

Respiratory symptoms and wheat flour exposure: a study of flour millers

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The objective of this study was to determine the prevalence of respiratory symptoms and their relationship to sensitization to wheat flour allergens and fungal amylase, in a group of workers from the UK flour milling industry. A cross-sectional study was used to evaluate symptoms, using a structured interview technique, and sensitization, using skin prick test findings, from 679 employees in flour milling and packing operations at 18 flour mills. A total of 147 workers (147/679, 22%) described upper respiratory tract symptoms of some kind. In the majority (139/147, 95%) these symptoms were of an occasional or transitory nature and were related to short-term exposures to high levels of dust. Three individuals (3/679, 0.4%) were identified whose symptoms were thought to be the result of allergy to wheat flour. The prevalence of positive skin prick tests to wheat flour allergens and to fungal amylase was 1.2% (8/678) and 0.9% (6/678), respectively. Measurements of total inhalable dust exposure for personnel exposed to flour dust were taken at 10 of the sites (116 samples). For production personnel the levels were typically between 1 and 10 mg/m³ (8-h time weighted average), with a median of 6.2 mg/m³. Hygiene operatives had appreciably higher exposure than production personnel, with a median of 18.7 mg/m³. Overall, 43% (50/116) of all samples exceeded 10 mg/m³ (8-h time weighted average). The findings suggest that the risk of sensitization to wheat flour allergens from current dust exposures in flour mills is very low. Wheat allergy was responsible in only a small proportion of the total who had respiratory symptoms. The principal causation of symptoms experienced by the workforce was considered to be a non-specific irritant effect related to short-term exposures to high levels of total inhalable dust.

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INTRODUCTION

Since Ramazzini, a Florentine physician, first described respiratory ill health in millers and baker in his treatise *De Morbis Artificum* circa 1700, a large body of work on baker's asthma has been published. Many of the studies have looked at workers in various types of bakery and have focused on the issue of allergy to wheat flour. However, the problem of respiratory ill health in bakers would seem to be considerably more complex than just an IgE-mediated sensitization to wheat flour allergens.¹

There are two reasons for the complexity. Firstly, exposure to sensitizing agents in bakeries takes place against a background of relatively high total inhalable dust levels.^{2–4} Thus, it is possible that some of the

symptoms which bakery workers describe are actually related to the large airborne dust burden rather than to allergy. Perhaps this might explain why some studies report a large excess of bakers with symptoms but without IgE markers of sensitization.^{5–7} Secondly, wheat flour allergens are not the only agents present in either the bread baking or the flour milling environment which can cause sensitization.¹ In bread bakeries there can be substantial exposure to enzymes from bread improvers, in addition to flour dust.⁸ The principal enzymes added to bread improvers are fungal amylase, which has been in use for some 30 years, and hemicellulase, which has been introduced in more recent years. In flour mills there is also potential exposure to grain dust, i.e. material from the surface of the wheat which is removed prior to the milling process itself. In some of the mills which produce flour for bread baking, there is also a potential for exposure to enzymes which are added to the flour, i.e. as flour improvers.

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Inferences drawn from studies on respiratory ill health, which include bread baking populations, are particularly prone to the confounding factors described above. In order to identify the risk of allergic and other symptoms from flour dust, whilst minimizing the confounding effects from other potential sensitizers, we have chosen a study group of flour millers and packers. Unlike groups from other flour-using industries, these workers will have total inhalable dust exposures which are made up almost entirely of wheat flour. Thus, the respiratory effects are much more likely to be the result of flour dust, rather than other agents. However, it must be said that even in this group some employees have exposure to enzymes, albeit generally at a much lower level than in bread baking operations.

METHODS

The study group

This consisted of 679 employees from 18 flour mills in the United Kingdom. The criterion for inclusion was exposure to flour dust for the whole or part of their normal working shift, i.e. employees who had a requirement to enter milling, production or packing areas as part of their job. The group was made up mainly of milling, engineering, cleaning, packing and other warehousing personnel, who experienced regular daily exposure. It also included a small number of administrative staff (17) with less frequent exposure. Employees whose exposure was limited to grain dust, and transport personnel who had possible intermittent exposure outside of the production or packing areas, were not included.

Recent data from the industry trade body (personal communication, N. Bennett, National Association of British and Irish Millers) suggests that there are currently some 3000 personnel employed in flour mills in the UK. Of these, it is estimated that only 75% (2250) are exposed to flour dust. The group of people who we have studied therefore represents around one third of the total flour dust-exposed employees in the UK flour milling industry.

Screening procedure

Each employee was screened by one of five occupational physicians, using a structured interview and skin prick testing. Where considered appropriate, serial peak flow readings were also performed. The interview covered occupational history in relation to ingredient exposure and enquiry regarding work-related or allergic respiratory symptoms. In particular, employees were asked about symptoms relating to possible rhinitis, conjunctivitis and asthma. The interview procedure covered the following points.

- Episodes of wheezing or chest tightness.
- Symptoms of shortness of breath or cough.
- Symptoms of sneezing, runny nose or blocked nose.
- Time of onset of symptoms.
- Duration of symptoms.
- Relationship of symptoms to work, i.e. whether they were worse at work or at home, whether only arose exclusively at work, whether they were connected with a particular task or ingredient.
- If the symptoms were associated with a particular task or use of a particular ingredient, the temporal relationship with dust exposure and the duration after exposure ceased.
- If symptoms were relatively persistent, whether there was an improvement while away from work during rest periods or on holiday.
- Whether treatment had been taken for the symptoms.

The prime purpose of the consultation was to probe, in some detail, the relationship between exposure to dust and the pattern of symptoms. We believe that a structured interview, backed up by positive skin prick tests, is the most appropriate method to distinguish asthma or rhinitis due to ingredient sensitization, from symptoms due to other causes. However, it has to be accepted that this form of data collection, based essentially on clinical acumen, can introduce bias. In order to minimize this, the participating occupational physicians operated to broadly agreed diagnostic criteria. In all cases, the diagnosis of occupational asthma or rhinitis required a history of work-related symptoms which were more than transient, plus a positive skin prick test to at least one work-related allergen.

It is important to note that, in this study, we were interested primarily in symptoms relating to flour dust. A proportion of the workforce in flour mills also have exposure to grain dust. However, there is usually a clear physical separation between most of the processes which give rise to either grain or flour dust. Furthermore, in discussing work-related symptoms with milling personnel, they are invariably able to make a distinction between grain- and flour-related causation.

Skin prick testing was performed against a standard set of solutions, namely: saline and histamine controls; commercially available common environmental allergens, i.e. house dust mite, cat fur, and mixed grass pollens (Biodiagnostics Ltd); and work-related allergens at a concentration of 1 mg/ml, i.e. wheat flour, soya flour, rice flour and *Aspergillus*-derived amylase (prepared from base ingredients by the National Heart and Lung Institute). The wheat flour used to make up the skin prick test solution was a standard bread-making variety with no fungal amylase added during milling. Skin prick tests were read after 10 min and were considered to be positive if there was a wheal of at least 3 mm diameter. For the purpose of this study, atopy was defined by positive skin prick tests to one or more of the common environmental allergens, i.e. house dust mite, cat fur, or mixed grass pollens.

Dust sampling

In choosing relevant exposure data, one of the considerations was the anticipated timescale of the sensitizing process. For high molecular weight sensitizers,

sensitization may take a number of months or even years to develop. In order to take account of the potentially long latent period between onset of exposure and development of sensitization, occupational hygiene measurements which had been taken in the mills from 1990 to the end of 1998 were included.

Although sampling for both flour and amylase aeroallergen has been reported,^{2,3,8} the techniques are essentially experimental and have not been standardized. For the purposes of this study, sampling consisted of full shift measurements of total inhalable dust. The method used was that described by the Health & Safety Executive.⁹ Measurements were taken at 10 of the 18 mills at various times from 1 January 1990 to 31 December 1998. Only samples where flour dust would be encountered were included. Measurements from areas where grain dust exposure arose were specifically excluded.

RESULTS

Prevalence of symptoms

The number of employees seen was 679, out of a total dust-exposed population at the sites of 850. This represented a response rate of 80%. A large proportion of the total group (147/679, 22%) reported respiratory symptoms. However, the majority (139/147, 95%) complained only of transient occasional symptoms which we have categorized as non-specific respiratory irritation. The type of symptom described by this subgroup varied from sneezing and blocked/runny nose to chest tightness with a feeling of difficulty breathing. On closer questioning, there was characteristically a clear temporal association between the symptoms and exposure to high levels of dust.

In contrast, symptoms which were thought to have an allergic basis were uncommon (8/679, 1%). Of those who were considered to have an allergic condition, four (prevalence, 0.6%) had occupational asthma and four (prevalence, 0.6%) had rhinitis. Four of these workers only had symptoms when they were exposed to grain dust. Wheat flour was responsible for two of the cases of asthma (prevalence, 0.3%) and one of the cases of rhinitis (prevalence, 0.1%). Fungal amylase was thought to be responsible for the other case of asthma (prevalence, 0.1%). The circumstances surrounding this case were perhaps somewhat unusual, in that the individual was employed as a test baker and he only had symptoms after handling bread improver.

Latency of symptoms

The mean latent period between the date of first exposure and the development of symptoms was 5 years for the eight individuals in the subgroup with allergic symptoms (median, 5 years; range, 1–15 years). The comparative figure for the 139 employees with non-specific irritant symptoms was 2 years (median, <1 year; range, 0–29 years). Perhaps of greater interest was the percentage in each category who developed symptoms in

the first year of exposure. For the non-specific irritant subgroup this was 71% (99/139), whereas none of the allergic individuals had symptoms in the first year.

Prevalence of specific IgE antibodies

All but one of the study group, who declined for personal reasons, underwent skin prick testing. The overall prevalence of atopy was 37% (248/678), which is broadly similar to the general population in the UK. Positive skin prick tests to wheat flour allergens were present in eight of the study group (prevalence, 1.2%). It is worth noting that a positive skin prick test can arise both in the presence and in the absence of symptoms. In the latter case it should be regarded simply as a marker of sufficient exposure to elicit a specific IgE response. Equally, the presence of a positive test in the presence of symptoms does not necessarily infer a causal relationship.

Of the eight who tested positive to wheat, three had respiratory symptoms which were thought to be due to allergy (two asthma, one rhinitis), two had non-specific irritant symptoms and three were asymptomatic. A further six (prevalence, 0.9%) had a positive response to fungal amylase, of whom one had allergic rhinitis, two had non-specific irritant symptoms and three were asymptomatic. None of those with positive skin prick tests to wheat flour allergens had concomitant positives to fungal amylase (and vice versa). The numbers who had positive skin prick tests to soya flour and rice flour were five (0.7%) and three (0.4%), respectively.

The total number of years worked in flour mills by the study population was 8518, with a mean of 12.5 years (median, 11 years; range, 2 months to 47 years). The relatively long average length of service is a reflection of the generally low turnover of flour milling employees in the UK. It is possible to calculate the number of years worked per positive wheat flour skin prick test. This figure is 1065 years per positive test.

Dust exposures

In total, 116 dust samples were collected from production and hygiene (cleaning) personnel exposed to flour dust. The median exposure for the whole group was 8.1 mg/m³ (8-h time weighted average), with a range of 0.5–217 mg/m³. Fifty (43%) of the samples exceeded 10 mg/m³. There were marked differences in exposure between the different job categories, with hygiene personnel having the highest exposures, both in terms of average and maximum figures (Table 1).

The data collected for production operatives largely reflect the levels of exposure when the mill is running normally, although some of the higher readings arose during unusual activities, such as clearing chokes. When milling and packing operations are running smoothly, personal exposures are largely a function of the background dust levels which, even on the roller floor or adjacent to sifters, are usually quite low. Under these conditions, exposures are typically in the 1–10 mg/m³ range. In contrast the results for hygiene personnel

Table 1. Flour dust exposure for different job categories

Parameter	Activity	
	Production	Hygiene
Number of samples	78	38
Maximum exposure (mg/m ³) (8-h TWA)	54.7	217
Minimum exposure (mg/m ³) (8-h TWA)	0.5	1.1
Median exposure (mg/m ³) (8-h TWA)	6.2	18.7
Geometric mean exposure (mg/m ³) (8-h TWA)	6.1	17.6
Percentage of samples exceeding 10 mg/m ³	32%	66%

reflect different circumstances where task-based exposures are often quite high, e.g. vacuuming or sweeping up spillages. Two-thirds of these samples exceeded 10 mg/m³ (8-h TWA).

DISCUSSION

The prevalence of both allergic symptoms and specific IgE to wheat flour in this study are quite low, suggesting that wheat flour allergens have only a weak sensitizing effect at current levels of flour mill exposure. The sensitizing effects which we have observed are smaller than those reported elsewhere.^{5,7} There are several possible explanations for the differences. The comparatively low prevalence of allergic respiratory symptoms when compared with other studies could be the result of a general under-reporting of symptoms. This seems an unlikely reason because the overall prevalence of respiratory symptoms in our study, taking the categories of allergic asthma/rhinitis and non-specific irritation together (i.e. 22%), is broadly comparable with the overall prevalence of symptoms from previously reported studies of milling and baking populations.^{5,7,10}

Undoubtedly one of the difficulties in comparing findings between research groups is that the definitions of clinical conditions vary. This is especially true when considering exactly what constitutes 'baker's asthma' and whether this condition has a single (allergic) aetiology. Many of the previous epidemiological works, particularly those relying on questionnaires to identify respiratory symptoms, have not been primarily concerned with the separation of potentially different mechanisms of causation. We would contend that there are two distinct aetiologies for respiratory symptoms, i.e. allergy and non-specific irritation. This view takes into consideration the fact that there are two exposure factors which need to be considered in milling and baking populations. In these industries there is concomitant exposure to allergens at sensitizing levels with a background of high levels of total inhalable dust. Although the total inhalable dust levels in the workplace areas covered by our study were generally in the range 1–10 mg/m³ (8-h time weighted average), 43% of all readings actually exceeded 10 mg/m³.

The category which we describe as non-specific

irritation might be considered as somewhat contentious. However, it is worth pointing out that, in our previous studies of baking populations,^{4,6} the prevalence of this subgroup has always been high (flour milling, 20%; bread baking, 17%; cake baking, 10%). Perhaps this is not surprising as we believe that these symptoms are related to high total inhalable dust levels and in these other groups some 20–50% of all exposures also exceed 10 mg/m³.

A further possible explanation of the low prevalence of allergic conditions in this study could be a survivor population effect, i.e. individuals who have developed problems have left the organization because of their symptoms. We believe that this can be discounted because the flour milling workforce has remained very stable. Although overall numbers in the industry have declined, the turnover of labour over the last 5–10 years has otherwise been low. In addition, the workforce has been subject to a systematic health surveillance programme for 5 years which has not identified any additional cases of allergy. There have been no medical retirements on account of occupational asthma during the same period. During the past 6 years the organization has applied a policy of excluding pre-existing asthmatics as new starters. The reason for this has been to prevent the risk of aggravating symptoms by exposure to substantial dust levels. The policy is unlikely to have had any effect on new cases of symptomatic sensitization but it may have reduced the numbers of those who are more susceptible to non-specific irritant symptoms.

The difference in prevalence of specific IgE to wheat flour between our study and others may be due to the method used to determine its presence. In this context, there are two important factors: the material used to prepare the allergen solution and the strength of the solution. As a source of wheat flour allergen, we have deliberately used a flour which is manufactured in large quantities within our own organization. Moreover, this particular flour does not contain any added fungal enzymes, such as amylase or hemicellulase, which could give a false positive result. We have chosen to use all of the skin prick test solutions at a strength of 1 mg/ml. This concentration is possibly less than that used by other research groups, although it is questionable whether this factor alone may account for the difference in reported response rates. There is no doubt that the availability of a standardized test solution would help comparability of studies in the definition of IgE positivity in the future.

The finding of positive skin prick tests to fungal α -amylase in flour millers has been noted before,¹⁰ although no source of exposure was identified in this study. The principal reason for amylase sensitization in our group is probably the exposure to relatively concentrated preparations, which can occur during their tipping, rather than to the amylase-containing flour, which is the final product. Amylase tipping is only carried out in mills which manufacture hard flour for bread making and is usually a fairly well controlled procedure. Typically less than ten bags of flour improver, whose concentration of amylase is less than 0.1%

by weight, will be tipped per week. Moreover, the tipping is performed in a small area within the mill and is done by only a few milling personnel. With one exception, all of those in our group who had positive skin prick tests to amylase had engaged in tipping amylase at some point. The exception was a test baker who had probably become sensitized by exposure to bread improver during small scale bread baking processes. He was the only symptomatic individual amongst those sensitized to amylase.

Despite the various issues which might set the findings in this study apart from others, it does attempt to eliminate some of the confounding factors which affect bakery populations when looking at wheat flour allergy. It is our belief that allergy to wheat flour is only an occasional cause of symptoms, even when substantial numbers of employees are exposed to total inhalable dust, which is wholly made up of flour dust, at levels in excess of 10 mg/m³. Our previous work has suggested that the principal sensitizers in flour mills and bread bakeries are grain dust and fungal amylase, respectively.¹¹ In comparison with both grain dust and fungal amylase, wheat flour would appear to have only a weak potential to produce sensitization.

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