Chapter 6
Traditional and Emerging Occupational Asthma in Japan

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Abstract Occupational asthma (OA) is one of the most common forms of occupational lung disease in many industrialized countries, and it accounts for 9–15 % of adult asthma. If a worker with an occupational allergic disease doesn't consider it an occupational disease, or if affected workers bear it and take no measures or treatment, extensive exposure at the workplace will persist. These cause the disease to worsen or become refractory. Sometimes, patients might lose their job and face economic difficulties. Therefore, we should always take the possibility of OA into consideration and obtain a detailed history from patients. When OA is diagnosed, patients should avoid allergen exposure, and the workplace environment should be improved, as well as adequate drug therapy being provided. This paper covers the history, current state, and the published first guideline for diagnosis and management of occupational allergic diseases in Japan.

Keywords Occupational asthma • Konjac asthma • Guideline • Japan

6.1 History of OA in Japan

Occupational asthma (OA) is one of the most common forms of occupational lung disease in many industrialized countries, and it accounts for 9–15 % of adult asthma [1].

The first case of OA in Japan was reported in 1926 as "Asthma attack induced by working with American red cedar wood." When large amounts of American red cedar were imported for reconstruction after the Great Kanto Earthquake, carpenters suffered from asthma when processing this cedar. An epidemiological study revealed that approximately 10 % of carpenters were suffering from OA due to cedar. Therefore, import of the cedar was stopped and such OA was no longer seen.

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After IgE was discovered in 1966, OA began to be studied from an immunological perspective. The first OA to be identified in Japan was konjac asthma. At that time, bronchial asthma apparently caused by "Maiko" powder was known among the residents living near konjac milling plants and the employees of these plants. A group from the First Department of Internal Medicine at Gunma University studied a detailed field survey in Shimonita that identified OA induced by inhaling Maiko powder, which they called konjac asthma and reported in 1951 [2]. After that, many OAs were reported as sea squirt asthma, silkworm phosphorus hair asthma, buckwheat asthma, silkworm cocoon asthma, and shiitake mushroom asthma in 1996, 1996, 1970, 1971, and 1985, respectively [3, 4].

6.2 Epidemiology of Occupational Asthma in Japan

The rate of the OAs is about 2–15 % of all asthmatics in Japan. However, we do not have correct data of incidence and prevalence of OA. Since it is possible that many patients are treated for asthma without diagnosis of OA, the actual prevalence is probably higher.

Among persons involved in specific types of work, the prevalence of OA depends on the allergens to which they are exposed or the work environment, and there are many reports about its prevalence (Table 6.1) [5, 6].

It is a serious problem that a high prevalence was shown around some factories because allergens released from the workplace cause residents living around the plants to develop asthma. We found that many residents living around a konjac factory had konjac asthma, and we proposed that this should be called "environmental asthma" (Table 6.2) [7].

Table 6.1 Estimated preverence of work-related asthma from cross-sectional studies in Japan

Type of work	Prevalence (%)
Konjac maker	5.0
Sericulturist	9.0
Polyurethane industry worker	16.4
Worker in plastic greenhouses of strawberry	4.6
Worker in plastic greenhouses of shiitake mushroom	5.0

Table 6.2 The number of Konjac asthma patients depend on the distance from the factories

Distance from factories	The number of Konjac asthma patients	The number of non-Konjac asthma patients
Within 300 m	46	17
300–1000 m	4	13
More than 1000 m	1	20

6.3 Allergens

The causative allergens are varied and sometimes unexpected. A part of substances that have been reported in Japan are summarized in Table 6.3 [7].

Causative allergens are divided into allergens of high molecular weight, such as those derived from animals and plants, and allergens of low molecular weight, such as chemicals and metals. According to the development of industry, the incidence of asthma induced by high molecular weight compounds is decreasing. On the other hand, asthma induced by low molecular weight substances is increasing and has become a serious problem, recently [5, 6]. The problems in OAs caused by chemicals are that the specific IgE antibody cannot be easily detected and diagnosis is difficult.

Table 6.3 Reported occupational allergens in Japan

		Allergen	Occupation	Year and author
Plants	Cereal	Amorphophallus konjac	Konjac maker	1951 Shichijo
		Buckwheat	Buckwheat miller. soba restaurant worker	1971 Nakamura
		Wheat flour	Baker. confectionary makers	1971 Jyo
		Barley flour	Miller	1991 Noda
	Wood particle	Western red cedar	Wood processing industry worker	1926 Seki
		Zelkova	Wood processing industry worker	1982 Katsuya
		Mulberry	Furniture making industry worker	1969 Nakamura
		White birch	Wood processing worker	1979 Takamoto
		Lauan	Wood processing worker	1968 Aoki
		Quince	Wood processing worker	1975 Takahashi
		Boxwood	Wood processing worker	1985 Tawara
	Others	Coffee beans powder	Manufacturing plant worker	1985 Shirakawa
		Sesame	Manufacturing plant worker sesame oil	1990 Tadokoro
		Tea leaf		
		Fresh top	Tea picking worker	1976 Ebihara
		Component of tea leaf	Tea manufacture worker	1989 Otsuka
		Tomato (component in stalk)	Worker in plastic greenhouses	1980 Saito
		Lettuce (component in stalk)	Worker in plastic greenhouses	1980 Saito
		Fuzz of melon	Worker in plastic greenhouses	1980 Masuyama

(continued)

Table 6.3 (continued)

		Allergen	Occupation	Year and author
Animal		Silk	Silk textile industry worker	1966 Nakamura
		Sea squirt	Oyster farm worker	1964 Jyo
		Alcyonarian	Japanese spiny lobster	1989 Onizuka
		Animal hair	Writing brush maker	1968 Kikuchi
		Mixed fertilizer (fish, crab)	Fertilizer factory worker	1982 Usami, 1991 Kasiwagi
		Sardine powder	Dried sardine factory worker	1987 Takamoto
		Coat of rat and guinea pig	Researcher	1972 Kobayashi
Pollen, spore	Pollen	Sugar beet	Researcher of sugar beet	1970 Matsuyama
		Rose	Researcher of rose	1978 Saito
		Orchard grass	Commercial grower of orchard grass	1971 Nakazawa
		Strawberry	Worker in plastic greenhouses of strawberry	1973 Kobayashi
		Peach	Commercial grower of peach	1973 shida
		Apple	Artificial pollination worker	1978 Sawada
		Grape	Worker in plastic greenhouses	1984 Tsukioka
		Pepper	Worker in plastic greenhouses	1985 Okumura
	Spore	Shiitake mushroom	Worker in plastic greenhouses	1968 Kondo
		Club moss	Dental technician	1969 Nakamura
		Smut fungus	Commercial grower of wheat.	1983 Asai
Metal, chemical	Drug	Diastase	Pharmacist; at drugstore;	1970 Fueki
		Pancreatin	Pharmacist; at drugstore;	1971 Nakamura
		Semisynthetic penicillin	Pharmacist; at drugstore;	1974 Kanetani
	Metal	Dichromate	Workers of cement producing industry	1972 Fueki
		Chloroplatinate	Industry worker	1984 Shima
	Chemical	TDI MDI	Polyurethane industry worker, painter	1970 Shima
		Ethylenediamine	Plastic processing worker	1979 Nakazawa
		Tetryl (explosive)	Pyrotechnist	1989 Inagaki
		Acrylic resin emulsion	Painter	1990 Nakamura

6.4 Traditional Occupational Asthma in Japan

6.4.1 Konjac Asthma

As I have described previously, the first OA to be identified immunologically in Japan was konjac asthma [2]. Konjac root is dried and ground into powder in the process of manufacturing the food known as konjac (no calorie food). Maiko is a fine konjac root powder that is blown by air pressure to obtain konjac powder for commercial use. Much of the Maiko powder is dispersed in the air and induces asthma in the plant workers by inhalation. The prevalence of konjac asthma was 16.6 % among employees in konjac mills, and the age of onset was different but mostly under 30 years.

The purified allergen of konjac asthma named Ag40D-2 is an acidic protein of about 24,000 daltons. Its ratio of basic to acidic amino acids is 1:3.7 and it induces a strong P-K reaction.

The immediate skin reaction to a purified Maiko powder allergen is positive in 100 % of konjac asthma patients, but negative in non-konjac asthma patients.

When the asthma was discovered, konjac making was an important industry in the Shimonita area and 40 % of the population were involved in producing konjac flour. Therefore, specific immunotherapy was developed because of the difficulty in changing jobs. When its efficacy was assessed, it was remarkably effective in 6/35 persons (17.1 %) and was effective in 18 (51.4 %) [3, 4].

After the konjac asthma was reported, companies began to improve the work environment. As a result of great effort, no one has developed konjac asthma since the late 1980s.

6.4.2 Sea Squirt Asthma

Sea squirt asthma is triggered by the inhalation of fluid from protochordate sea squirts that is adherent to cultured oysters. Cultivation of oysters in the Hiroshima region has been done for 400 years, and many people are engaged in the task of oyster husking. There were no reports before World War II, but employees complained of the onset of asthma associated with their work from around 1960. This asthma was reported in 1963 by Mitsui. In addition, detailed studies revealed that this type of asthma was induced by the inhalation of sea squirt components adherent to oysters. Such OA was named sea squirt asthma in 1966 [8].

The cause of its onset was improved farming methods that allowed farming of oysters in deep water since around 1952, so that sea squirts became attached to the oysters. Because work was often done under rough conditions with poor ventilation, workers inhaled a lot of sea squirt components.

From the investigation done at the time, the prevalence was 29 % (443 out of 1,528 people) and it reached 45.8 % in some towns. Because the industry has mostly

female employees, there is a majority of female patients. Half of the patients develop asthma within 5 years of starting work.

Separation and purification of sea squirt allergen was carried out and four allergens (H, Gi-rep, Ei-M, and DIIIa) were identified. Especially Gi-rep and Ei-M were effective for immunotherapy.

The skin reaction to sea squirt allergen is positive in 91.3 % of sea squirt asthma patients. When an allergen inhalation challenge test was done with sea squirt allergen, four out of nine sea squirt asthma patients were positive.

Initially immunotherapy was done with the crude allergen and the efficacy rate was high at about 75 %. However, immunotherapy with the crude allergen caused side effects such as induction of asthma or urticaria. In contrast, therapy with the purified allergen has a higher efficacy rate of 91.5 % and causes fewer side effects [8].

As a result of great effort to improve work environments, the number of patients has recently shown a significant decrease due to improvement of the work environment.

6.5 Emerging Occupational Asthma

6.5.1 High Molecular Weight Allergen

The pollen of vegetables and fruits or spores of mushrooms have become causative allergens along with the increase of greenhouse culture. Especially, shiitake mushroom, tomato, and strawberry were not recognized as causing asthma when open-field cultivation was common.

Furthermore, it was reported that a furniture craftsman developed asthma by inhalation of the dust of *Albizia falcataria* (Falcata wood), which is a broad-leafed tree and began to be imported recently.

6.5.2 Low Molecular Allergen

There have been reports about occupational allergy induced by ortho-phthalaldehyde, which is used as a disinfectant solution for fiberscopes. Cases of ortho-phthalaldehyde-induced anaphylaxis began to be reported from around 2006. For example, anaphylaxis has occurred immediately after observation by a laryngeal fiberscope. Since various new chemicals will be developed in the future, we always have to pay attention to allergies caused by chemicals.

6.6 The First Guidelines for Occupational Allergic Diseases in Japan

6.6.1 Necessity of Guideline

It is extremely important to identify occupational allergic disease cases in their early stages and take appropriate preventive measures for the social lives of patients. A guideline was released in Canada as long ago as 1998, while the American Thoracic Society (ATS) guidelines were published in 2005 [1]. In the same year, other guidelines were published in the United Kingdom. Other guidelines that described diagnosis and management in detail were published by The American College of Chest Physicians, while more guidelines were released in Spain (in 2006) and in Singapore (in 2008). These guidelines show wide recognition of the importance of occupational asthma.

In Japan, a large number of case reports have been accumulated on occupational allergic diseases. However, because of the occupational features of the diseases, only case reports have been presented in many cases. Although guidelines for individual allergic diseases have been published by allergologic associations, the descriptions of occupational factors are generally minimal. It is extremely important that the guideline for diagnosis and management of occupational allergic diseases have been published in 2013 for the first time in Japan [5] (Fig. 6.1).

This guideline is designed to assist healthcare professionals engaging in ordinary diagnosis and management of allergic diseases to practice early detection and treatment and early prevention in patients with allergic diseases induced and worsened by occupational factors. We hope that this guideline will be used for ordinary diagnosis and management of occupational allergic diseases and help the patients.

6.6.2 The Structure of the Guideline

The guideline has a basic structure in which clinical questions are set with reference to Medical Information Network Distribution Service (MINDS); statements by the committee are listed; recommendation grades and evidence levels are defined; descriptions and references are indicated. Also, legal aspects are written in full.

As for occupational allergic diseases, because new substances have been continually produced due to technical innovation and working environments have been changing due to changes in industrial structures, new OAs can always arise. We have revised the guideline in 2016 and will continue to revise it every 3 years, in order to maintein a high level of evidence for the guideline.

Fig. 6.1 First Japanese guideline for occupational allergic diseases 2014

6.7 Problems Related to Occupational Asthma in Japan

1. Due to advances in medication, achieving control of symptoms medically tends to be emphasized, and the search for causative allergens tends to be neglected. Thus, physicians often do not try to identify the causative allergen.
2. Poor surveillance data.
3. Poor regulation by law.
4. The work environment has improved in large enterprises under the direction of the government, but the smaller companies are not considered to have made enough effort in some cases.

6.8 Action Plans

1. Make surveillance system/checkup lung conditions of workers regularly.
2. Revise the guidelines of prevention and control of OA at stated periods.
3. OA information center and homepage are required.
4. Share information on OA in other countries.
5. Education about OA for workers, employers, healthcare providers, and government agencies.

References

1. Mapp CE, et al. Occupational asthma. Am J Respir Crit Care Med. 2005;172(3):280–305.
2. Shitijyo K. The study of Konnyaku asthma. Kitakannto Med J. 1951;1:29–30.
3. allergy, J.c.o.o, editor. Occupational asthma. Tokyo: Asakura Publishing Co., LTD; 1973.
4. allergy, J.c.o.o, editor. Occupational allergy. Tokyo: Buneido Publishing Co., LTD; 1983.
5. Committee for Japanese Guideline for Diagnosis and Management of Occupational Allergic Diseases. Japanese guideline for diagnosis and management of occupational allergic diseases 2013. Tokyo: Kyowa Kikaku; 2013 (in Japanese).
6. Dobashi K, et al. Japanese guideline for occupational allergic diseases 2014. Allergol Int. 2014;63(3):421–42.
7. Dobashi K. Occupational allergy. In: Fukuda T, editor. Sogo allergy-gaku. Tokyo: Nanzando; 2010.
8. Katsuya T. Hoya (Sea-Squirt) asthma (Japanese). Occup Environ Allergy. 2005;12:1–15.