

CASE REPORT

Occupational buckwheat allergy as a cause of allergic rhinitis, asthma, contact urticaria and anaphylaxis—An emerging problem in food-handling occupations?

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Email: soile.jungewelter@ttl.fi**Abstract**

Buckwheat is a known, though uncommon, allergen in occupational settings. It has recently gained popularity as healthy food and as an ingredient in gluten-free diets. We describe a series of six patient cases with occupational immediate allergy to buckwheat. Three cooks, two bakers, and a worker in a grocery store were occupationally exposed to buckwheat flour and developed immediate allergy to buckwheat, which was confirmed by skin prick testing and measurement of specific immunoglobulin E antibodies. Four of the patients were diagnosed with occupational asthma, four with occupational rhinitis, and two with occupational contact urticaria caused by buckwheat. Three of the six patients suffered anaphylaxis as consequence of their occupational buckwheat allergy after ingestion of food that contained buckwheat. The high rate of life-threatening reactions, together with a short exposure time to buckwheat before sensitization occurred in these cases, highlights the importance of a detailed occupational history and a high index of suspicion for occupational food allergens.

KEYWORDS

anaphylaxis, bakers, cooks, immediate allergy, immunoglobulin E, nasal provocation test, skin prick test

1 | INTRODUCTION

Common buckwheat (*Fagopyrum esculentum*) is a grain-like seed native to Central Asia. It is unrelated to wheat, does not contain gluten, and is therefore suitable for people with coeliac disease. Buckwheat flour may be used in products like gluten-free pastry, bread and other bakery products, noodles, pasta or pizza, crepes, blinis, Dutch pancakes (poffertjes), and beer. Buckwheat chaff is used as filling in pillows.¹ With globalization and the grown interest in ethnic foods, buckwheat considered as a healthy food has become popular.² Gluten-free diets, where buckwheat is a common ingredient, have recently gained popularity in Western countries.³ Consequently, gluten-free baking in professional bakeries has become more common. Occupational exposure to buckwheat is therefore likely to increase in bakeries and other trades involved in handling and processing food.

Buckwheat is a known food allergen, and a cause of immunoglobulin E (IgE)-mediated allergy.⁴ We report six patients with occupationally related immediate allergy to buckwheat examined at our clinic within a single year, 2019. Three of our patients had suffered anaphylaxis caused by ingested buckwheat as a sequel of their occupational allergy to buckwheat.

2 | CASE REPORTS

The occupational medicine clinic at the Finnish Institute of Occupational Health is a tertiary referral center that evaluates patients with suspected occupational diseases from throughout the country. We describe six patients with occupational immediate allergy to buckwheat who presented for examinations at our clinic during 2019. The details of the patients' histories, results of their clinical examinations,

TABLE 1 Symptoms at workplace and after ingestion of buckwheat products, and results of measurements of serum immunoglobulin E (IgE), skin prick tests, open skin application tests, lung function tests, specific inhalation challenge tests, and nasal provocation tests

Patient case number	1	2	3	4	5	6
Age (years)	25	43	23	35	27	42
Occupation	Cook	Worker in a grocery store	Cook	Cook	Baker	Baker in a gluten-free bakery
Exposure to buckwheat before symptoms occurred	1½ years	3½ years	2 Months	1 Year	5 Years	2 Years
Work tasks with exposure to buckwheat	Baking buckwheat dough	Shelving buckwheat flour packages that leaked flour	Baking buckwheat bread, breading fish pins and vegetable balls	Preparing buckwheat blinis	Baking buckwheat dough	Baking buckwheat dough
Symptoms at work associated with inhalation exposure to buckwheat	Recurrent watery rhinitis, cough, and dyspnea	Recurrent watery rhinitis, cough, and dyspnea contact urticaria	Recurrent watery rhinitis, cough, and dyspnea	Recurrent watery rhinitis, cough, and dyspnea	Recurrent watery rhinitis, cough, dyspnea and contact urticaria	Recurrent watery rhinitis, cough, dyspnea and contact urticaria
Symptoms of anaphylaxis associated with ingestion of buckwheat	Nausea, vomiting, strong dyspnea, urticaria, and itching of the throat after eating buckwheat crepes	None	Itching of whole body, swelling of lips, dysphagia, and hoarseness after eating buckwheat bread	Dyspnea, itching of eyes, face, and hands and swelling of eyelids after preparing buckwheat blinis (under former employer)	None	None
Regular asthma medication	Budesonide 200 µg	Budesonide/formoterol 160/4 µg, montelukast 10 mg	Salbutamol 200 µg for symptom relief if needed	Fluticasone furoate/vilanterol 92/22 µg, montelukast 10 mg	Ciclesonide 160 µg	Ciclesonide 160 µg
Serum IgE measurements (kU/l) ^a						
Serum total IgE	13	569	175	18	703	162
Buckwheat flour IgE	0.92	>100	4.6	2.4	74	0.63
IgE to other flours	Wheat flour 0.13	Wheat flour 1.5	Wheat flour 0.65, rye flour 0.70, oat flour 0.68	Wheat flour, rye flour, barley flour <0.1	Rice flour 4.9, barley flour 3.4, rye flour 2.6, wheat flour 2.2, soy flour 1.8, oat flour 1.8	Rice flour <0.1
Skin prick tests (wheal diameter in mm)						
Histamine 10 mg/ml	8	6	6	7	5	6
Diluent control	Negative	2	Negative	Negative	2	Negative
Work-related allergens ^b	Buckwheat flour 10, wheat flour 3,	Buckwheat flour 11, barley flour 4,	Buckwheat flour 11, wheat flour 4, oat	Wheat flour 4, barley flour 4, rye flour 3,	Wheat flour 5, barley flour 7, rye flour 6, oat flour 4, soy	Negative (buckwheat flour not tested).

TABLE 1 (Continued)

Patient case number	1	2	3	4	5	6
	garlic 5, almond 7, hazel nut 4	wheat flour 5, hazel nut 4	flour 4, paprika 4, coriander 4, garlic 6, almond 7, hazel nut 7, clove 4, fenugreek 6	soy flour 3, paprika 4, almond 7, fenugreek 3, hazel nut 6	flour 4, rice flour 4, lupin flour 5, psyllium 5	
Patient's own materials from the workplace	NT	Buckwheat flour 11, wheat flour 6, barley flour 8	NT	Cornmeal 4, wheat flour 3, rye flour 4	Rice flour 4	Buckwheat flour 4
Common aeroallergens ^c	Negative	Timothy 4, horse 3, alder 6, timothy 6, dog 4, cat 7	Birch 11, alder 6, timothy 5, cat 9	Negative	Negative	Birch 5, alder 3, timothy 15, horse 4, dog 5, cat 7, Dermatophagoides pteronyssinus 6, Dermatophagoides farinae 4
Open skin application tests						
20, 40, 60 min	NT	Buckwheat and wheat flour positive	NT	NT	Buckwheat, oat and rice flour positive, soy flour and psyllium negative	Buckwheat flour negative
Nasal provocation test (bilaterally)						
Control with lactose powder 0.03 g	NT	NT	NT	Negative	NT	Negative
Nasal findings after provocation with flours 0.03–0.04 g	NT	NT	NT	Positive for rye flour	NT	Buckwheat flour positive; VAS increase from 2 to 4, rhinorrhea 1.22 g, no relevant rhinometric changes
Lung function tests						
Spirometry	Mild reversible obstruction	Mild reversible obstruction	Mild reversible obstruction	Normal	Normal	Normal
FeNO _{ex} (ppb)	29.5	19.5	13.0	11	142.5	17.0
Bronchial hyperresponsiveness ^d	Mild, PD ₁₅ FEV ₁ 0.706 mg	Moderate, PD ₁₅ FEV ₁ 0.164 mg	Normal, PD ₂₀ FEV ₁ > 2600 µg	Moderate, PD ₂₀ FEV ₁ 239 µg	Normal, PD ₂₀ FEV ₁ > 2600 µg	Normal, PD ₂₀ FEV ₁ > 2600 µg
PEF monitoring at workplace	Declining while handling buckwheat flour on workdays	NT	No exposure to buckwheat during monitoring	NT	NT	NT
Specific inhalation challenge tests	NT	Negative for wheat flour	NT	Positive for rye flour	Positive for rice flour	Negative for buckwheat flour and for potato fiber

(Continues)

TABLE 1 (Continued)

Patient case number	1	2	3	4	5	6
Diagnosis of occupational disease (cause)	Occupational asthma (buckwheat), occupational anaphylaxis (buckwheat)	Occupational asthma (buckwheat), occupational asthma (buckwheat), occupational contact urticaria (buckwheat and wheat)	Occupational rhinitis (buckwheat), occupational asthma (buckwheat), occupational anaphylaxis (buckwheat)	Occupational rhinitis (buckwheat), occupational asthma (buckwheat), occupational anaphylaxis (buckwheat), occupational rhinitis (rye), occupational asthma (rye)	Occupational rhinitis (buckwheat), occupational asthma (buckwheat and rice), occupational contact urticaria (buckwheat, rice, oat)	Occupational rhinitis (buckwheat), contact urticaria to buckwheat suspected but not confirmed

Note: Serum IgE >0.35 kU/l was considered elevated; only positive skin prick test reactions to allergens are shown; all patients were female.

Abbreviations: FeNO_{ex}, fractional exhaled nitric oxide (normal <25 ppb); FEV₁, forced expiratory volume in 1 s; PD₁₅FEV₁, the dose of histamine that caused a 15% decrease in forced expiratory volume in 1 s; PD₂₀FEV₁, the dose of metacholine that caused a 20% decrease in forced expiratory volume in 1 s; PEF, peak expiratory flow; ppb, parts per billion; NT, not tested; VAS, visual analog scale (range: 0–10).

^aImmuno-CAP, Phadia AB.

^bIn-house test substances.

^cCommercial test substances (ALK-Abelló Nordic A/S).

^dPD₁₅FEV₁, PD₂₀FEV₁.

and diagnoses are summarized in Table 1. All six were women. Two of our patients were bakers, three were cooks, and one worked in a grocery store where she handled packages of buckwheat flour. According to this patient, the packages leaked some flour, which spread locally, in her breathing zone, on her arms, and on the nearby shelves and other surfaces. All patients had used disposable rubber gloves as hand protection, but none had used respiratory protection at work. None of the patients had a previous history of symptoms associated with ingestion of buckwheat before their occupational exposure. Severe symptoms of anaphylaxis with typical skin features, respiratory symptoms or angioedema (Table 1) occurred after three of our patients (Patient 1, 3, and 4) consumed buckwheat-containing crepes, blinis, or bread subsequent to their occupational exposure to buckwheat. These patients were treated in emergency clinics with intramuscular epinephrine, intravenous cortisone, and oral antihistamines. All patients experienced rhinitis, cough, and dyspnea in association with their occupational exposure to buckwheat. Three also reported symptoms suggestive of contact urticaria from skin contact to buckwheat flour. In one patient (Patient 4), exposure to buckwheat had occurred in her previous work, and during that time she also had an episode of anaphylaxis when eating blinis which contained buckwheat at her workplace. She was examined at our clinic for symptoms caused by rye flour in her present work, where there was no exposure to buckwheat. Because of her history of work-related respiratory symptoms and anaphylaxis in her previous work in a blini-restaurant, we also tested her for buckwheat allergy.

Immediate allergy to buckwheat was diagnosed based on skin prick testing in four patients, and on serum-specific buckwheat IgE >0.35 kU/l in two patients (Table 1). We performed skin prick tests according to the European guideline⁵ with a series of common aeroallergens, in-house test substances selected on individual basis according to the patient's occupational exposure, and the patient's own materials from the workplace. Specific IgE to buckwheat varied between 0.63 and >100 kU/l in our patients. The patients with a history of buckwheat anaphylaxis had only moderately elevated buckwheat IgE, in all three of them below 5 kU/l. Total IgE in these patients varied between 13 and 703 kU/l.

Diagnosis of occupational rhinitis was based on history of exposure and symptoms at work, sensitization in all patients, and a positive nasal provocation test with the patient's own buckwheat flour (Patient 6) or with rye flour (Patient 4) and negative control provocation. A quantity of 0.02 g buckwheat flour or 0.03 g rye flour was set bilaterally on the nasal mucosa. Before the provocation, and after 20 min, we measured nasal volume change (2–6 cm) with acoustic rhinometry, nasal inspiratory resistance change with anterior rhinomanometry, and patients' blown nasal secretion weight.⁶ Patients assessed their rhinitis symptoms with a visual analog scale.⁷ In three patients (Patients 2, 3, and 5), the diagnosis was based on medical history and sensitization.

The diagnosis of occupational asthma caused by buckwheat was based on medical history, sensitization test results, and peak expiratory flow (PEF) monitoring at the workplace. Lower PEF values on workdays were seen in Patient 1, while diagnosis was made solely on history and sensitization in Patients 2, 3, and 5.

Diagnosis of occupational asthma caused by other exposures than buckwheat (rye and rice flours) was based on history of exposure and symptoms at work, sensitization testing, and a positive specific inhalation challenge test with rye flour dust (Patient 4) and with rice flour (Patient 5) for 45 min in a challenge chamber, and measuring forced expiratory volume in 1 s, fractional exhaled nitric oxide, and the methacholine dose that caused a 20% decrease in forced expiratory volume in 1 s before the challenge test and afterwards.

Diagnosis of occupational anaphylaxis to buckwheat was based on history of occupational exposure to buckwheat, symptoms consistent with anaphylaxis in association with ingestion of buckwheat, and sensitization indicated by skin prick test positivity or specific IgE to buckwheat (Patients 1, 3, and 4; Table 1).⁸

The three patients (Patients 2, 5, and 6; Table 1) with suspected contact urticaria underwent open skin application test. Buckwheat flour mixed with water was applied on a 5 × 5 cm area of healthy skin on the forearm. The test area was inspected at 20 min, and if the result was negative, the application was repeated in the same area for another 20 min. The test area was then reinspected and if it was negative, the application was repeated for third time for another 20 min and then reinspected. A positive open skin application test reaction was defined as one or several urticarial wheals appearing on the test area at 20, 40, or 60 min. Open skin application test with buckwheat was positive in two patients and confirmed their diagnoses of occupational contact urticaria. In the third one, the diagnosis of contact urticaria was considered possible but could not be confirmed since the open skin application test remained negative and the clinical characteristics of her previous work-related dermatitis were not documented at a doctor's office.

As measures to prevent further occupational allergen exposure and the persistent symptoms of asthma and rhinitis caused by allergen exposure, all our patients had to change work tasks or work site. Patient 1 still had persistent asthma symptoms 6 months after the diagnosis, and further work task changes were planned at her worksite. Patient 2 changed her worksite and has since been symptom-free. Patient 3 continued working in the same restaurant but avoided handling buckwheat flour. Patient 4 who had occupational rhinitis and asthma caused by rye flour and a previous occupational anaphylaxis to buckwheat flour moved to another work environment because of the symptoms caused by rye flour. Patient 5 was moved to office work under the same employer. Patient 6 continued her work with altered work tasks to avoid contact with buckwheat flour and products made from it.

3 | DISCUSSION

IgE-mediated allergy to foods, such as cereals, vegetables, fruits, seafood, and meat may cause occupational allergic rhinitis, asthma, contact urticaria, and protein contact dermatitis in food industry workers and other food handlers.^{9–16} Occupational exposure to buckwheat has previously been reported to cause occupational allergic asthma, rhinitis, and contact urticaria in occupations involved in food handling, such as bakers, cooks, noodle makers, workers

in creperies, pancake and noodle shops, and in the food industry.^{3,4,17–21}

Nonoccupational immediate allergy to buckwheat is commonly reported in Eastern Asia^{22–24} as well as in Europe, North America, and Australia, where it is considered a rare food allergen, though possibly with increasing importance.^{3,25–27} Allergic reactions to buckwheat often occur after consumption of specific regional foods.^{28–30} Buckwheat may also be a hidden or unsuspected food allergen.^{29,31} Pillows filled with buckwheat chaff have reportedly caused asthma exacerbations by inhalation of small amounts of buckwheat flour present in the pillows.^{1,27}

Buckwheat is a very potent immediate-hypersensitivity allergen which may induce allergic symptoms through ingestion, inhalation, and skin contact. Sensitization by inhalation can cause severe allergic reactions associated with usage of buckwheat pillows, and subsequent anaphylaxis when ingesting buckwheat-containing food.^{32,33} Buckwheat allergy is a common cause of anaphylaxis.^{23,24,34} In children with buckwheat allergy, as many as 65.4% were reported to have a history of anaphylaxis.³⁵ In line with the literature, three of our six patients with occupational buckwheat allergy who probably had been sensitized through inhalation exposure at work had suffered anaphylaxis caused by ingested buckwheat.

One of the patients with occupational rhinitis caused by buckwheat was diagnosed by nasal provocation test, which to our knowledge has not been previously reported. Nasal provocation test has been established as an international standard for evaluating occupational rhinitis.^{7,36,37} It is noteworthy that in general, occupational rhinitis seems to be more common than occupational asthma.³⁸ To prevent more severe allergic reactions, it is important to notice early symptoms that indicate sensitization.

The identified main allergens in buckwheat include Fag e 1 (buckwheat legumin), Fag e 2 (2S albumin) and Fag e 3, a terminal fragment of a vicilin-like protein, while other known buckwheat allergens include Fag e 4, a hevein-like antimicrobial peptide with potential cross-reactivity to latex, and Fag e 5, a vicilin-like protein.^{39–46} Concomitant sensitization to Fag e 1, Fag e 2, and Fag e 5, has been suggested to predict symptomatic buckwheat allergy.⁴⁷ On the other hand, Fag e 3-IgE has been reported to predict oral food challenge results and anaphylaxis.⁴⁸ Cross-reactivity between buckwheat and several other allergens, including natural rubber latex, poppy seed, and coconut has been described.^{49–52} Allergies to other food and inhaled allergens are common in patients allergic to buckwheat, and only a minority are sensitized to buckwheat only.^{30,45} In line with the previous reports, concomitant allergy to other flours and foods was common in our buckwheat-allergic patients. Four had an occupationally relevant allergy to wheat flour. Allergy to pollen and animal dander was seen in three patients, whereas three buckwheat-allergic patients were uniformly negative to the test series of common aeroallergens.

Previously, the usefulness of buckwheat IgE has been critically evaluated,^{53,54} and a study on patients aged 2–16 years found skin prick test to be superior to specific IgE in diagnosing buckwheat allergy.⁴⁸ This seemed to be the case in our patients as well. Skin prick test with buckwheat produced relatively strong reactions, with

a reaction diameter of 10–11 mm in the first three of our patients, two of whom had a history of anaphylaxis. As a safety measure, we then refrained from skin prick testing the following three patients with buckwheat flour and instead, relied on serum-specific IgE measurements. However, in Patient 6, buckwheat IgE was only slightly above the cut-off for a positive result. We used the patient's own buckwheat flour sample from the worksite for skin prick testing to confirm immediate allergy to buckwheat. The buckwheat IgE level varied considerably in our patients, from 0.63 to >100 kU/l, which is in accordance with previous findings.⁴⁵

Noteworthy is that our patients with a history of buckwheat anaphylaxis had only moderately elevated buckwheat IgE, in all three of them below 5 kU/l. As is evident, the level of specific IgE does not directly indicate the severity of the patient's allergic response and should not be interpreted as such. As discussed elsewhere, more precise in vitro diagnostic tools based on allergen components of buckwheat are needed.^{44,47} These would be useful in diagnosing buckwheat allergy in cases where skin prick testing is not feasible or must be refrained from performing. We suggest that the safety of respiratory provocation tests and skin prick tests with buckwheat flour should be carefully weighed on an individual basis.

Planning and implementing measures to prevent exposure to buckwheat as well as to other potentially harmful workplace substances is the employer's responsibility. Prevention combines four elements: systemic, technical, organizational, and personal measures. Although product substitution generally represents the first and most desirable means of exposure prevention, it may not be applicable in preparation of buckwheat-based food and baking. Systemic preventive measures may include easy-to-clean surfaces and sufficient cleaning of workplaces to minimize exposure to flour dust. Technical measures might include, for example, use of local- or area-based exhaust ventilation and dust removal via air filtration. Technical measures need to be planned according to the nature of baking work and the requirements of individual workplaces.⁵⁵ Importantly, organizational measures should include health and safety information dissemination to workers and training to promote safe working habits. Personal protective measures are focused on clothing, gloves, and respiratory protection, which must be made available at the workplace with workers instructed in their proper use. However, wearing respiratory protection with particulate filters for allergen protection can be difficult due to the working environment, where fine dusts, high temperatures, humidity, physical burden, or food hygiene regulations may all be problematic for their use. Regular workplace visits by occupational health services, preferably in co-operation with a safety engineer, may enable timely detection of an increased risk of exposure and introduction of targeted prevention measures, and may promote awareness of work-related health risks and the methods to control them.

In conclusion, buckwheat is a potent allergen in food and in occupational settings, and may cause allergic rhinitis, asthma, contact urticaria, and severe anaphylactic reactions. Recognition of buckwheat as an occupational and consumer allergen may be gaining importance because of the increasing popularity of gluten-free diets and of buckwheat as a health food, which in turn may lead to increased exposure to buckwheat flour in food-handling occupations,

such as bakers, cooks, and workers in food manufacture and preparation. Early identification of work-related symptoms is important. The possibility of buckwheat allergy should be kept in mind when examining workers from food-handling occupations with symptoms suggestive of immediate (Type I) allergy.

CONFLICTS OF INTEREST

All authors declare that there are no conflicts of interest.

DISCLOSURE BY AJIM EDITOR OF RECORD

John Meyer declares that he has no conflict of interest in the review and publication decision regarding this article.

AUTHOR CONTRIBUTIONS

All authors participated in drafting the work or revising it critically for important intellectual content and also participated in the final approval of the version to be published.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

ETHICS STATEMENT

All patients gave their oral informed consent for case reporting.

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