawa 252-0392, Japan.  
Tel.: +81-42-742-8311  
Fax: +81-42-742-7990  
E-mail: y-fukutomi@sagamihara-hosp.gr.jp

Accepted for publication 4 July 2014

DOI:10.1111/all.12481

Edited by: Antonella Muraro

### Abstract

**Background:** Recent studies have highlighted the importance of extra-intestinal routes of sensitization to food-related allergens as the cause of epidemics of food allergy. Instances of Japanese women developing food allergy to wheat after exposure to hydrolyzed wheat protein (HWP) present in facial soap have been reported. However, the epidemiologic impact of these ingredients as a cause of food allergy has not been well studied.

**Methods:** To clarify the epidemiological relationship between food allergy to wheat and contact exposure to HWP, a case–control study of Japanese women aged 20–54 years with self-reported wheat allergy (WA) (cases,  $n = 157$ ) and age-matched control subjects without WA (controls,  $n = 449$ ) was performed using a large-scale Web-based research panel. Subjects answered a Web-based questionnaire regarding the use of skin and hair care products, as well as other possible risk factors.

**Results:** Current use of an HWP-containing facial soap (Cha no Shizuku; Yuka) was significantly associated with an increased risk of WA (adjusted odds ratio, 2.6; 95% confidence interval, 1.2–5.7; frequencies of current use in cases and controls; 11% and 6%, respectively). Use of Cha no Shizuku was more common in subjects with more recent-onset WA, implying that this soap may have contributed to the recent epidemic of WA.

**Conclusions:** An epidemiological relationship between WA and contact exposure to HWP has been documented. This study implicates a possible role of contact exposure to food-derived protein hydrolysates as a risk factor for the development of food allergy manifesting itself as anaphylaxis.

The burden of food allergy is an emerging public health problem worldwide (1, 2). The prevalence of adult-onset food allergy as well as childhood allergy has increased in recent decades (3). However, little is known about the cause of this increase, especially in adults. Recently, some studies have highlighted the importance of an extra-intestinal route of sensitization to food-related allergens, that is, environmental allergens, as the cause of food allergy (4–6). Birch pollen-related food

allergy (7–9) and latex–fruit allergy syndrome (10, 11) are well-studied and characterized examples of this.

Reflecting the worldwide trend toward the use of ‘natural materials’ as ingredients of skin and hair care products including facial soaps, body soaps, cosmetics, shampoo, hair treatments and hair conditioner, food-derived protein hydrolysates is becoming increasingly commonly used as moisturizers or emulsifiers. Considering the potential importance of the extra-intestinal route of sensitization, it can be hypothesized that skin and/or rhinoconjunctival exposure to these ingredients may be a cause of the development of food allergy (12–16). However, epidemiological evidence supporting this hypothesis has been limited so far.

In late 2010, a small number of cases of Japanese women with wheat-dependent exercise-induced anaphylaxis (WDEIA)

### Abbreviations

AD, atopic dermatitis; AR, allergic rhinitis; BA, bronchial asthma; CIs, confidence intervals; HWP, hydrolyzed wheat protein; OR, odds ratio; WA, wheat allergy; WDEIA, wheat-dependent exercise-induced anaphylaxis.

associated with skin and/or rhinoconjunctival contact exposure to hydrolyzed wheat protein (HWP) in facial soap were reported (17, 18). After the publication of these papers, numerous similar cases have been reported from various institutions in Japan (19–23). This suggests that primary sensitization to HWP contained in skin and hair care products resulting in the development of food allergy to wheat may be relatively common in Japanese women. It is hypothesized that HWP contained in these products might be contributing to the epidemic of wheat allergy (WA) in women.

The aim of this study was to elucidate the epidemiological link between WA and exposure to HWP contained in skin and hair care products. Because WA is relatively rare in the general population, a case–control design was chosen. We used a large-scale Web-based research panel to recruit wheat-allergic patients and age-matched controls. The use of skin and hair care products containing HWP was compared between the cases and controls.

## Methods

### Study design

A case–control study of Japanese women aged 20–54 years was performed. Both wheat-allergic subjects (cases) and control subjects were selected from the population living in Japan, which was obtained using a large-scale Web-based

research panel. Characteristics of the studied Internet research monitor population are shown in the Supporting information. The ethics committee of Sagamihara National Hospital approved the study protocol (No. 7 in 2010).

### Web-based survey

Figure 1 shows the protocol for the Web-based survey. First, the research company sent e-mails inviting participation in the screening survey. These were sent to an age-stratified random sample of subjects in the research panel between January 14 and January 25, 2011. No further invitations were sent once 200 000 responses had been obtained. The Web-based screening questionnaire consisted of five questions regarding WA (Q1–Q5, shown in the Appendix S1). Subjects (hereafter, cases) were considered as having self-reported WA if they met the following three criteria: (i) affirmative response to Q1, ‘Do you experience any allergic symptoms after eating certain foods?’; (ii) indicating ‘wheat’ in the response to Q2, ‘Which of the foods listed below are you allergic to?’; and (iii) indicating <2 h in their response to Q3, ‘How many hours after eating wheat do your allergic symptoms appear?’. Three times as many age-matched controls were also chosen from subjects who denied food allergy in Q1. Consequently, e-mail of invitations to the secondary survey was sent to 328 cases and 984 controls.

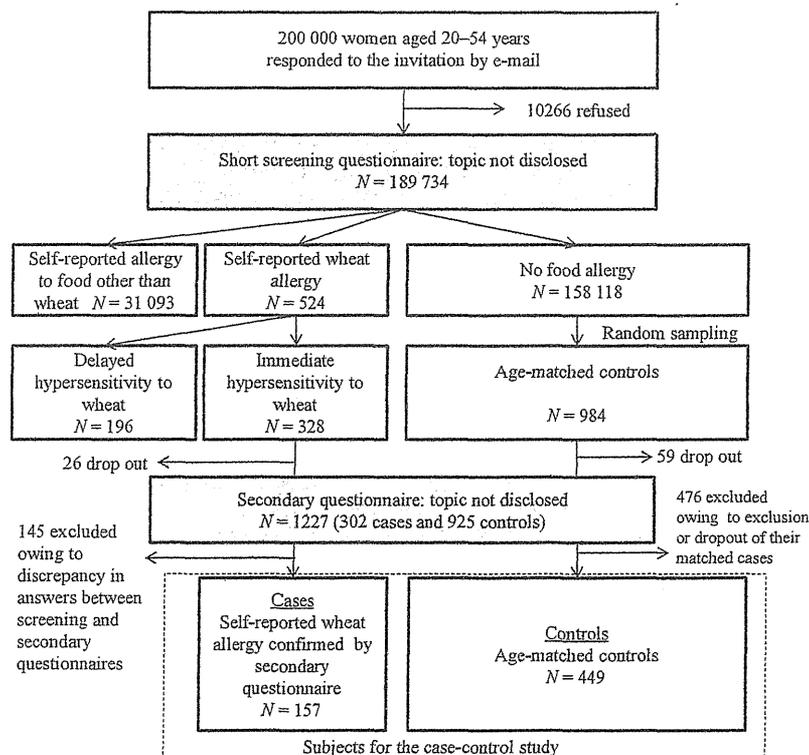


Figure 1 Protocol of Web-based survey.

The first e-mail inviting participation in the secondary survey was sent on January 28, 2011, and reminders were sent up to three times until we received answers. The secondary survey ended on February 7, 2011. The secondary questionnaire contained detailed questions regarding WA, allergic diseases other than food allergy, and use of skin and hair care products. To ensure the validity of the answers in the screening questionnaire, the secondary questionnaire included the same questions as Q1 and Q2 of the former and in addition the question 'At what age did you become allergic to wheat?', which was almost the same as Q5 of the screening questionnaire. Of the 328 cases to whom an invitation to the secondary survey was sent, 302 responded (for a response rate of 92%). We excluded 145 cases that showed discrepancies between the answers to these three questions in the screening and secondary questionnaires. Finally, data from 157 cases and 449 matched controls could be analyzed here.

### Questions in the secondary questionnaire

The secondary questionnaire included questions about the use of soap, shampoo, hair treatment and conditioner, and cosmetics. All the popular brands of skin and hair care products in Japan were listed on the questionnaire, and subjects were asked to indicate which product they were 'currently using' or 'have used before' in the past 5 years. If the currently used brand was not listed, subjects were asked to provide the name of the brand they were using. If subjects gave an affirmative response for current or past use of the HWP-containing facial soap 'Cha no Shizuku' (Yuka, Fukuoka, Japan), the causal brand in most of the cases reported (17, 21), additional questions were posed on when they started to use and when they discontinued use of this brand and whether they experienced allergic symptoms after contact with the soap.

The questionnaire also included questions about possible risk factors associated with WA, namely smoking status, weight, height, allergic rhinitis (AR), atopic dermatitis (AD), and bronchial asthma (BA) comorbidities. Cases with WA were also asked whether their allergic symptoms were induced or exacerbated by exercise, whether they had been diagnosed as having WDEIA by their doctor, the frequency of WA episodes over the last 12 months, how much wheat product they consumed, and the type of symptoms induced by wheat ingestion.

### Statistical analysis

The collected data were analyzed using SPSS ver. 21.0 (IBM, Tokyo, Japan). Descriptive statistics were used to characterize the cases and control subjects. Conditional logistic regression was used to compare the demographics of cases and controls and determine adjusted odds ratios (OR) and 95% confidence intervals (CIs) for the association between use of skin and hair care product and risk of WA.

The chi-square test and Fisher's exact test were used to determine whether distributions of categorical variables significantly differed from each other. Trend analysis was tested with the use of SPSS CROSSTAB command's linear-by-linear

association test. A *P*-value of  $\leq 0.05$  was considered statistically significant.

## Results

### Characteristics of cases and controls

Demographic characteristics of 157 subjects with self-reported WA and the age-matched controls are shown in Table 1. Cases were significantly more likely to have AR, BA, and AD than control subjects. In 85% of the cases, the onset of WA was in adolescence or adulthood and 52% had their WA diagnosed by a doctor.

**Table 1** Demographic characteristics of cases with self-reported WA and their age-matched control subjects

	Cases ( <i>n</i> = 157)	Control subjects ( <i>n</i> = 449)	<i>P</i> - value
Gender (=female), <i>n</i> (%)	157 (100)	449 (100)	N.A.
Age, years, mean $\pm$ SD	35.2 $\pm$ 7.9	35.3 $\pm$ 7.8	N.A.
Allergic diseases, <i>n</i> (%)			
Allergic rhinitis	119 (76)	226 (50)	<0.001
Asthma	37 (24)	23 (5)	<0.001
Atopic dermatitis	58 (37)	56 (12)	<0.001
Smoking status, <i>n</i> (%)			
Non-smoker	117 (75)	326 (73)	0.164
Past smoker	13 (8)	62 (14)	
Current smoker	27 (17)	61 (14)	
Body mass index, kg/m <sup>2</sup> , mean $\pm$ SD	21.6 $\pm$ 3.6	21.0 $\pm$ 3.2	0.067
Presentation of WA			
Onset age >12 years, <i>n</i> (%)	133 (85)	–	
WA diagnosed by doctor, <i>n</i> (%)	81 (52)	–	
Exacerbation of WA symptoms by exercise, <i>n</i> (%)	67 (43)	–	
WDEIA diagnosed by doctor, <i>n</i> (%)	31 (20)	–	
Frequency of episodes of WA during the last 12 months, <i>n</i> (%)			
0	28 (18)	–	
1–2	46 (29)	–	
3–5	37 (24)	–	
6–10	16 (10)	–	
11–	30 (19)	–	
How much wheat have you eaten recently?			
No wheat	13 (8)	–	
A small amount of wheat	45 (29)	–	
A usual amount of wheat	90 (57)	–	
Avoid eating only before exercise	9 (6)	–	

WA, wheat allergy; WDEIA, wheat-dependent exercise-induced anaphylaxis; N.A., not assessed.

## Use of skin and hair care products as risk factors for WA

Frequencies of the use of different skin and hair care products are shown in Table 2. All brands which were currently used by more than 3% of the cases are shown in the table and were analyzed. Because comorbid allergic diseases were associated with the use of some brands of skin and hair care products (data not shown), statistical analysis of the association between the use of these products and risk of WA was performed after adjustment for AR, BA, and AD. The

**Table 2** Frequency of current use of each skin and hair care product and associations with self-reported wheat allergy

Name of brand*	No. of current users (%)		Adjusted OR† (95%CI)	P-value
	Cases (n = 157)	Controls (n = 449)		
<b>Facial soaps and body soaps</b>				
K.B.	31 (19.7)	118 (26.3)	0.7 (0.4–1.1)	0.111
U.D.	18 (11.5)	60 (13.4)	0.8 (0.4–1.5)	0.506
Cha no Shizuku‡	17 (10.8)	26 (5.8)	2.6 (1.2–5.6)	0.014
G.C.	15 (9.6)	56 (12.5)	0.9 (0.5–1.9)	0.866
D.C.	10 (6.4)	16 (3.6)	2.2 (0.2–23.1)	0.519
U.L.	5 (3.2)	11 (2.4)	1.2 (0.4–3.7)	0.817
<b>Shampoo</b>				
U.L.	19 (12.1)	70 (15.6)	1.1 (0.8–1.5)	0.607
P.P.	13 (8.3)	67 (14.9)	0.7 (0.3–1.3)	0.207
S.W.‡	13 (8.3)	17 (3.8)	1.8 (0.8–4.3)	0.184
S.R.	10 (6.4)	34 (7.6)	0.8 (0.4–1.8)	0.577
C.I.‡	8 (5.1)	24 (5.3)	1.2 (0.5–3.0)	0.736
P.H.	8 (5.1)	21 (4.7)	1.3 (0.5–3.4)	0.542
S.G.	5 (3.2)	12 (2.7)	1.6 (0.5–5.1)	0.416
<b>Hair treatment</b>				
U.L.	17 (10.8)	66 (14.7)	0.9 (0.5–1.7)	0.755
P.P.	16 (10.2)	73 (16.3)	0.8 (0.4–1.4)	0.392
S.W.‡	12 (7.6)	17 (3.8)	1.5 (0.6–3.6)	0.416
S.R.	9 (5.7)	32 (7.1)	0.8 (0.4–1.9)	0.678
P.H.	8 (5.1)	21 (4.7)	1.5 (0.6–3.7)	0.430
C.I.‡	7 (4.5)	28 (6.2)	0.9 (0.4–2.3)	0.844
K.E.	6 (3.8)	23 (5.1)	0.5 (0.2–1.5)	0.246
K.A.	6 (3.8)	23 (5.1)	0.6 (0.2–1.6)	0.295
S.G.	5 (3.2)	11 (2.4)	1.6 (0.5–5.2)	0.404
P.V.	5 (3.2)	9 (2.0)	1.1 (0.3–4.6)	0.844
<b>Cosmetics</b>				
R.H.	18 (11.5)	62 (13.8)	0.8 (0.4–1.5)	0.531
D.S.‡	17 (10.8)	28 (6.2)	1.7 (0.8–3.7)	0.136
D.C.	12 (7.6)	34 (7.6)	1.2 (0.6–2.5)	0.610
F.N.	8 (5.1)	16 (3.6)	1.0 (0.4–2.6)	0.996
O.R.	7 (4.5)	24 (5.3)	0.8 (0.3–2.0)	0.581
S.E.	7 (4.5)	16 (3.6)	0.9 (0.3–2.8)	0.903
A.L.	5 (3.2)	10 (2.2)	1.3 (0.4–4.7)	0.667

OR, odds ratio.

\*Names of brands other than 'Cha no Shizuku' (Yuka) are indicated by their initials.

†Adjusted for allergic rhinitis, atopic dermatitis, and asthma.

‡Some products of this brand contain hydrolyzed wheat protein.

frequency of cases currently using the HWP-containing soap, 'Cha no Shizuku', was 11%, significantly higher than in control subjects (5%,  $P = 0.014$ ), with an adjusted OR of 2.6 (95% CIs, 1.2–5.6). As shown in Table 2, some other brands also contained HWP. However, use of no other brand showed a statistically significant association with WA. To compare the risk of WA between users of 'Cha no Shizuku' soap and users of other HWP-containing products, we performed an unconditional multivariate logistic regression analysis after adjustment for AR, BA, and AD and after limiting the subjects to those who were currently using any of the HWP-containing brands listed in Table 2. When compared with the use of other HWP-containing brands, use of 'Cha no Shizuku' was associated with an increased risk of WA with an adjusted OR of 2.3 (95%CI, 0.94–5.56) (data not shown). However, this difference did not reach statistical significance ( $P = 0.07$ ).

Associations between the use of 'Cha no Shizuku' and WA were also evaluated using different exposure parameters. The subjects were divided into three groups according to their history of product use as follows: (i) subjects who were currently using the product (current users), (ii) those who had used it before but not currently (past users), and (iii) those who had never used it (never users). We found that only current use was associated with WA with an OR of 2.6 (1.2–5.7) (Table 3, model 1). Subjects were then divided into four groups according to the duration of use of the product. It can be seen that the duration of use  $\geq 2$  years was associated with an increased risk of WA with an OR of 4.2 (1.6–10.7) (Table 3, model 2). In an analysis of all subjects who had ever used the soap (current or past users), current users were more likely to have used it for  $\geq 2$  years ( $P = 0.005$ ).

Of the 29 subjects who had ever used the soap (current or past users) in the allergic group, seven experienced itchiness of the face and/or eyes, sneezing, a runny nose, or

**Table 3** Association between use of the facial soap 'Cha no Shizuku' containing HWP and self-reported wheat allergy

Facial soap containing HWP, 'Cha no Shizuku'	Cases (n = 157) No. (%)	Controls (n = 449) No. (%)	Adjusted OR* (95% CI)
<b>Model 1</b>			
History of use			
Never used	128 (82)	383 (85)	1
Ever used	12 (8)	40 (9)	1.0 (0.4–2.1)
Currently using	17 (11)	26 (6)	2.6 (1.2–5.7)
<b>Model 2</b>			
Duration of use			
Never used	128 (82)	383 (85)	1
<1 year	12 (8)	41 (9)	0.9 (0.4–2.1)
1 year	4 (3)	14 (3)	1.0 (0.3–3.5)
$\geq 2$ years	13 (8)	11 (2)	4.2 (1.6–10.7)

OR, odds ratio; 95% CI, 95% confidence interval; HWP, hydrolyzed wheat protein.

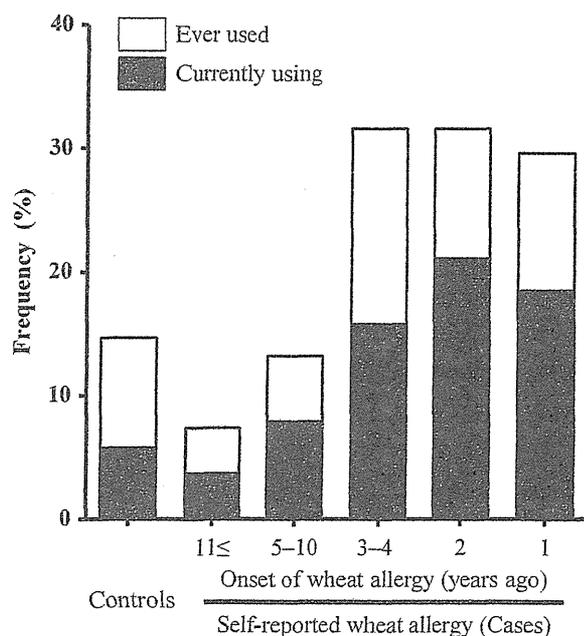
\*Adjusted for allergic rhinitis, atopic dermatitis, and asthma.

swelling of the eyelids after using it (24%). This was significantly higher than in the control group (5%, 3/66) ( $P = 0.008$ ).

#### Presentation of WA in relation to the use of 'Cha no Shizuku'

To further elucidate the relationship between the use of the soap and WA, we assessed associations between history of use and the presentation of WA. Figure 2 shows the frequency of current users and past users relative to the time of onset of WA. Frequencies of current users were higher in more recent-onset WA ( $P$  for trend = 0.002), suggesting that the use of the soap is associated with the recent epidemic of WA. Compared with the frequency of current users in the controls, a significantly higher frequency was observed only in cases who had developed WA within the last 4 years ( $P = 0.001$ ). This might be explained by the fact that this facial soap started to be sold in 2004, namely 7 years before this study.

Associations between history of soap use and presentation with WA are shown in Table 4. Current use of the soap was associated with doctor-diagnosed WA. Although the overall frequency of diagnosed WA was 52%, it was as high as 76% among the current users. Additionally, eye and nose symptoms after wheat ingestion were more common among current users than never users, and about half of the current users were also diagnosed as having WDEIA by their doctor. These presentations of WA were compatible with those of



**Figure 2** Frequencies of subjects who were currently using or had ever used the facial soap 'Cha no Shizuku' containing hydrolyzed wheat protein according to time of onset of wheat allergy.

cases who were clinically diagnosed as suffering from WDEIA induced by this soap (17, 21).

#### Discussion

This Web-based case-control study explored epidemiological relationships between the use of the HWP-containing facial soap 'Cha no Shizuku' and risk of WA. Current use of the soap was significantly associated with increased risk of WA with an adjusted OR of 2.6. Additionally, current use of this soap was more common in cases with more recent-onset WA, implying that it may have contributed to the recent epidemic of WA. To the best of our knowledge, this is the first study that shows the epidemiological impact of contact exposure to food-derived protein in skin and hair care products on the epidemic of adult-onset food allergy.

'Cha no Shizuku' was a popular facial soap in Japan. The company (Yuka) sold more than 40 million bars to more than 4 million customers up to 2010. This product contained an acid-HWP named Glupearl 19S (Katayama Chemical, Inc, Osaka, Japan) included for its moisturizing effect and emulsification function. The soap started to be sold in 2004, and sales increased with time. A minority of allergists and dermatologists began to become aware of the potential role of HWP in this soap as an inducer of WA in 2009–2010. However, this was not recognized by the general allergist and the public until the company started a voluntary recall of the HWP-containing soap on May 25, 2011. After the voluntary recall, the allergy problem induced by this soap was publicized by the media and in the meantime has grown to be recognized as a major public health problem in Japan. Therefore, the current study was performed before the general recognition of the allergy problem. In October 2011, the Japanese Society of Allergology (JSA) determined the diagnostic criteria for the immediate WA induced by exposure to Glupearl 19S contained in this soap (21). To date, more than 2000 patients meeting these criteria have been reported to the JSA.

Among the skin and hair care products containing HWP, a statistically significant association with WA was observed only for 'Cha no Shizuku' soap. The reason for this cannot be determined from the present study. Differences in the amount of HWP in the different products may explain this, because 'Cha no Shizuku' contained the relatively high level of 0.3% of HWP. Another possibility may relate to the high volume of sales of this soap, resulting in a sufficient sample size for reliable statistical analysis. One more explanation may relate to the difference in biochemical properties between Glupearl 19S and the HWPs in other products. HWPs produced by different companies have been used in skin and hair care products in Japan. A strong sensitizing capacity of Glupearl 19S has been shown in animal models, although not in a direct comparison with other HWPs (24). Glupearl 19S contains higher molecular weight proteins, which may increase its allergenicity (25, 26). More recently, studies have shown that the deamidation of glutamine residues in gluten by acid-heat treatment also contributes to the

**Table 4** Use of the facial soap 'Cha no Shizuku' containing hydrolyzed wheat protein and the presentation of WA

	History of use			P-value
	Currently using (n = 17)	Ever used (n = 12)	Never used (n = 128)	
Onset age >12 years	17 (100)	11 (92)	102 (80)	0.079
WA diagnosed by doctor	13 (76)*	6 (50)	62 (48)	0.094
Exacerbation of WA symptoms by exercise	10 (59)	5 (42)	52 (41)	0.361
WDEIA diagnosed by doctor	8 (47)*	2 (17)	21 (16)	0.011
Frequency of episodes during the last 12 months				
0	3 (18)	2 (17)	23 (18)	0.679
1–2	3 (18)	4 (33)	39 (30)	
3–5	7 (41)	1 (8)	29 (23)	
6–10	2 (12)	2 (17)	12 (9)	
11–	2 (12)	3 (25)	25 (20)	
How much wheat have you eaten recently?				
No wheat	0 (0)	1 (8)	12 (9)	0.170
A small amount of wheat	9 (53)	2 (17)	34 (27)	
A usual amount of wheat	6 (35)	8 (67)	76 (59)	
Avoid eating only before the exercise	1 (12)*	1 (8)	6 (5)	
Self-reported symptoms of WA				
Swelling of the eyelid	9 (53)*	4 (33)	17 (13)	<0.001
Itchiness of the eyes	9 (53)*	4 (33)	25 (20)	0.008
Red swelling of the face	2 (12)	2 (17)	15 (12)	0.880
Itchiness of the face	6 (35)	2 (17)	31 (24)	0.484
Sneezing/runny nose/stuffy nose	5 (29)*	3 (25)	14 (11)	0.062
Swelling of the lips	2 (12)	2 (17)	20 (16)	0.909
Generalized itchiness	9 (53)	4 (33)	39 (30)	0.181
Generalized urticaria	8 (47)	3 (25)	32 (25)	0.157
Generalized redness	4 (24)	2 (17)	15 (12)	0.381
Discomfort or itchiness of the throat	6 (35)	3 (25)	31 (24)	0.615
Dyspnea	4 (24)	1 (8)	19 (15)	0.507
Cough	3 (18)	1 (8)	14 (11)	0.673
Wheeze/stridor	2 (12)	0 (0)	14 (11)	0.476
Abdominal pain	4 (24)*	1 (8)	8 (6)	0.052
Nausea and vomiting	3 (18)	1 (8)	9 (7)	0.328
Diarrhea	4 (24)	1 (8)	10 (8)	0.116
Blurring of vision	0 (0)	0 (0)	6 (5)	0.493
Weakness	0 (0)	0 (0)	8 (6)	0.385
Loss of consciousness	0 (0)	0 (0)	3 (2)	0.707
Palpitation	2 (12)	1 (8)	12 (9)	0.941
Headache	1 (6)	0 (0)	7 (5)	0.704
Feeling sluggish or drowsy	1 (6)	0 (0)	14 (11)	0.403

WA, wheat allergy; WDEIA, wheat-dependent exercise-induced anaphylaxis.

Data are expressed as number (%).

\* $P < 0.05$  when compared with never used group.

allergenicity of acid-HWP (27–30). Additionally, the possibility remains that ingredients other than HWP in 'Cha no Shizuku' soap caused allergic contact dermatitis to disrupt the skin barrier and facilitated the penetration of higher molecular weight proteins of Glupearl 19S into an inflammatory milieu (31, 32). Indeed, the soap contained more than 10 kinds of ingredients including phenoxyethanol and 1,3-butylene glycol, which are known contact sensitizers (33, 34).

The main limitation of this study relates to the definition of WA, which was self-reported, not doctor-diagnosed. It is generally recognized that diagnosis by an allergist after provocation testing is more reliable than the definition of diseases by self-report. However, especially in the case of WDEIA, the sensitivity of the provocation test is not always very good. Using patients diagnosed by provocation test as cases may not be suitable for epidemiological studies that estimate the effect of exposure on the general population, because such patients are different from the general set of patients with WA. This study was a Web-based survey; such surveys have the advantage that both cases and controls can be recruited from the same cohort of the general population, and patients with rare diseases are identifiable in large-scale cohorts.

In conclusion, this Web-based case-control study documents an epidemiological relationship between WA and contact exposure to HWP in Japanese women. These findings imply a possible role of contact exposure to food-derived protein hydrolysates in skin and hair care products in the epidemic of adult-onset food allergy. We urge that more attention should be paid to the possible role of food-derived protein in skin and hair care products in the induction of food allergy.

#### Author contributions

YF designed the study and wrote the manuscript. MT, HN, and KA contributed to the critical revision of the manuscript. All authors read and approved the final manuscript.

#### Conflicts of interest

The authors declare that they have no conflicts of interest.

#### Supporting Information

Additional Supporting Information may be found in the online version of this article:

**Figure S1.** Distribution of the population of 20–54 year-old women in Japan according to the national population census (A), the number of women aged 20–54 years who were registered to MACROMILL research panel in 2011 (B), and number of studied subjects in the screening survey (C).

**Appendix S1.** Screening questionnaire.

**Data S1.** Characteristics of the studied internet research monitor population.

## References

1. Sicherer SH. Epidemiology of food allergy. *J Allergy Clin Immunol* 2011;127:594–602.
2. Zuberbier T, Edenharter G, Worm M, Ehlers I, Reimann S, Hantke T et al. Prevalence of adverse reactions to food in Germany – a population study. *Allergy* 2004;59:338–345.
3. Gupta R, Sheikh A, Strachan DP, Anderson HR. Time trends in allergic disorders in the UK. *Thorax* 2007;62:91–96.
4. Lack G. Epidemiologic risks for food allergy. *J Allergy Clin Immunol* 2008;121:1331–1336.
5. Lack G, Fox D, Northstone K, Golding J. Factors associated with the development of peanut allergy in childhood. *N Engl J Med* 2003;348:977–985.
6. Asero R, Antonicelli L. Does sensitization to foods in adults occur always in the gut? *Int Arch Allergy Immunol* 2011;154:6–14.
7. Bohle B. The impact of pollen-related food allergens on pollen allergy. *Allergy* 2007;62:3–10.
8. Skypala LJ, Bull S, Deegan K, Gruffydd-Jones K, Holmes S, Small I et al. The prevalence of PFS and prevalence and characteristics of reported food allergy; a survey of UK adults aged 18–75 incorporating a validated PFS diagnostic questionnaire. *Clin Exp Allergy* 2013;43:928–940.
9. Fukutomi Y, Sjolander S, Nakazawa T, Borres MP, Ishii T, Nakayama S et al. Clinical relevance of IgE to recombinant Gly m 4 in the diagnosis of adult soybean allergy. *J Allergy Clin Immunol* 2012;129:860–863.
10. Cabanes N, Igea JM, de la Hoz B, Agustin P, Bianco C, Dominguez J et al. Latex allergy: position paper. *J Investig Allergol Clin Immunol* 2012;22:313–330.
11. Blanco C. Latex-fruit syndrome. *Curr Allergy Asthma Rep* 2003;3:47–53.
12. Codreanu F, Morisset M, Cordebar V, Kanny G, Moneret-Vautrin DA. Risk of allergy to food proteins in topical medicinal agents and cosmetics. *Eur Ann Allergy Clin Immunol* 2006;38:126–130.
13. Niinimäki A, Niinimäki M, Makinen-Kiljunen S, Hannuksela M. Contact urticaria from protein hydrolysates in hair conditioners. *Allergy* 1998;53:1078–1082.
14. Pecquet C, Lauriere M, Huet S, Leynadier F. Is the application of cosmetics containing protein-derived products safe? *Contact Dermatitis* 2002;46:123.
15. Lauriere M, Pecquet C, Bouchez-Mahiou I, Snegaroff J, Bayrou O, Raison-Peyron N et al. Hydrolysed wheat proteins present in cosmetics can induce immediate hypersensitivities. *Contact Dermatitis* 2006;54:283–289.
16. Lauriere M, Pecquet C, Boulenc E, Bouchez-Mahiou I, Snegaroff J, Choudat D et al. Genetic differences in omega-gliadins involved in two different immediate food hypersensitivities to wheat. *Allergy* 2007;62:890–896.
17. Fukutomi Y, Itagaki Y, Taniguchi M, Saito A, Yasueda H, Nakazawa T et al. Rhinconjunctival sensitization to hydrolyzed wheat protein in facial soap can induce wheat-dependent exercise-induced anaphylaxis. *J Allergy Clin Immunol* 2011;127:531–533.
18. Chinuki Y, Kaneko S, Sakieda K, Murata S, Yoshida Y, Morita E. A case of wheat-dependent exercise-induced anaphylaxis sensitized with hydrolyzed wheat protein in a soap. *Contact Dermatitis* 2011;65:55–57.
19. Sugiyama A, Kishikawa R, Nishie H, Takeuchi S, Shimoda T, Iwanaga T et al. [Wheat anaphylaxis or wheat-dependent exercise-induced anaphylaxis caused by use of a soap product which contains hydrolyzed wheat proteins. – a report of 12 cases–]. *Arerugi* 2011;60:1532–1542.
20. Hiragun M, Ishii K, Hiragun T, Shindo H, Mihara S, Matsuo H et al. The sensitivity and clinical course of patients with wheat-dependent exercise-induced anaphylaxis sensitized to hydrolyzed wheat protein in facial soap – secondary publication. *Allergol Int* 2013;62:351–358.
21. Chinuki Y, Morita E. Wheat-dependent exercise-induced anaphylaxis sensitized with hydrolyzed wheat protein in soap. *Allergol Int* 2012;61:529–537.
22. Iwamoto S, Hagino N, Tanimoto T, Kusumi E. Wheat-dependent exercise-induced anaphylaxis associated with a facial soap. *BMJ Case Rep* 2012. Available from: <http://case-reports.bmj.com/content/2012/bcr.01.2012.5641.full>. Last accessed 26 February 2014.
23. Kobayashi M, Okura R, Yoshioka H, Hiro-masa K, Yoshioka M, Nakamura M. [Wheat dependent exercise induced anaphylaxis possibly sensitized by the hydrolyzed wheat proteins in a facial cleansing soap]. *J UOEH* 2012;34:85–89.
24. Adachi R, Nakamura R, Sakai S, Fukutomi Y, Teshima R. Sensitization to acid-hydrolyzed wheat protein by transdermal administration to BALB/c mice, and comparison with gluten. *Allergy* 2012;67:1392–1399.
25. Chinuki Y, Takahashi H, Dekio I, Kaneko S, Tokuda R, Nagao M et al. Higher allergenicity of high molecular weight hydrolyzed wheat protein in cosmetics for percutaneous sensitization. *Contact Dermatitis* 2013;68:86–93.
26. Nakamura R, Nakamura R, Adachi R, Itagaki Y, Fukutomi Y, Teshima R. Evaluation of allergenicity of acid-hydrolyzed wheat protein using an in vitro elicitation test. *Int Arch Allergy Immunol* 2013;160:259–264.
27. Denery-Papini S, Bodinier M, Larre C, Brossard C, Pineau F, Triballeau S et al. Allergy to deamidated gluten in patients tolerant to wheat: specific epitopes linked to deamidation. *Allergy* 2012;67:1023–1032.
28. Gourbeyre P, Denery-Papini S, Larre C, Gaudin JC, Brossard C, Bodinier M. Wheat gliadins modified by deamidation are more efficient than native gliadins in inducing a Th2 response in Balb/c mice experimentally sensitized to wheat allergens. *Mol Nutr Food Res* 2012;56:336–344.
29. Yokooji T, Kurihara S, Murakami T, Chinuki Y, Takahashi H, Morita E et al. Characterization of causative allergens for wheat-dependent exercise-induced anaphylaxis sensitized with hydrolyzed wheat proteins in facial soap. *Allergol Int* 2013;62:435–445.
30. Nakamura R, Nakamura R, Sakai S, Adachi R, Hachisuka A, Urisu A et al. Tissue transglutaminase generates deamidated epitopes on gluten, increasing reactivity with hydrolyzed wheat protein-sensitized IgE. *J Allergy Clin Immunol* 2013;132:1436–1438.
31. Strid J, Hourihane J, Kimber I, Callard R, Strobel S. Disruption of the stratum corneum allows potent epicutaneous immunization with protein antigens resulting in a dominant systemic Th2 response. *Eur J Immunol* 2004;34:2100–2109.
32. Spiewak R. Contact dermatitis in atopic individuals. *Curr Opin Allergy Clin Immunol* 2012;12:491–497.
33. Uter W, Yazar K, Kratz EM, Mildau G, Liden C. Coupled exposure to ingredients of cosmetic products: II. Preservatives. *Contact Dermatitis* 2014;70:219–226.
34. Tamagawa-Mineoka R, Katoh N, Kishimoto S. Allergic contact dermatitis due to 1,3-butylene glycol and glycerol. *Contact Dermatitis* 2007;56:297–298.

原 著

## 北海道上士幌町における成人喘息，アレルギー性鼻炎有病率の検討 —2006年，2011年の比較—

1)北海道大学病院内科I

2)筑波大学医学医療系呼吸器内科

3)国立病院機構相模原病院

4)東京都立小児総合医療センター

清水 薫子<sup>1)</sup> 今野 哲<sup>1)</sup> 木村 孔一<sup>1)</sup> 荻 喬博<sup>1)</sup>  
谷口葉津子<sup>1)</sup> 清水 健一<sup>1)</sup> 伊佐田 朗<sup>1)</sup> 服部 健史<sup>1)</sup>  
檜澤 伸之<sup>2)</sup> 谷口 正実<sup>3)</sup> 赤澤 晃<sup>4)</sup> 西村 正治<sup>1)</sup>

【目的】北海道上士幌町の成人喘息，アレルギー性鼻炎有病率の推移を把握する。

【方法】2006年(3096名)と2011年(1472名)のEuropean Community Respiratory Health Survey 日本語版による調査結果を比較検討した。

【結果】回収率は，2006年は95.8%，2011年は98.1%。喘息期間有症率は，2006年は男性12.9%，女性9.8%，2011年は10.7%，8.3%。過去に喘息と言われたことがあり，医師による診断がある群は，2006年は男性5.7%，女性6.3%，2011年は7.9%，7.5%と増加。喫煙群は，2006年，2011年それぞれ男性42.8%，34.8%，女性17.2%，14.7%と減少。鼻アレルギーのある群は，男性が17.6%から23.2%，女性が23.0%から25.4%と増加。

【結論，考察】

医師の診断がある喘息，アレルギー性鼻炎は増加した。一方で喘息期間有症率は減少し，適切な加療による変化と予想された。

Key words: allergic rhinitis — asthma — obesity — prevalence — smoking

### 緒 言

近年，諸外国において，成人のアレルギー性鼻炎有病率の増加が報告されている<sup>1)2)</sup>。一方で，成人気管支喘息の有病率は，近年増加を示すという報告もあるが，先進国においては，横ばいの傾向であるとの報告も存在する<sup>1)3)~7)</sup>。

2006年に，厚生労働科学研究免疫アレルギー疾患予防・治療研究事業「気管支喘息の有病率・罹患率およびQOLに関する全年齢階級別全国調

査]がおこなわれ，全国10地区における，我が国の成人気管支喘息，アレルギー性鼻炎の有(症)有病率が報告された<sup>8)9)</sup>。この研究の一環として，当科では北海道十勝郡上士幌町住民を対象とした調査を担当し，成人気管支喘息，アレルギー性鼻炎の有病率調査をおこない，また両疾患の危険因子に関する検討を行った<sup>10)</sup>。

本研究では，前回の調査より5年経過した2011年に，2006年時と同一のEuropean Community Respiratory Health Survey (ECRHS) 調査用紙日

Received: February 19, 2014, Accepted: May 23, 2014

Abbreviations: BMI “body mass index”, ECRHS “European Community Respiratory Health Survey”

今野 哲：北海道大学病院内科I〔〒060-8638 北海道札幌市北区北14条西5丁目〕

E-mail: satkonno@med.hokudai.ac.jp

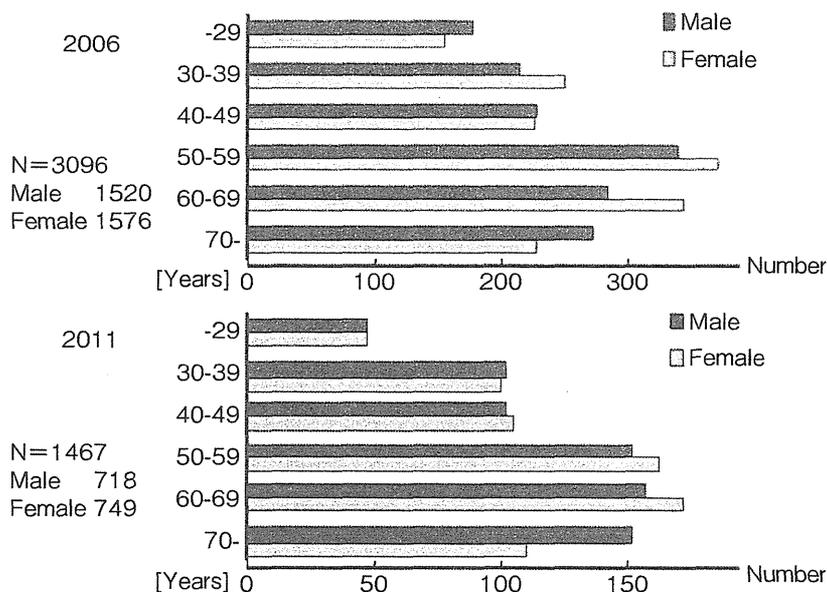


Fig. 1. Age distribution of respondents.

The distribution of residents aged from 20 to 81 years old in 2011 was similar to that in 2006.

本語版を用いたアンケート調査をおこない、同町における、近年の成人気管支喘息、アレルギー性鼻炎の有病率の推移を検討した。

### 対象と方法

2006年の調査対象の年齢分布に一致するように上士幌町の住民基本台帳からランダムに抽出された20歳から81歳の男女計1500名に対し、2006年の調査と全く同一のECRHS調査用紙日本語版を用い、アンケートを施行した。調査は、2006年と同時期の10月に、全例訪問調査員による自宅への訪問調査にておこなわれた。

喘息、アレルギー性鼻炎、喫煙率については、20歳から39歳、40歳から59歳、60歳以上の3群に分けて比較検討した。喘息、アレルギー性鼻炎と喫煙、肥満との関連については、 $\chi^2$ 検定を用いた。有意水準は $p < 0.05$ を有意差ありとし、統計解析には統計プログラムJMP Pro10<sup>®</sup>を用いた。

尚、本研究はヘルシンキ宣言を遵守し、「北海道上士幌町民における、アレルギー疾患有病率調査に関する研究」に関して、平成23年5月31日付で、北海道大

学大学院医学研究科・医学部医の倫理委員会の承認を得ておこなわれた。

### 結果

アンケート用紙は1500人（男性738人、女性762人）に配布し、男性718人、女性749人、計1467人より回収され、回収率は98.1%であり、これは該当年齢の全町民（男性1864人、女性1946人、計3810人）の38.5%（男性38.5%、女性38.5%）に相当する（Fig. 1）。また、調査対象の年齢分布は全町民の分布とほぼ同様であった。

「あなたは、最近12カ月の間に一度でも胸がゼーゼー、ヒューヒューしたことがありますか？」の質問に「はい」と答えた人（喘息期間有症率）は、2006年は男性12.9%、女性9.8%であったが、2011年は10.7%、8.3%であり、減少傾向であり、この傾向は高齢男性で顕著であった（Fig. 2）。次に「あなたは、今までに喘息に罹ったことがありますか？」、「あなたの喘息は医師によって確認されましたか？」にいずれも「はい」と答えた人を喘息あり（current asthma）と定義したところ、2006

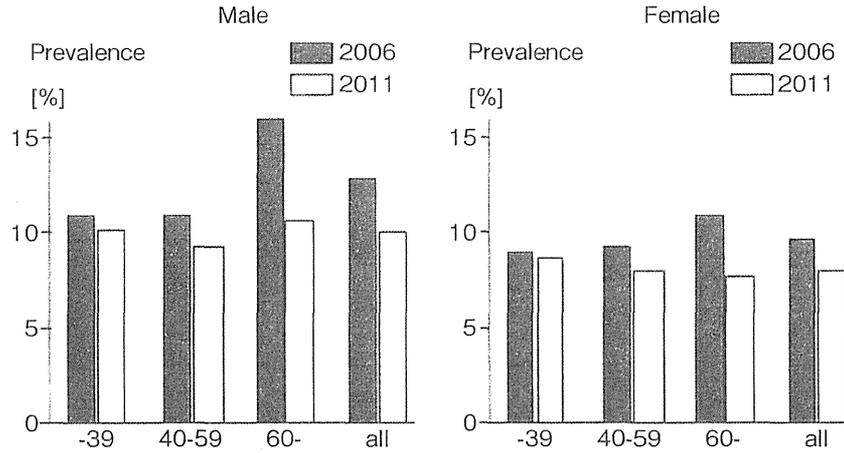


Fig. 2. Prevalence of wheezing over the last 12 months.  
Prevalence was decreased in 2011 compared with that in 2006.

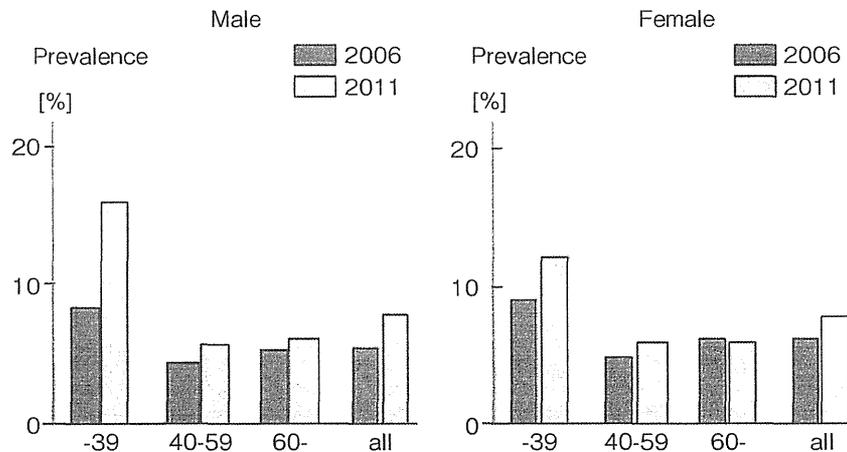


Fig. 3. Prevalence of respondents who answered "Yes" to the questions "Have you ever had asthma?" and "Was this confirmed by a doctor?".  
Prevalence, especially among younger respondents, was increased in 2011 compared with 2006.

年は男性 5.7%, 女性 6.3% であったが, 2011 年は 7.9%, 7.5% であり, 軽度増加傾向であった (Fig. 3). 特に 39 歳以下では 2006 年は男性 8.1%, 女性 9.1% であったが, 2011 年 15.8%, 12.2% と他の年代と比較し増加を認めた. また, 医師により喘息と診断された群で「あなたは, 最近 12 カ月の間に一度でも胸がゼーゼー, ヒューヒューしたことがありますか?」の質問に「はい」と答えた人は 2006

年 65.4% (男性 70.9%, 女性 60.6%), 2011 年 57.4% (男性 55.1%, 女性 58.9%) と減少しており, 「あなたは, 最近 12 カ月の間に一度でも胸がゼーゼー, ヒューヒューしたことがありますか?」の質問に「はい」と答えた人のうち医師により喘息と診断された割合は 2006 年 34.5% (男性 31.1%, 女性 38.7%), 2011 年 47.1% (男性 41.6%, 女性 53.2%) と増加していた.

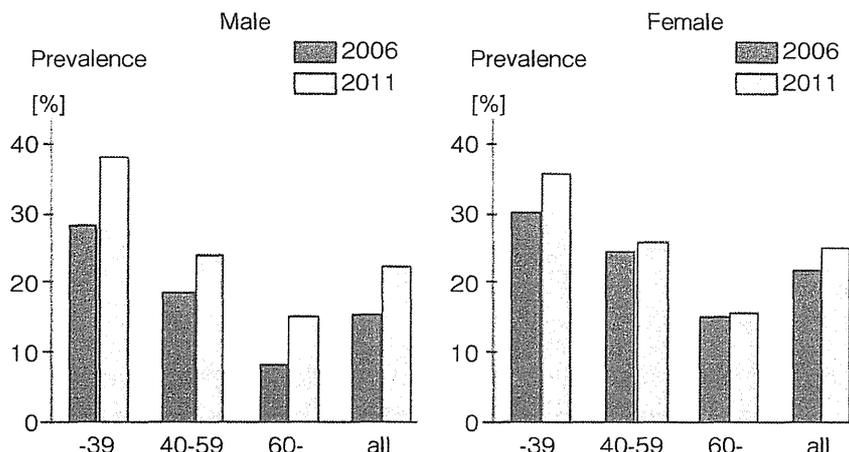


Fig. 4. Prevalence of allergic rhinitis.  
The prevalence was increased in 2011 compared with that in 2006.

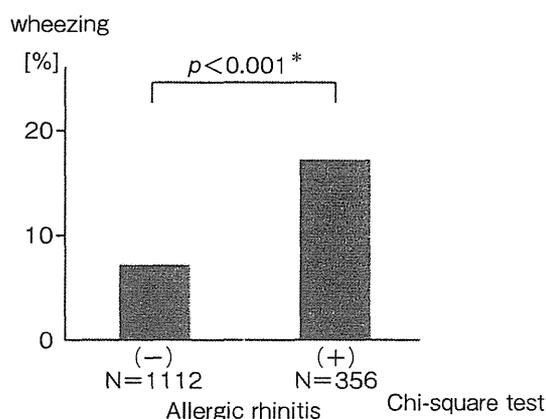


Fig. 5. Association between wheezing over the last 12 months and allergic rhinitis.

A significant association was found between wheezing over the last 12 months and allergic rhinitis.

「あなたは、花粉症を含む何らかの鼻アレルギーがありますか？」の質問に「はい」と答えた人（アレルギー性鼻炎群）は男性が17.6%から23.2%へ、女性が23.0%から25.4%と増加を認めた（Fig. 4）。20から39歳、40から59歳、60歳以上の全年齢層で同様の傾向であった。

過去12カ月の喘鳴と鼻炎との関係を検討したところ、アレルギー性鼻炎が有る群において「あ

なたは、最近12カ月の間に一度でも胸がゼーゼー、ヒューヒューしたことがありますか？」の質問に「はい」と答えた人は非鼻炎群と比べて有意に多かった（鼻炎群18.0%、非鼻炎群6.7%  $\chi^2: p < 0.001$ ）（Fig. 5）。

喫煙に関するアンケート結果では、「あなたはこれまでに少なくとも1年以上タバコを吸っていたことがありますか？」という質問に対し、「はい」と答えた人が、2006年、2011年それぞれ男性67.7%、69.3%、女性23.9%、24.1%と著変を認めなかった（Fig. 6）。一方、現在喫煙している人の割合は、2006年、2011年それぞれ男性42.8%、34.8%、女性17.2%、14.7%と全体としてみると低下傾向であったが、60歳以下の女性においては低下は認めなかった。（Fig. 7）また肥満者（BMI 25以上）の割合は、2006年、2011年それぞれ男性33.4%、33.8%、女性21.8%、21.8%と著変を認めなかった（Fig. 8）。

過去12カ月の喘鳴と喫煙との関係を全年齢、20～44歳を対象に検討したところ、「あなたはこれまでに少なくとも1年以上タバコを吸っていたことがありますか？」という質問に「はい」と答えた人と「いいえ」と答えた人との過去12カ月の喘鳴がある割合に有意差を認め、1年以上の喫煙がある群で有意に高かった（ $\chi^2: \text{Population1}$ ；

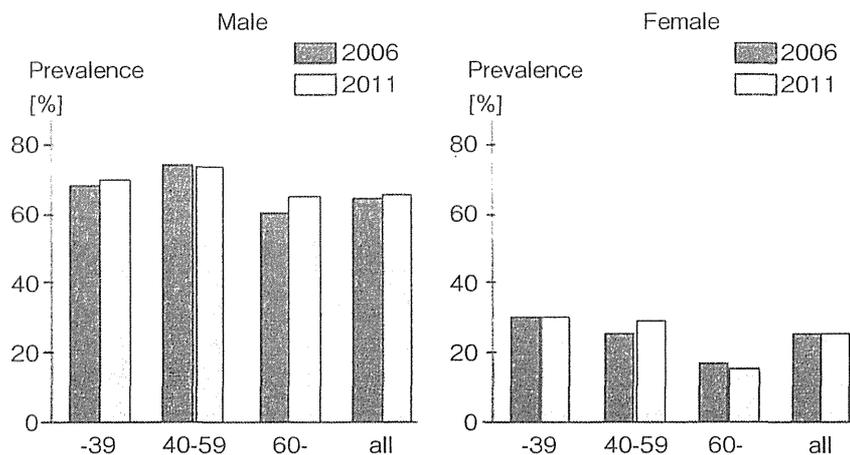


Fig. 6. Prevalence of respondents who answered "Yes" to the question "Have you ever smoked for as long as one year?".

The prevalence in 2011 was similar to that in 2006.

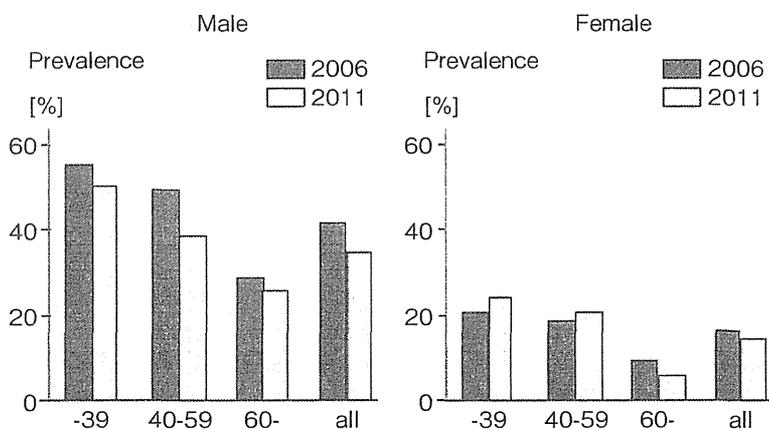


Fig. 7. Prevalence of respondents who answered "Yes" to the question "Are you a current smoker?".

The prevalence was decreased slightly in 2011 compared with that in 2006.

全体  $p = 0.029$ , Population2 ; 22~44 歳  $p < 0.001$ ) (Fig. 9). 一方, 現在喫煙している人における過去 12 カ月の喘鳴の割合は全年齢を対象とした場合, 有意差を認めなかったが, 20~44 歳において有意差を認めた. ( $\chi^2 : p < 0.001$ ) (Fig. 10) また, 肥満との関連においては, 全年齢で検討した場合, 肥満群において, 過去 12 カ月の喘鳴が有意に多い結果であった ( $\chi^2 : p = 0.001$ ) (Fig. 11). 一方, アレル

ギー性鼻炎と喫煙, 肥満の間には有意な関連は認められなかった.

## 考 察

今回の調査は, 北海道上士幌町の成人住民 1500 人に対しアンケート調査を依頼し, 実際 1427 人より回答が得られた. 2006 年の調査では 3096 人を対象としたが, 北海道大学と上士幌町とが, 訪問

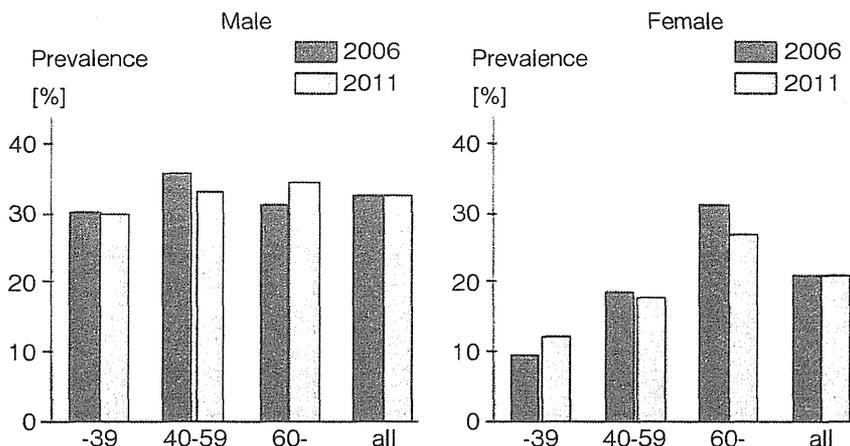


Fig. 8. Prevalence of obesity, defined as BMI  $\geq$  25. The prevalence in 2011 was similar to that in 2006.

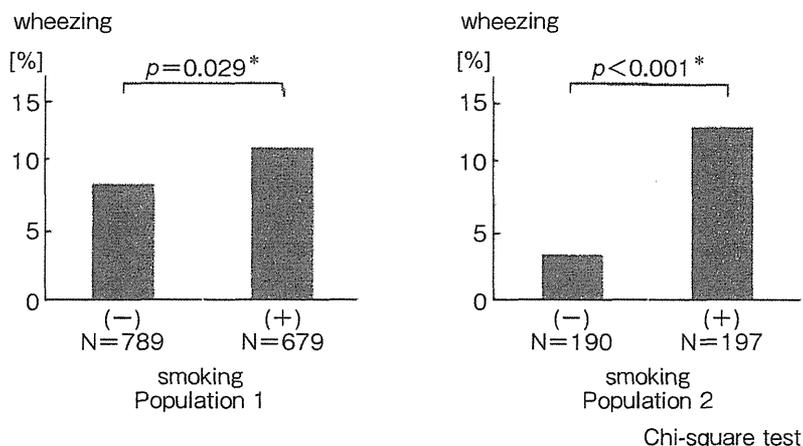


Fig. 9. Association between smoking habit for as long as 1 year and wheezing over the last 12 months. Population 1: Total number of respondents. Population 2: 20-44 years old. Smoking habit was significantly associated with wheezing over the last 12 months in both Populations 1 and 2.

研究員派遣の予算や、本研究の今後の長期的な継続の可能性を考慮した結果、約半数を調査対象とした。今回の調査でも回収率は98.1%と高く(前回95.8%)、年齢別にみると全対象住民の38.5%を対象とすることができた。また年齢分布、性差についても2006年と一致させることにより、過去5年間の推移を考察するにあたっての妥当性は充

分なものと考えられた。

気管支喘息は、発作性の喘鳴、可逆性の気道狭窄、非特異的気道過敏性の亢進といった特徴を有する疾患であるが、診断において客観的な指標に基づく明確な定義が存在しない。そのために、その有病率、有症率の把握には、ある程度の限界を許容せざるを得ない。今回の調査では全世界の標

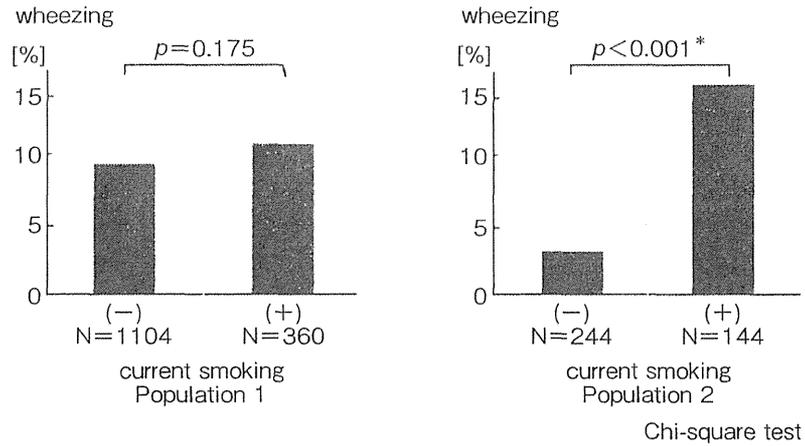


Fig. 10. Association between current smoking and wheezing over the last 12 months.

Population 1: Total number of respondents.

Population 2: 20-44 years old.

Current smoking was significantly associated with wheezing over the last 12 months in Population 2.

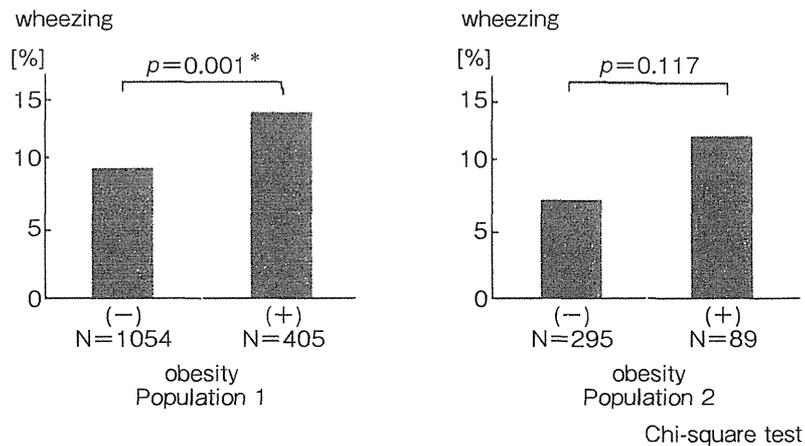


Fig. 11. Association between obesity and wheezing over the last 12 months.

Population 1: Total number of respondents.

Population 2: 20-44 years old.

Obesity was significantly associated with wheezing over the last 12 months in Population 1.

準アンケートの一つとされる ECRHS を用いた。「あなたは、最近 12 カ月の間に一度でも胸がゼーゼー、ヒューヒューしたことがありますか?」と

いう質問が喘息期間有症率の国際比較の指標として用いられ、喘息患者、非喘息健康人との鑑別に最も信頼されている<sup>11)-13)</sup>。本邦でも渡辺らがその

日本語訳の妥当性を報告している<sup>14)</sup>。更には、喘息の診断の信頼性を高めるために「あなたは、今までに喘息に罹ったことがありますか?」、「あなたの喘息は医師によって確認されましたか?」という質問も用いた。

1990年代までは全世界的に喘息の割合が増加傾向であることが示されてきたが、特に先進国において2000年代から頭打ちの状態となったとの報告も見られる<sup>13)</sup>。1990年と2008年のスウェーデンにおける調査において、喘鳴の割合は低下していたが、喘息発作、喘息治療薬の使用率は軽度増加していたことが示された<sup>3)</sup>。今回12カ月の喘鳴の頻度は2006年と比較し軽度減少傾向を呈していた。しかし医師による診断を受けた者の割合は増加傾向であり、その傾向は特に39歳以下で顕著であった。さらには医師により喘息と診断された群において喘鳴を有する割合は2006年65.4%、2011年57.4%と減少しており、このことは、若年者に多いアトピー素因を背景とするアトピー性喘息<sup>15)</sup>の罹患率は増加しているが、一方で、喘息のコントロールは向上している現代の医療環境を反映している可能性がある。この現象は先に述べた海外の既報とも合致し、世界的なガイドラインの普及とICSの使用率の増加が背景にあると推測された。

アレルギー性鼻炎においては、5年間で、男性は17.6%から23.2%へ、女性は23.0%から25.4%と著明な増加を認めた。この傾向は男性においては全年代で認められ、女性では39歳以下の年代でより顕著であった。結果として、今回の調査により、上士幌町のような非都市部においても、海外の既報と同様に若い世代におけるアレルギー性鼻炎の増加が示された<sup>12)</sup>。

本調査の結果の解釈に関してはいくつかの問題点があげられる。一つは、今回の調査対象は2006年時と一部は重複してはいるが、異なる対象者も多数含まれている。中には、スギ花粉症の多い本州からの転入者も含まれている可能性があり、このことが、特にアレルギー性鼻炎の増加に寄与している可能性がある。また、北海道大学では調査地区である上士幌町において、継続的に講演を行

うなどの啓発活動を行っていることが結果に影響した可能性も否定出来ない。町民に対し、2006年の調査結果や喫煙によるリスクを説明したことが、結果として現喫煙率の低下をもたらし、医療機関の受診や、適切な治療の普及にも至ったかもしれない。そのため、本調査の結果を他の地域や本邦全体に当てはめることはできないかもしれない。しかし、本地区での今後の調査の継続により得られる知見の価値は高く、本邦の成人気管支喘息、アレルギー性鼻炎の有病率の経年的変化の把握に、寄与しうると考える。

## 結 語

非都市部に位置する北海道上士幌町では、2006年より2011年の5年間で、過去12カ月の喘鳴を有する者の割合が減少したが、医師の診断がある喘息は軽度増加していた。これは喘息に関わる医療環境の変化が関連しているかもしれない。一方、アレルギー性鼻炎の有病率は明らかに増加した。また、2006年の調査と同様に、過去1年の喫煙歴及び肥満(BMI 25以上)と過去12カ月の喘鳴とに有意な関連を認めた。

本結果は、第62回日本アレルギー学会学術大会で発表した。

利益相反 (conflict of interest) に関する開示：著者全員は本論文の研究内容について他者との利害関係を有しません。

## 文 献

- 1) Asher MI, Montefort S, Bjorksten B, Lai CK, Strachan DP, Weiland SK, et al; ISAAC Phase Three Study Group. Worldwide time trends in the prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and eczema in childhood: ISAAC Phases One and Three repeat multicountry cross-sectional surveys. *Lancet* 2006; 368: 733-43.
- 2) Lee YL, Shaw CK, Su HJ, Lai JS, Ko YC, Huang SL, et al. Climate, traffic-related air pollutants and allergic rhinitis prevalence in middle-school children in Taiwan. *Eur Respir*

- J* 2003; 21: 964-70.
- 3) Bjerg A, Ekerljung L, Middelveld R, Dahlén SE, Forsberg B, Franklin K, et al. Increased prevalence of symptoms of rhinitis but not of asthma between 1990 and 2008 in Swedish adults comparisons of the ECRHS and GA2LEN surveys. *PLoS One* 2011 17; 6: e16082.
  - 4) Bjerg A, Sandström T, Lundbäck B, Rönmark E. Time trends in asthma and wheeze in Swedish children 1996-2006: prevalence and risk factors by sex. *Allergy* 2010; 65: 48-55.
  - 5) Lötvall J, Ekerljung L, Rönmark EP, Wennergren G, Linden A, Ronmark E, et al. West Sweden Asthma Study: Prevalence trends over the last 18 years argues no recent increase in asthma. *Respir Res* 2009; 10: 94.
  - 6) Verlato G, Corsico A, Villani S, Cerveri I, Migliore E, Accordini S, et al. Is the prevalence of adult asthma and allergic rhinitis still increasing? Results of an Italian study. *J Allergy Clin Immunol* 2003; 111: 1232-8.
  - 7) Anderson H, Gupta R, Strachan D, Limb E. 50 years of asthma: UK trends from 1955 to 2004. *Thorax* 2007; 62: 85-90.
  - 8) Fukutomi Y, Taniguchi M, Watanabe J, Nakamura H, Komase Y, Ohta K, et al. Time trend in the prevalence of adult asthma in Japan: findings from population-based surveys in Fujieda City in 1985, 1999, and 2006. *Allergol Int* 2011; 60: 443-8.
  - 9) Fukutomi Y, Nakamura H, Kobayashi F, Taniguchi M, Konno S, Nishimura M, et al. Nationwide cross-sectional population-based study on the prevalences of asthma and asthma symptoms among Japanese adults. *Int Arch Allergy Immunol* 2010; 153: 280-7.
  - 10) 清水薫子, 今野 哲, 清水健一, 伊佐田朗, 高橋 歩, 服部健史, 他. 北海道上士幌町における成人喘息, アレルギー性鼻炎有病率—特に喫煙及び肥満との関連について—. *アレルギー* 2008; 57: 835-42.
  - 11) Janson C, Chinn S, Jarvis D, Burney P. Physician-diagnosed asthma and drug utilization in the European community respiratory health survey. *Eur Respir J* 1997; 10: 1795-802.
  - 12) Burney PGJ, Luczynska C, Chinn S, Jarvis D. The European Community Respiratory Health Survey. *Eur Respir J* 1994; 7: 954-60.
  - 13) European Community Respiratory Health Survey. Variations in the prevalence of respiratory symptoms, self-reported asthma attacks, and use of asthma medication in the European Community Respiratory Health Survey (ECRHS). *Eur Respir J* 1996; 9: 687-95.
  - 14) 渡辺淳子, 谷口正実, 高橋 清, 中川武正, 大矢幸弘, 赤澤 晃, 他. European Community Respiratory Health Survey 調査用紙日本語版の作成と検証. *アレルギー* 2006; 55: 1421-8.
  - 15) Masoli M, Fabian D, Holt S, Beasley R. Global Initiative for Asthma (GINA) Program. *Allergy* 2004; 59: 469-78.

PREVALENCE OF ADULT ASTHMA AND ALLERGIC RHINITIS IN KAMISHIHORO, HOKKAIDO  
—TRENDS FROM 2006 THROUGH 2011—

Kaoruko Shimizu<sup>1)</sup>, Satoshi Konno<sup>1)</sup>, Hirokazu Kimura<sup>1)</sup>, Takahiro Ogi<sup>1)</sup>,  
Natsuko Taniguchi<sup>1)</sup>, Kenichi Shimizu<sup>1)</sup>, Akira Isada<sup>1)</sup>, Takeshi Hattori<sup>1)</sup>,  
Nobuyuki Hizawa<sup>2)</sup>, Masami Taniguchi<sup>3)</sup>, Akira Akazawa<sup>4)</sup> and Masaharu Nishimura<sup>1)</sup>

<sup>1)</sup>*First Department of Medicine, Hokkaido University School of Medicine*

<sup>2)</sup>*Department of Pulmonary Medicine, Institute of Clinical Medicine, University of Tsukuba*

<sup>3)</sup>*Clinical research Center for Allergy and Rheumatology, National Hospital Organization,  
Sagamihara National Hospital*

<sup>4)</sup>*National Center for Child Health and Development*

**Purpose:** To investigate changes in the prevalence of adult asthma and allergic rhinitis from 2006 to 2011 in Kamishihoro, a town in Hokkaido, Japan.

**Methods:** The Japanese edition of the European Community Respiratory Health Survey questionnaire was completed by 1472 residents aged from 20 to 81 years old. (718 men, 749 women). The age and gender distribution of respondents matched that of respondents in 2006.

**Results:** Response rates were 98.1% in 2011 and 95.8% in 2006. Wheezing in the last 12 months was reported by 10.7% of men and 8.3% of women in 2011, compared to 12.9% and 9.8%, respectively, in 2006. The questions “Have you ever had asthma?” followed by “Was this confirmed by a doctor?” both received positive answers from 7.9% of men and 7.5% of women in 2011, compared to 5.7% and 6.3%, respectively, in 2006. The rate of current smoking was 34.8% in men and 14.7% in women in 2011, compared to 42.8% and 17.2%, respectively, in 2006. A “Yes” answer to the questionnaire item, “Do you have any nasal allergies, including hay fever?” (defining allergic rhinitis) was given by 23.2% of men and 25.4% of women in 2011, compared to 17.6% and 23.0%, respectively, in 2006. The prevalence of allergic rhinitis was increased, particularly among younger respondents.

**Conclusion:** Rates of current asthma and allergic rhinitis increased, whereas the rate of wheezing in the past 12 months decreased from 2006 to 2011. Optimal treatment of asthma might be related to these trends.

## Factors associated with asthma control in children: findings from a national Web-based survey

Mari Sasaki<sup>1</sup>, Koichi Yoshida<sup>1</sup>, Yuichi Adachi<sup>2</sup>, Mayumi Furukawa<sup>1</sup>, Toshiko Itazawa<sup>2</sup>, Hiroshi Odajima<sup>3</sup>, Hirohisa Saito<sup>4</sup> & Akira Akasawa<sup>1</sup>

<sup>1</sup>Division of Allergy, Tokyo Metropolitan Children's Medical Center, Tokyo, Japan; <sup>2</sup>Department of Pediatrics, University of Toyama, Toyama, Japan; <sup>3</sup>Department of Pediatrics, Fukuoka National Hospital, Fukuoka, Japan; <sup>4</sup>Department of Allergy and Immunology, National Research Institute for Child Health and Development, Tokyo, Japan

**To cite this article:** Sasaki M, Yoshida K, Adachi Y, Furukawa M, Itazawa T, Odajima H, Saito H, Akasawa A. Factors associated with asthma control in children: findings from a national Web-based survey. *Pediatr Allergy Immunol* 2015; **25**: 804–809.

### Keywords

asthma; asthma control; childhood asthma control test; rhinitis; web survey

### Correspondence

Mari Sasaki, Tokyo Metropolitan Children's Medical Center, 2-8-29 Musashidai, Fuchu, Tokyo, Japan  
Tel.: +81 42 300 5111  
Fax: +81 42 312 8143  
E-mail: mari\_sasaki@tmhp.jp

Accepted for publication 29 November 2014

DOI:10.1111/pai.12316

### Abstract

**Background:** Although achieving and maintaining control of asthma is considered to be the goal of asthma treatment, determinants of asthma control are not fully understood. Our aim was to assess factors associated with asthma control among paediatric patients in the general population.

**Methods:** In June 2012, a Web-based survey was conducted to identify Japanese children aged 6 to 11 yr who currently have asthma and evaluate control of their disease using the Childhood Asthma Control Test (C-ACT). Associations were evaluated among uncontrolled asthma (C-ACT score <20) between environmental factors, demographics and comorbid allergic diseases.

**Results:** Among the 3066 children with current asthma, 447 (14.6%) had uncontrolled asthma. Multivariable analysis identified factors such as low birthweight (adjusted OR 1.65, 95% CI 1.25–2.18), obesity (adjusted OR 1.44, 95% CI 1.05–1.99) and pet ownership before birth (adjusted OR 1.68, 95% CI 1.24–2.29) to be associated with uncontrolled disease. Comorbid allergic diseases, especially rhinitis were a significant risk of uncontrolled asthma (adjusted OR for severe rhinitis: 3.88, 95% CI 2.50–6.00). The severity of rhinitis symptoms was inversely correlated with the C-ACT score ( $p < 0.001$ ).

**Conclusions:** A population-based Web survey showed an association between several factors and the control of paediatric asthma. The assessment of these factors may help identify the children at risk with uncontrolled asthma.

Asthma is one of the most common chronic pulmonary diseases of childhood and is a cause of poor quality of life (QOL) due to emergency department visits, school absences and impairment of daily activities (1). Achieving and maintaining asthma control has been identified as the goal of asthma treatment in current guidelines (2). This goal benefits patients not only in regard to improving quality of life, but also in reducing the risk of future exacerbations (3).

Studies suggest that a proportion of patients with asthma continue to have poorly controlled disease, despite advances in therapies such as inhaled corticosteroids. A worldwide study in 2004 showed that asthma patients who report restriction of normal daily activities ranged from 17% to 68% (4), and later studies have reported similar results both in adults and children (5, 6).

Other than higher asthma severity, comorbidities such as allergic rhinitis and socioeconomic status are reported to have a role in disease control in adult and paediatric asthma patients (5, 7, 8). The relationship of asthma control with active or passive smoking and obesity has also been suggested (9, 10). However, determinants of asthma control are not fully understood. Moreover, few studies have evaluated multiple factors among the general population in paediatric asthma. Previous community-based surveys among children (11) are often conducted with limited sample sizes, which could be due to the method of sample collection.

Web-based surveys are regarded as a useful tool for allowing large numbers of participants to respond with a higher and faster response rate than conventional methods (12). These advantages have also been utilized recently in epidemiological