

Baker's asthma

Andrew Brant

Purpose of review

Baker's asthma is one of the leading causes of occupational asthma and this review describes recent developments in the field.

Recent findings

The location of bakery production has undergone change and, subsequently, so has the location of baker's asthma. Innovations in the baking industry have also led to new, potentially allergenic, ingredients. A new family of cereal allergens has been identified, including wheat thioredoxin hb (Tri a25). New enzymes are being added to bread that may have allergic potential. The relationship of specific sensitization and baker's asthma has been confirmed in further studies. Measuring specific sensitization to bakery allergens is an essential part of making the diagnosis but there is a lack of standardization of allergen tests. Advancements are being made in the measurement of airborne allergens through the Measurement of Occupational Allergen Exposure project and the development of novel measurement techniques. This will enable better exposure-response relationships and more accurate risk assessment.

Summary

Progress is being made to better identify bakery allergens and measure exposures accurately. Changes in the location of bread production and new allergens mean that the distribution and determinants of baker's asthma are changing.

Keywords

baker's asthma, flour, fungal alpha-amylase, wheat

Introduction

Baker's asthma is one of the most common causes of occupational asthma, and annual incidence of disease ranges between one and 10 cases per 1000 bakery workers [1,2]. Any worker who is exposed to bakery allergens can develop the disease (including confectioners, flour miller and food processors), not only bakers. The main agents that cause baker's asthma are cereal flours (wheat, rye and barley) and enzymes, but new allergens are being used. Baker's asthma is mediated through the classical IgE allergic pathway, and accurate measurement of sensitization to bakery allergens is essential for diagnosis.

Epidemiology

Reports from different countries have confirmed that baker's asthma is one of the leading causes of occupational asthma. In Great Britain, the most recent findings from the Surveillance of Work-Related and Occupational Respiratory Disease (SWORD) have identified baker's asthma as the second most common cause of occupational asthma [3]. The Norwegian National Insurance Scheme contains a comprehensive database for occupational disease. Recent analysis of the data shows that bakery allergens were the second most common cause of occupational asthma, second only to aluminium, where the industry is undergoing an active screening programme [4]. The incidence of occupational asthma in male bakers/confectioners was 2.46 per 1000 person-years, and in females it was 1.00 per 1000 person-years. In France, baker's asthma is the most common cause of occupational asthma [5], and a population-based incident case-control study from Finland investigating work-related respiratory disease found that bakers and food processors had the strongest association of work and asthma [6].

Many supermarkets make bread in-store from raw ingredients in circumstances similar to the traditional craft bakery. As a result, a large part of the bakery workforce is based in supermarkets in many countries. They are a group of workers not previously identified to be at risk of disease. The growth of supermarket bakeries in the UK has been progressing steadily for over 20 years, however, and the market share of bread production has increased from 3% by volume in 1984 to 15% in 1999, probably at the expense of the small craft bakeries. This change has paralleled the broader dominance of the supermarkets in the food sector, a phenomenon seen in many countries.

A cross-sectional survey of supermarket bakery workers found that 9% of bakers and 4% of bakery workers overall

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Wellington Hospital, University of Otago, Wellington, New Zealand

Correspondence to Dr Andrew Brant, Respiratory Physician, Wellington Hospital, University of Otago, Private Bag 7902, Wellington, New Zealand
Tel: +64 43855816; fax: +64 43855550; e-mail: andrewbrant@hotmail.com

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Abbreviations

EIA enzyme immunoassay
MOCALEX Measurement of Occupational Allergen Exposure project
NSBH nonspecific bronchial hyperresponsiveness

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(including managers, confectioners and assistants) had a combination of work-related chest symptoms and specific IgE to either flour or fungal alpha-amylase [7^{••}]. Using this definition, the study found that supermarket bakery workers had a burden of disease comparable with studies in traditional craft bakeries. It highlights that the location of baker's asthma (and other occupational disease) follows changes within the industry. In retrospect, the problem within supermarket workers should not be surprising, but it took some time to be identified. As production methods change and the location of production changes at different levels of the supply chain, so will the location of the disease. Following business and market trends within an industry may help facilitate proactive measures in baker's asthma, and allow predictions about where future problems may arise.

Allergens in baker's asthma

The main agents that cause occupational asthma are cereal flours (wheat, rye and barley) and enzymes. In wheat flour, more than 100 IgE-binding protein spots have been detected and sera from sensitized bakers show not only reactions to many of these antigens but also considerable variability in individual sensitization patterns [8]. Wheat is composed of four protein classes, including water-soluble albumins and globulins, gliadins and glutenins, with the strongest IgE response in baker's asthma being to the water-soluble albumins and globulins, particularly those within the 12–17 kD range. Other proteins that cause an IgE response have been identified but there remains uncertainty as to which proteins are the major allergens in wheat flour-induced baker's asthma.

Weichel *et al.* [9^{••}] used a novel approach to investigate major allergens and found a new family of wheat allergens. They screened a wheat cDNA phage display library against serum from individuals with confirmed baker's asthma. They found that wheat thioredoxin hb (Tri a25) was an allergen in eight out of 17 patient sera. Thioredoxin hb is a 13.4-kD protein, within a commonly observed range of proteins that are immunogenic. The same eight sera also reacted against a Tri a25 homologue from maize called Zea m 25. In addition, two sera samples reacted against human thioredoxin, and the authors speculated that this family of allergens might play a role in the maintenance of allergic inflammation in baker's asthma.

Innovations in the baking industry have led to the introduction of new ingredients, including enzymes. Experience from other workplace settings shows enzymes to have a strong potential to cause allergy [10]. Elms *et al.* [11[•]] took 195 personal air samples from 55 baking establishments and, using polyclonal antibodies, were able to measure fungal and bacterial alpha-amylases

and amyloglucosidases from some of the samples. Fungal alpha-amylase is a well recognized cause of baker's asthma but the others' allergic potential is largely unknown and needs future evaluation.

Diagnosis

The diagnosis of baker's asthma depends on a history of work-related asthma symptoms, specific sensitization to bakery allergens and evidence of variability in lung function. Peak flows or spirometry should demonstrate variability consistent with asthma and improvement in periods away from work. Occasionally a specific bronchial challenge is required to make the diagnosis.

The association of sensitization to bakery allergens and work-related symptoms in baker's asthma has been confirmed in two studies: a nested case-control of bakery students [12], and in a cross-sectional survey in an industrial and small bakery setting with a referent population from the petrochemical industry [13].

A longitudinal study of apprentice bakers found that work-related chest symptoms with sensitization had an incidence rate of 4% after the first year and 9% after the second year of training [14]. It was also demonstrated that sensitization to bakery allergens commonly occurred before the onset of symptoms, confirming that sensitization to occupational allergens precedes the development of asthma, as suggested by others [15,16].

Demonstrating specific IgE to an allergen is important for diagnosing baker's asthma. Previously, Sander *et al.* [8] demonstrated how many potential allergens there are in wheat flour. The same group compared three different commercial skin prick-test preparations on individuals who had baker's asthma confirmed by specific bronchial challenge [17]. Of concern was the low sensitivity of the individual commercial preparations, and that the different preparations recognized different proteins. Therefore, these preparations need to be used with caution in the diagnosis of baker's asthma or as a screening tool for occupational sensitization.

In a series of patients with suspected baker's asthma on the basis of work-related respiratory symptoms, Quirce *et al.* [18[•]] demonstrated that a positive skin prick test to an occupational allergen and nonspecific bronchial hyper-responsiveness (NSBH) correlate with a positive specific inhalation testing. The authors demonstrate that a work-related history and NSBH with specific sensitization are predictive of occupational asthma. The question of NSBH in occupational asthma is interesting. In the study by Quirce *et al.*, all but two of the 24 subjects were still working with the allergen, and a positive NSBH response may depend upon on whether the individual is currently exposed to allergen.

Measurement of airborne allergens

The Measurement of Occupational Allergen Exposure project (MOCALEX) endeavours to optimize and compare immunoassay methods for assessment of occupational bio-allergen exposure in the workplace, and this includes bakery allergens. The project is being conducted by a number of European laboratories. Standardizing airborne measurements will help to better define exposure-response relationships and consequently improve risk assessment in baker's asthma.

Tests for airborne wheat allergens include a human IgE inhibition RAST, a rabbit IgG inhibition radio-immunoassay, a human IgG4 inhibition enzyme immunoassay (EIA) and a monoclonal antibody-based test. The authors of MOCALEX chose to use polyclonal rabbit antibodies to potentially overcome the difficulties of getting enough suitable human serum, and to avoid variability of assay test results (within and between laboratories) that can arise using human serum-based tests [19[•]]. The authors compared the results of a rabbit IgG inhibition EIA with those using human IgG4 inhibition EIA and found that their results were comparable. The rabbit IgG inhibition EIA predominantly measured water-soluble albumins and globulins and was less efficient in measuring gliadins and glutenins. As bakers' sera with specific IgE antibodies to gliadins or glutenins nearly always also react to albumins or globulins, however, the rabbit IgG-based EIA is not likely to underestimate wheat-flour allergen exposure. The authors concluded that the rabbit IgG inhibition EIA is a sensitive test and measures allergens of clinical relevance.

The MOCALEX authors also developed a sandwich EIA technique and found it more sensitive than the inhibition assays, and thus could be useful in short-term exposure measurements and low exposure environments. The test is less reproducible and so needs further evaluation before widespread use is recommended.

Dust-particle size determines how far dust can penetrate into the lungs. Probably only particles in the respirable particle size smaller than 4 μm are responsible for baker's asthma. Being able to size-select different particle sizes in personal dust measurements would improve exposure-response assessments in baker's asthma. Porous foams enable measurement of different sizes of dust particles and since they are lightweight and portable, they could be suitable for personal sampling. Bogdanovic *et al.* [20[•]] have been able to demonstrate that measurement of wheat-flour dust and wheat allergen of respirable and thoracic particle sizes using these foams is feasible. This is a promising method for capturing relevant exposure to bakery allergens, but further validation work is still required.

A rapid and simple method for measuring airborne fungal alpha-amylase, an important bakery allergen, has been

reported by Koets *et al.* [21]. They used immunochromatography based on the principle of a lateral flow immunoassay. This seems to be a sensitive test and could be used to measure both airborne and static samples, within the workplace. It is a semi-quantitative measure. Its advantage is that it does not require particular expertise for its use compared with the usual EIA, which requires skilled personnel and laboratories.

Renstrom *et al.* [22] studied the efficacy of nasal air sampling of bakery dust in bakery workers. They found that the measurements from these samplers correlated well with measurements from the commonly used Institute of Occupational Medicine personal inhalable samplers. The nasal samplers, however, measured few particles in the respirable dust range, which is the particle size of most clinical relevance. The nasal method could be useful in assessing real-life dust exposure in bakery workers who use facemasks.

Surveillance

Health surveillance is considered a cornerstone in the prevention of occupational asthma. Gordon *et al.* demonstrated that bakery workers who reported respiratory symptoms in a screening questionnaire were no more likely to have asthma (or occupational asthma) than those who responded negatively [23]. The effectiveness of health surveillance in the baking industry (or in any other field of occupational asthma) has not been systematically investigated, however. To address this issue, the results from an epidemiological cross-sectional survey of supermarket bakery workers were compared with the company's own routine health surveillance [24[•]]. This study showed that surveillance underestimated the extent of potential disease by a factor of 4 for all bakery workers and a factor of 7 for bakers. Reasons for these findings included differences in response rates and differences in types of responses given in the two circumstances. The authors speculated that workforce education and information, assurances of confidentiality, and protection of employment conditions for those with occupational illness, could address some of these issues.

Maternal exposure

An interesting suggestion has been made that the impact of a woman's workplace allergen exposure may be passed on to their offspring [25]. Magnusson *et al.* [25] found that women who had worked as bakers, pastry cooks and confectioners during pregnancy are more likely to have atopic offspring. Conceivably, the transfer of maternal antibodies to the offspring during pregnancy could affect immune development and response.

Conclusion

Baker's asthma continues to be one of the most common causes of occupational asthma and strategies are required

to reduce the prevalence of disease. Progress is being made in the characterization of bakery allergens and the standardization of allergen tests and airborne exposures measurements. This should be very helpful in the diagnosis of patients, and in better assessing exposure–response relationships.

Changes in the location of bakery production and innovations in the baking industry mean that the distribution and determinants of baker's asthma will continually change. These changes need to be tracked and monitored in order to help predict and prevent baker's asthma in the future.

References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:

- of special interest
- of outstanding interest

Additional references related to this topic can also be found in the Current World Literature section in this issue (p. 209).

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