

## Baker's asthma: An allergic occupational disease

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### Abstract

Baker's asthma is an allergic occupational disease, caused most often from wheat flour inhalation. Herewith we present a case of new-onset work-related asthma in a 27-year-old patient who works in a pizzeria. The patient with nasal congestion, sneezing over and over, runny nose, dyspnea and wheezing, was recently followed up in our clinic. He reported a history of five years with these complaints, or three years after he began to work in a pizzeria. These complaints were present especially in the morning, when he was working. He was free of symptoms when he is not working. Skin prick tests and specific IgE measurements for aeroallergens and trofoallergenes were positive for wheat and wheat flour. Spirometry showed a moderate airflow obstruction. He was diagnosed with baker's asthma. The treatment with inhaled corticosteroids, intranasal corticosteroids and antihistamines was recommended.

## Introduction

Baker's asthma is an allergic occupational disease, caused most often from wheat flour inhalation. Baker's asthma is one of the most common forms of occupational asthma, which affects 1-10% of bakery workers (1). It is still a serious occupationally related obstructive airway disease worldwide.

In 1700 Bernardo Ramazzini described respiratory symptoms among bakers caused by exposure to flour dust. However, there are anecdotal references from antiquity describing how Roman slaves working in bakeries protected themselves by using cloth as a primitive respirator to cover their faces because their breathing suffered from inhaling flour (2).

The incidence of baker's asthma among young bakers has been reported to range from 0.3-2.4 cases per 1000 person-years, and an increasing number of asthma cases are being reported among supermarket bakery workers (3). Sixty percent to 70% of bakers with rhinitis or asthma have increased specific IgE levels to wheat, rye, or both flour extracts (4). In France, baker's asthma was ranked the first among cases reported to the national observatory of occupational asthma (5).

The most common cause of baker's asthma is wheat flour sensitization. The specific IgE antibodies most often found in Baker's asthma are against cereal flours such as wheat, rye or barley (table 1).

**Table 1. Allergens associated with baker's asthma and rhinitis**

<b>Cereal flours</b>	Wheat
	Rye
	Barley
	Hops
	Rice
	Maize
<b>Non-cereal flours</b>	Buckwheat
	Soybean flour
<b>Additives/Enzymes</b>	Amylase
	Cellulase
	Xylanase
	Papain, other proteases
	Glucose, Oxidase
<b>Nuts</b>	Almonds, Hazelnuts
<b>Color</b>	Carmine red
<b>Egg powder</b>	
<b>Milk powder</b>	
<b>Insects</b>	Flour beetle ( <i>tribolum confusum</i> )
	Flour moth ( <i>ephestia Kuenhilla</i> )
	Cockroach ( <i>Blatella spp</i> )
	Granary Weevill ( <i>Sitophilus granaris</i> )
<b>Moulds</b>	Alternaria, Aspergillus
<b>Sesame seeds</b>	

Since the 1970s a variety of enzymes can be added to flour in order to enhance the baking process. Although in minute quantities (typically mg/kg flour), they can cause sensitization and baker's asthma (table 1). The most common enzyme is an amylase of fungal origin. The use of a amylase varies between countries and bakeries; in some enterprises the amylase is routinely added to the flour, in others it is used for some

products only, and in some it is not used at all (6). Other potential sensitizers can be moulds, yeast, eggs, sesame seeds, nuts, and insects, for example (table 1). The occurrence of sensitization to these allergens is less well known than the cases caused by cereal flours or enzymes, and seems to be of marginal importance to the burden of disease in bakers. However, they should be kept in mind in the clinical setting if no sensitization to common

bakery allergens is found. Wheat proteins are subdivided in two fractions: the water/salt-soluble (including albumins and globulins)

and the water/ salt insoluble gluten (containing gliadins and glutenins). The latter represent about

**Table 2. The function of main allergens from wheat flour associated with baker's asthma**

Protein	S.N	AA	Cys	Function
<b>Acyl-CoA-Oxydase</b>	ACX	644	11	Catalyzes the desaturation of long-chain Acyl-CoAs to 2-trans-enoyl-CoAs
<b>Fructose biphosphate aldolase</b>	FBA	358	7	Fructose-biphosphate aldolase activity
<b>Glycerinaldehyde-3-phosphate dehydrogenases</b>	GAPDH	496	13	Important as a means for generating NADPH for biosynthetic reactions
<b>Thioredoxin</b>	TRX	125	2	Participates in various redox reactions through the reversible oxidation of the active center dithiol to disulfide
<b>Triosephosphate isomerase</b>	TPIS	253	4	Triose-phosphate isomerase activity
<b>Serpin(Serin proteinase inhibitor)</b>	WSZ	398	1	Molecular function:Serine type endopeptidase inhibitor activity
<b>Peroxidase</b>	WSP	332	8	Removal of H <sub>2</sub> O <sub>2</sub> , biosynthesis and degradation of lignin, response to environmental stresses
<b>Monomeric alpha-amylase inhibitor</b>	WMAI	121	10	Inhibits exo-alpha-amylase
<b>Dimeric alpha-amylase inhibitor</b>	WDAI	124	10	Inhibits exo-alpha-amylase
<b>Tetrameric alpha-amylase inhibitor</b>	WTAI	119-143	10	Inhibits exo-alpha-amylase
<b>Agglutinine</b>	WGA	186	32	Carbohydrate binding protein that selectively recognizes sialic acid and N-acetylglucosaminyl sugar residues
<b>Lipid transfer protein</b>	LTP	90	8	Enhances the in vitro transfer of phospholipids between membranes and can bind acyl chains
<b>Chymotripsin inhibitor (serine proteinase inhibitor)</b>	WSCI	84	0	Inhibits chymotripsine

80% of all wheat proteins (7). It was assumed a relation between protein solubility and the various clinical manifestations of wheat allergy (8):

- Salt-insoluble proteins might be resistant to digestion during the passage through the stomach and intestines and might cause specific symptoms of food allergy.

- Salt-soluble proteins can be reabsorbed in the respiratory tract, eliciting IgE-mediated allergic reactions. Among bakers the whole flour particles are deposited on the mucosa of bronchi, where the allergens most readily dissolve in bronchial lining fluids.

- Water-soluble proteins can reach mast cells and initiate IgE-mediated reactions.

In addition, however, some insoluble allergens on

the surface of the foreign particles are likely to trigger IgE reactions; either because of direct contact with local mast cells or after enzymes (particularly proteases) or detergents contained in alveolar surfactant or present on the mucosa permits access of allergens that are less readily extractable. Thus far, only few flour allergens have been described at the molecular level:  $\alpha$ -amylase inhibitors, acyl-CoA oxidase and fructose-bisphosphate aldolase, a wheat glycoprotein with peroxidase activity, triose-phosphate isomerase (TPIS), and recently thioredoxin, all of which belong to the water/ salt-soluble protein fraction. The water-soluble albumin fractions were believed to represent the most relevant allergens

Current immunological and clinical data point to the  $\alpha$ -amylase/trypsin inhibitor family as the main culprit of baker's asthma. The cereal  $\alpha$ -amylase/trypsin inhibitor subunits are 12-16-kDa polypeptides with 4-5 intrachain disulphide bridges that are essential for their inhibitory activity. Members of the inhibitor family are restricted to the seed storage tissue (endosperm), and seem to have a common fold (4-5  $\alpha$ -helices and a short antiparallel  $\beta$ -sheet).

Amino acid sequence identity between members of the family ranges from around 30% to 95%. Based on their degree of aggregation, 3 types of  $\alpha$ -amylase inhibitors have been identified in wheat flour, namely, monomeric (1 subunit), homodimeric (2 identical subunits), and heterotetrameric (3 different subunits, one of them in two copies) (9). Trypsin inhibitors belong to the monomeric type. Additionally, the interaction between wheat inhibitors and the  $\alpha$ -amylase from *Dermatophagoides pteronyssinus* (Der p 4 allergen) suggests that wheat/mite allergen complexes might be present in house-dust mite-infected flours (10).

Besides the salt-soluble allergens discussed above, several of the major water/salt-insoluble wheat flour proteins (prolamins) also appear to be implicated in baker's asthma.

The subunits of the gliadin family are the  $\alpha\beta$ -,  $\gamma$ -, and  $\omega$ -gliadins based on their electrophoresis mobility. The different gliadin subunits share amino acid sequence and 3-dimensional structure homologies (11).

*Gliadins can be considered possible allergens associated with baker's asthma. In the case of negative results on routine IgE testing with wheat extract, diagnostic tests with water-insoluble allergens, such as gliadins, should be considered.*

Baker's asthma is often preceded by rhinitis, and skin symptoms are often concomitant.

Frequently there is atopy and sensitization to flour and/or enzyme (for example, an amylase).

Immediate hypersensitivity reactions to the ingestion of wheat are not very common and can be divided into two types:

1. Typical IgE-mediated food allergy, in which patients display a variety of clinical symptoms ranging from urticaria/angioedema to vomiting and anaphylaxis, and, sometimes, atopic dermatitis;
2. Wheat-dependent exercise-induced anaphylaxis

(WDEIA), which is a well-defined clinical picture commonly associated with sensitization to a major grain allergen,  $\omega$ 5-gliadin (Tri a 19), whose IgE-binding epitopes have been identified. Measurement of serum IgE antibodies to recombinant  $\omega$ 5-gliadin has been proposed as a marker of WDEIA (12). Wheat proteins have also been shown to induce contact urticaria (13) and protein contact dermatitis (14). Cereals form part of the Poaceae family, and there is wide allergenic cross-reactivity between wheat flour and grass pollen (15).

Current diagnostic tests for Baker's asthma include; history, physical examination, skin prick tests, specific IgE measurements, Specific Inhalation Challenge, and bronchial provocation test with methacoline.

The treatment of baker's asthma, as the other forms of asthma consists in the causative agent eviction, drug therapy, and allergen-specific immunotherapy (but other studies are necessary to prove the efficacy of specific immunotherapy with wheat in a patient with baker's asthma).

### Case description

A 27-year-old man complaints of nasal congestion, sneezing over and over especially in the morning, runny nose, dyspnea during the night and at work, and wheezing, was recently followed up to our clinic. He has five years with these symptoms, which began after three years that he began working in the pizzeria. At the beginning, for two years he had only runny nose, sneezing and nasal congestion. He was treated several times with antihistamines. The symptoms were present during all the year. The patient reported that the complaints were commonly present when he was working in the pizzeria. He is free of symptoms when he is not working in the pizzeria. His symptoms gradually got worse. Actually, the patient has nasal congestion, sneezing, dry cough, wheezing and dyspnea. The patient has been afebrile. On chest examination sibilances and sonore ronchi were present. The hematological and biochemical profile was normal. Taking into consideration his medical history, we made skin prick tests and specific IgE measurements for aeroallergens and trophoallergenes. The results were the following: skin prick tests for aeroallergens were positive for plantago, helianthus ann, and four cereals mix; skin prick tests for trofoallergenes were positive for wheat and wheat flour; and also prick by prick

with wheat flour resulted positive. The spirometry showed a moderate airflow obstruction, but methacoline test provocation was positive.

The recommended treatment was with inhaled/intranasal corticosteroids and antihistamines. A month after the treatment, a relevant improvement of his symptoms and on spirometry was observed. Taking into consideration his medical history: profession, respiratory symptoms during his work, disappearance of symptoms out of his workplace, positivity of skin tests, spirometry examinations, and results of treatments, Baker's asthma diagnosis was considered.

Our recommendation for the patient was to change his profession; with no wheat flour inhalation. We believe that the eviction of wheat flour inhalation results in clinical recovery of this patient.

### Conclusion

Baker's asthma is an important allergic occupational disease, most often caused by wheat flour inhalation. In our case, after the diagnosis, the eviction of the causative agent and treatment (inhaled/intranasal corticosteroids and antihistamines) resulted in a significant improvement of the symptoms.

### References

- Houba R, Doekes G, Heederick DJJ. Occupational respiratory allergy in bakery workers: a review of the literature. *Am J Ind Med* 1998; 34:529-546.
- Brisman J. Baker's asthma. *Occup Environ Med* 2002; 59:498-502.
- Rémen T, Coevoet V, Acouetey DS, Guéant JL, Guéant- Rodriguez RM, Paris C, Zmirou-Navier D. Early incidence of occupational asthma among young bakers, pastry-makers and hairdressers: design of a retrospective cohort study. *BMC Public Health* 2010; 10:206.
- Baur X, Degens PO, Sander I. Baker's asthma: still among the most frequent occupational respiratory disorders. *J Allergy Clin Immunol* 1998; 102: 984-997.
- Palacin A, Quirce S, Armentia A, et al. Wheat lipid transfer protein is a major allergen associated with baker's asthma. *J Allergy Clin Immunol* 2007; 120:1132-1138.
- Brisman J. Baker's asthma. *Occup Environ Med* 2002; 59:498-502.
- Bietz JA, Huebner FR, Sanderson JE, Wall JS. Wheat gliadin homology revealed through N-terminal amino acid sequence analysis. *Cereal Chem* 1977; 54:1070-83.
- Mittag D, Niggemann B, Sander I, et al. Immunoglobulin E-reactivity of wheat-allergic subjects (baker's asthma, food allergy, wheat-dependent, exercise-induced anaphylaxis) to wheat protein fractions with different solubility and digestibility. *Mol Nutr Food Res* 2004; 48:380-389.
- Wheat Allergens Associated With Baker's Asthma G Salcedo,1 S Quirce,2 A Diaz-Perales1 *J Invest Allergol Clin Immunol* 2011; 21:81-92.
- Sanchez-Monge R, Garcia-Casado G, Barber D, Salcedo G. Interaction of allergens from house dust mite and from cereals: Dermatophagoides pteronyssinus  $\alpha$ -amylase (Der p 4) and wheat and rye  $\alpha$ -amylase inhibitors. *Allergy* 1996; 51:176-180.
- Palosuo K, Varjonen E, Kekki OM, Klemola T, Kalkkinen N, Alenius H, et al. Wheat omega-5 gliadin is a major allergen in children with immediate allergy to ingested wheat. *J Allergy Clin Immunol* 2001; 108:634-638.
- Morita E, Matsuo H, Mihara S, Morimoto K, Savage AW, Tatham AS. Fast omega-gliadin is a major allergen in wheat-dependent exercise-induced anaphylaxis. *J Dermatol Sci* 2003; 33:99-104.
- Laurière M, Pecquet C, Bouchez-Mahiout I, Snégaroff J, Bayrou O, Raison- Peyron N, Vigan M. Hydrolysed wheat proteins present in cosmetics can induce immediate hypersensitivities. *Contact Dermatitis* 2006; 54:283-289.
- Matsuo H, Uemura M, Yorozuya M, Adachi A, Morita E. Identification of IgE-reactive proteins in patients with wheat protein contact dermatitis. *Contact Dermatitis* 2010; 63:23-30.
- Sander I, Raulf-Heimsoth M, Düser M, Flagge A, Czuppon AB, Baur X. Differentiation between cosensitization and crossreactivity in wheat flour and grass pollen-sensitized subjects. *Int Arch Allergy Immunol* 1997; 112:378-385.