

Current best practice for the health surveillance of enzyme workers in the soap and detergent industry

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This study defines current best practice for the health surveillance of workers who are potentially exposed to enzymes in the manufacture of enzymatic detergent products. It is recommended that health surveillance is performed 6-monthly for the first 2 years and annually thereafter. The health surveillance programme should include a respiratory questionnaire to detect symptoms, assessment of lung function to detect pre-symptomatic changes and an immunological test to detect specific immunoglobulin E (IgE) to enzymes. The International Union Against Tuberculosis and Lung Disease respiratory questionnaire should be used since it has been validated extensively for detecting asthma. Operators should observe the American Thoracic Society performance criteria for spirometers and standardized procedures for conducting spirometry. Since current airborne monitoring techniques for enzymes do not detect short-duration peak exposures, the incidence of employee sensitizations remains the most reliable measure of the integrity of environmental control. The Pepys skin prick test has been validated as a sensitive, specific and practical test for detecting specific IgE to many inhalant allergens including enzymes. For newly sensitized workers, a multi-cause investigation should be conducted to identify potential sources of exposure. Group results of immunological test results assist in the evaluation of workplace control measures, and should be used to monitor the effectiveness of hygiene and engineering programmes and to help prioritize areas for improvement. Positive responses to a questionnaire or abnormal spirometry should be assessed further. Occupational asthma should be excluded in any case of adult-onset asthma that starts or deteriorates during working life. This is particularly important because an accurate diagnosis of occupational asthma with early avoidance of exposure to its cause can result in remission of symptoms and restoration of lung function.

Key words: Asthma; enzymes; health surveillance.

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Introduction

The first reports of asthma in workers heavily exposed to proteolytic enzyme dust appeared over 30 years ago [1,2]. Since then, other enzymes, i.e. amylases, lipases and cellulases, have been introduced into detergent products.

Most detergent manufacturers have controlled enzyme exposure successfully, preventing allergic occupational disorders [3,4]. In the early 1970s, 40% of the workforce were sensitized to enzyme and 15% had respiratory symptoms. By 1995, the prevalence of sensitizations was only 7% among enzyme workers in one large company and there were no cases of respiratory symptoms [4]. The reduced prevalence of sensitizations and symptoms was associated with reduced airborne enzyme of three orders of magnitude. Enzyme asthma remains avoidable,

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provided that programmes are robust in relation to raw product specification, plant design and maintenance, operational and exposure guidelines, control of short-term peak exposures, air monitoring and employee training and health surveillance [4].

Background

Enzyme raw material is supplied as non-friable granular encapsulates or as liquid slurry to minimize dust or aerosol formation. Enzymes are added to the process in a dedicated room under negative pressure with local exhaust ventilation at the dosing point. The manufacturing process is enclosed and automated, and all equipment couplings are encased. Any accidental spills are cleaned up immediately. Granular spills are removed using central vacuum cleaning or portable high-efficiency vacuum cleaners, whilst liquid spills are removed using low-pressure water hoses. Equipment is designed and operated such that workers only need to wear respiratory protective equipment during direct handling of enzymes, cleaning of spills and maintenance work. Workplace air is monitored by area sampling for total dust and for enzyme to confirm that control measures are satisfactory. Exposure is monitored by high-volume air sampling at locations of potential exposure, e.g. the enzyme dosing area, packing machine filler heads and the product recovery and bulk storage areas. Workers undergo periodic health surveillance, and are trained with respect to safe practice and the health effects of enzymes.

Unfortunately, sensitizations and symptoms have not been avoided uniformly within the industry. A recent report revealed a high prevalence of sensitization and symptoms in workers in a detergent factory in Finland [5]. Furthermore, a large outbreak of amylase-induced asthma occurred in a single UK factory where exposures were not well controlled [6]. That outbreak at a single factory prompted this review and its recommendations for current best practice for the health surveillance of enzyme workers in the soap and detergent industry. The aim of this paper is to encourage consistent application of best practice for the health surveillance of workers potentially exposed to enzymes in the manufacture of enzymatic detergent products, in order to detect pre-symptomatic and early changes in immunological and respiratory status. These recommendations reflect current best practice, but this is not always applied uniformly, particularly in small and medium-sized establishments, which accounts for recent reported outbreaks. This review aims to define those procedures that can be undertaken within the occupational health setting and does not aim to define in any detail hospital-based procedures.

Health assessments

Regulators such as the UK Health & Safety Executive issue guidance for the prevention of and health surveillance for occupational asthma, and industry-specific guidance is available from the soap and detergent industry [7,8]. Such industry publications are intended as guidance to assist member companies. Responsibility for operating safe programmes of work and fulfilling obligations under appropriate legislation is the responsibility of each individual company. Guidance for the health surveillance of workers exposed to respiratory sensitizers is also available in the medical literature [9–12].

Health surveillance is performed pre-placement and periodically thereafter on all workers potentially exposed to enzymes in the workplace. Since the incidence of sensitization is highest in the first 2 years of exposure [13], health surveillance should be performed 6-monthly for the first 2 years of exposure and annually thereafter. Workers should also be tested at 6-monthly intervals if there are operational changes, such as the introduction of new enzymes, increased concentration of enzymes in product or loss of hygiene control measures. Furthermore, exit health surveillance should be performed on all workers who leave or transfer to non-enzyme areas.

The health surveillance programme should include a standardized and validated respiratory questionnaire, assessment of lung function by spirometry and identification of specific immunoglobulin E (IgE) (Table 1). No one component of the health surveillance programme should be considered in isolation. A health surveillance programme of high sensitivity is provided by the combination of a validated questionnaire, spirometry and immunological tests, provided the tests are conducted by properly trained and qualified occupational health nurses who have access to an accredited specialist occupational physician. The nurse and the physician must be trained, and should demonstrate competency in performing and interpreting results of all such investigations.

The respiratory questionnaire

It is anticipated that applicants complete a general health questionnaire at pre-placement, and that this questionnaire will include questions relating to previous employment and any exposures to chemicals, fumes or dust. The intent of the respiratory questionnaire is solely to detect respiratory and related symptoms. The wording of the questions should be standardized.

Standardized respiratory questionnaires, such as those published by the UK Medical Research Council [14] and the American Thoracic Society [15], contain a few questions that elicit symptoms of asthma or a history of asthma. They are not used widely in health assessments of those exposed to respiratory sensitizers, where enquiries

Table 1. Summary of recommendations

1	All workers potentially exposed to enzymes should undergo periodic health surveillance
2	Health surveillance should include - Administration of a validated questionnaire (i.e. modified IUATLD) - Spirometry according to American Thoracic Society guidelines - Immunological test (e.g. skin prick test or RAST)
3	Health surveillance should be a quality assured process with appropriate protocols and procedures in place
4	Health surveillance should be performed/interpreted by competent, qualified occupational health professionals

are directed more specifically toward asthma symptoms and less toward other respiratory symptoms. Many other questionnaires have been used, but their sensitivities and specificities have been questioned [16–18].

In the health surveillance of those working with respiratory sensitizers, sensitivity is more important than specificity, i.e. a low false-negative but high false-positive rate. If the surveillance procedure identifies false-positive results, these can be eliminated by subsequent clinical assessment. Unidentified false-negative results will place some workers at risk of ill-health by continuing to expose them to the same environment and chemical hazard. To aim for maximum sensitivity, the authors recommend the use of a questionnaire based on that published by the International Union Against Tuberculosis and Lung Disease (IUATLD) [19,20] and which has been validated extensively [20–22]. Our modifications (see Appendices 1 and 2) include:

- minor rewording to produce separate pre-placement and periodic questionnaires and to allow their use at intervals other than annually;
- the removal of questions to elicit symptoms of chronic bronchitis;
- the addition of questions to elicit symptoms of rhinitis and conjunctivitis;
- rewording to amalgamate very similar questions into one question;
- the addition of enquiry about smoking habit.

The nurse should assess the significance of any reported symptoms and should identify any smokers. Smoking cessation advice is particularly important for those working with respiratory sensitizers, since smoking promotes IgE production, damages the respiratory mucosa and impairs mucociliary clearance [23].

Spirometry

Spirometry is a reproducible method of measuring lung volume and expiratory flow rate that can be used to detect slowly developing lung function losses that may

characterize occupational asthma. The advantage over serial measurement of peak expiratory flow rate is that each procedure can be observed directly to detect any bias due to a subject using variable effort. Generally accepted standardized procedures and protocols [24–27] are available and should be followed to reduce measurement errors.

We recommend the following standardized approach to spirometry at pre-placement and periodic health surveillance. The spirometer should conform to the performance criteria of the American Thoracic Society [27]. A volumetric spirometer is preferred, since this allows direct observation of the graph during the performance of the forced expiratory manoeuvre. Volumetric and flow-type spirometers each have advantages and disadvantages. Volumetric spirometers are precise, operate simply and are easily maintained. The chief disadvantage of volume spirometers is their size. Flow-type spirometers, on the other hand, are lightweight and portable, but in general are less precise than volumetric spirometers and this can adversely affect interpretation of the serial spirometry measurements of medical surveillance programmes [28]. Inexpensive ‘office spirometers’ are not acceptable for diagnostic spirometry or for occupational screening, surveillance and impairment evaluations [28].

Guidelines should be followed for calibration procedures, maintenance of calibration records, leak checks, BTPS (body temperature, ambient pressure, saturated with water vapour) correction factors and standards for nurse competence and training [29]. The nurse should enquire about current illness and/or medication that may affect test results or dictate postponement of the procedure [30]. Although there is no standard requirement to record weight, forced vital capacity (FVC) may fall 16 ml for every kilogram of weight gained [31] and this should be considered in individuals who experience considerable changes in body weight. As part of a quality control process, nurses should receive systematic feedback regarding performance in obtaining satisfactory spirometry results [30].

Transmission of respiratory pathogens is reported to be a possible complication of lung function testing [32]. Although respiratory pathogens have been recovered from mouthpieces and proximal spirometer tubing [33], there is no clinical evidence of transmission of respiratory pathogens between subjects undergoing spirometry [34], particularly if at least 5 min is allowed between tests [35]. In the absence of good evidence for or against the use of filters, it is prudent to use them.

The subject should perform a forced vital capacity manoeuvre in a standing position [27,29]. The subject takes the deepest possible inspiration and, without hesitation, blows into the spirometer using maximal effort. The nurse should be alert for any signs of dizziness or syncope, which occur in ~6.5 and 1% of subjects, respectively

Table 2. Performance of FVC (adapted from American Thoracic Society) [26]

Check spirometer calibration
Explain test
Prepare subject
Ask about smoking
Instruct and demonstrate test to subject
Correct posture with head elevated
Inhale completely
Position mouthpiece
Exhale with maximal force
Perform manoeuvres
Have subject assume correct posture
Inhale completely; the inhalation should be rapid but not forced
Place mouthpiece in mouth and close lips around mouthpiece
Exhale maximally as soon as lips are sealed around mouthpiece
Repeat instructions as necessary
Repeat for a minimum of three manoeuvres: no more than eight are usually required
Check test reproducibility and perform more manoeuvres as necessary

[36]. The stages in performing and obtaining acceptable and reproducible forced vital capacity manoeuvres are outlined in Table 2.

For an FVC manoeuvre to be considered acceptable there should not be:

1. an unsatisfactory start to expiration characterized by excessive hesitation, false start or an excessive extrapolated [26,27] volume >5% of forced vital capacity or 0.15 l, whichever is the greater;
2. coughing during the first second of expiration;
3. early termination of expiration—a plateau on the volume–time curve should be observed for at least 1 s and expiration length should be at least 6 s and optimally 10 s;
4. Valsalva manoeuvre;
5. leak;
6. obstructed mouthpiece, e.g. due to the tongue or false teeth.

The largest forced expiratory volume in 1 s (FEV₁) and FVC are recorded, even if they are derived from separate manoeuvres. For FEV₁ and FVC to be considered reproducible [27]:

1. at least three and up to eight acceptable manoeuvres should be performed;
2. the two highest measurements of FEV₁ and FVC must not vary by >200 ml;
3. the greatest single values for FEV₁ and FVC must not come from the last test performed.

Once acceptable and reproducible spirometry results have been obtained, an assessment must be made as to whether observed lung volumes are within the normal range. The number of test indices [FVC, FEV₁,

FEV₁/FVC ratio, peak expiratory flow rate (PEFR)] should be limited, since the use of other indices is likely to add to the false-positive rate.

Lung function tests are carried out usually to decide whether an individual's lung function is normal or abnormal. Interpretation of individual results therefore requires knowledge of what would be expected as normal for the individual, which can only be obtained from results of tests carried out in a representative sample of a healthy general population. The findings from several such studies have been surprisingly consistent: FEV₁ and FVC increase until the third decade, after which they decline slowly; and the major determinants of FEV₁ and FVC in adult life are age, height, sex and race. After these have been taken into account, the results in healthy population samples are distributed normally around the mean ('predicted') value, with a standard deviation for FEV₁ of ~0.5 l in men and ~0.45 l in women [37]. Such studies provide predicted values of FEV₁ and FVC for individuals by age, sex, height and, on occasion, race.

The counter-intuitive observation, that FEV₁ has the same distribution at different heights possibly throughout adult life and certainly during working life, has considerable importance. It implies that abnormal lung function should be defined in absolute terms, probably most understandably as a difference from the mean, e.g. >1.96 standard deviations (SD) (below 2.5th percentile) or 1.64 SD (below 5th percentile) below the average ('predicted') value. In fact, however, abnormal FEV₁ is usually defined as a proportion (e.g. <80% predicted). Whereas the absolute value of 2 SD (~1 l) is the same for all values of FEV₁, the value of a proportion falls for lower 'predicted' values of FEV₁. For instance, for a man whose predicted FEV₁ is 5 l, 80% is 4 l, i.e. 1 l and 2 SD below the mean value. For a man whose predicted FEV₁ is 2.5 l, however, 80% is 2 l and only 1 SD (500 ml) below the mean value. In the case of the second man, values between 1 and 2 SD below the predicted would be classified as abnormal (i.e. below the 15th percentile).

For these reasons, it is preferable to express FEV₁ (and FVC) as an absolute difference from the 'predicted' mean, rather than as a proportion of it, which classifies a greater proportion of those with a lower predicted FEV₁, e.g. older and shorter individuals, as abnormal. Although it is not certain that a constant spread of distribution holds for the elderly, it has been found in several different studies in those of working age.

The bottom 5th percentile from the 'predicted' (mean) expected value can be calculated for an individual of known age, sex and height, using the value of 0.5 l for men and 0.45 l for women as 1 SD from the mean in the normal population.

For example, for a man whose 'predicted' FEV₁ is 5 l:

$$\begin{aligned}
 \text{5th percentile for FEV}_1 &= \text{predicted mean FEV}_1 - \\
 &\quad (1.64 \times \text{SD}) \\
 &= 5 - (1.64 \times 0.5) \\
 &= 5 - 0.82 \\
 &= 4.18 \text{ l}
 \end{aligned}$$

i.e. any value of $\text{FEV}_1 < 4.18 \text{ l}$ is below the 5th percentile for a man of his age and height.

Although different reference populations do provide different 'predicted' values, these differences are generally small, with the exception of the effect of race when this has not been taken into account. In the UK, Cotes's references values remain a reliable basis for expectation; other reference populations, particularly those that have included hospital patients, are less representative of 'normal' lung function in the general population.

The use of a fixed percentage (e.g. 75%) of the FEV_1/FVC ratio as the basis for defining normal lung function has the merit that a reduction in the ratio indicates airflow limitation, the characteristic functional abnormality of asthma. It has the disadvantage, however, that the FEV_1/FVC ratio declines with age and can be reduced in tall, fit individuals with a normal FEV_1 and disproportionately large FVC.

During periodic health surveillance, a fall in FEV_1 or FVC that exceeds 15% in 1 year should be regarded as statistically significant. Assuming measurement error has been excluded, such reductions in lung volume warrant further investigation [37].

Immunological tests

Enzymes are allergenic at very low concentrations in air. The American Conference of Governmental Industrial Hygienists' threshold limit value and the UK Health & Safety Executive occupational exposure standard for 'subtilisins' (serine endopeptidases derived mainly from *Bacillus* spp.) is 0.00006 mg/m^3 (60 ng/m^3). Consequently, workplace exposure needs to be maintained at very low concentrations and currently available airborne monitoring is reliant on high-volume sampling collected typically over periods of at least 1 h. Such monitoring is unable to detect short-duration peak exposures, which may be responsible for producing sensitizations and allergic symptoms [38]. Accordingly, the incidence of employee sensitizations is the most reliable measure of the integrity of environmental control and exposure to enzymes.

Sensitization to an allergen is defined as the development of specific IgE, which is detected by immunological tests such as the skin prick test and serological tests such as the radioallergosorbent test (RAST) and enzyme-linked immunosorbent assay (ELISA). The demonstration of an immunological response to an allergen

indicates sufficient exposure to the allergen to stimulate a detectable immunological response [39,40]. It does not establish the presence of disease, nor does it predict the likelihood that a person will develop enzyme asthma.

The results of immunological tests are of practical relevance for individual employees. They permit the identification and correction of individual contributory or causative factors, such as failure to follow job safe practices. Group immunological test results assist in the evaluation of workplace control measures. Group data can be used to monitor the effectiveness of hygiene and engineering programmes and to prioritize areas for improvement. The effectiveness of the use of health surveillance data to monitor compliance is affected by group size.

Specific IgE measured directly in serum involves venepuncture, is relatively costly and the results are not available immediately. The skin prick test is a less expensive, direct and practical method of detecting specific IgE that provides immediate results [41–44].

Skin prick tests

The skin prick test is painless, compliance is high, it can be performed in health centres [45] and it has a low risk of side-effects, apart from occasional minor localized itching. Several disposable devices are available for such tests. However, none shows any advantage over disposable hypodermic needles when used properly [46–49]. The Pepys skin prick test method has been validated as a sensitive and specific test to identify specific IgE to inhalant allergens, including enzymes [42]. Although skin prick tests with inhalant allergens are safe [42], anaphylaxis has been reported with food allergens in those with a past history of anaphylaxis [50] and so i.m. adrenaline should be available [45]. Skin prick tests for food allergy should not usually be undertaken in occupational health practice.

The skin prick test is performed on the volar surface of the forearm, avoiding the wrist and antecubital fossa. The test should be performed with standardized allergen solutions [45]. Drops of allergen solution are placed on the skin at least 2 cm apart [51] and with a separate disposable 20–26 G hypodermic needle for each allergen site, the needle tip is inserted gently into the superficial epidermis at an angle of $15\text{--}30^\circ$. The needle is gently lifted away from the skin to form a tent-like elevation of skin, which is then allowed to fall away from the needle tip. The allergen solutions are thereafter blotted off as soon as possible with tissue, taking care not to mix the solutions. This test introduces $\sim 1/3\ 000\ 000$ th of a millilitre of allergen extract into the epidermis, so that the test dose is in the picogram range [42]. The skin prick test is specific and sensitive at a range of concentrations [43,52]. The

concentration of the allergen extract is important. It should be high enough to elicit a response to specific IgE and low enough to avoid non-specific primary irritant effects, which occur at concentrations >1 mg/ml [52]. Thus, the lowest concentrations of allergen extract that remain sensitive should be used [53,54]. There is no evidence that the skin prick test leads to sensitization [54], which is corroborated by >25 years of experience of use in industry.

Tests should be performed with 50:50 glycerol/saline solutions of enzyme allergen to which workers are potentially exposed, i.e. specific protease, amylase, lipase and cellulase. Baseline skin prick tests may include common allergens, e.g. *Dermatophagoides pteronyssinus*, mixed grass pollen and cat fur, to determine whether individuals are atopic. Skin prick tests to common allergens may be useful as an epidemiological tool to quantify the importance of atopy as a predisposing factor for disease [55]. Although atopics are at increased risk—atopy affects around 40% of the population—it is a poor discriminator of future cases of asthma (i.e. high false-positive rate) and the workplace should be made equally safe for atopics and non-atopics. Therefore, a positive skin prick test to common inhalant allergens is not a basis for exclusion. A positive control (1:1000 histamine phosphate) is used to confirm a normal vasoactive response to histamine. A negative control (glycerol/saline) is used to determine if any reaction occurs to the skin prick test itself, as in dermatographism. Results are read after 15 min and a positive reaction is recorded if there is a wheal 3 mm greater than the diameter of the negative control plus a flare. A wheal size of 3 mm is generally regarded to be clinically relevant [42]. Enquiry should be made about the use of anti-allergic medications and H₂ antagonists. Antihistamines inhibit the wheal and flare response to a variable extent [56–63], H₂ antagonists less so [64–67], as may ketotifen [56,57] and oral beta-agonists [56,68]. However, if a wheal reaction is detectable to the histamine positive control, then a negative skin prick test to allergen is probably reliable [63]. The skin prick test is not affected by oral corticosteroid medication [56,69,70] or by inhaled medication [56].

Although sensitization to an occupational allergen may be a precursor of symptoms, the development of symptoms is not an inevitable consequence and workers who develop a specific IgE to enzymes are able to continue working in a controlled enzyme area. Sensitization to enzyme is reason to initiate a multi-cause investigation to identify any remediable causes. The multi-cause investigation should seek to identify sensitizations among other workers, mechanical failures, abnormal results from routine atmospheric monitoring, change in work practices or behaviours, change in quality of raw material or failure of control systems or of respiratory protective equipment.

Investigation of suspected cases

There is good reason for rapid investigation of cases of rhinitis, conjunctivitis, new-onset asthma and aggravation of underlying allergic disorder. Occupational asthma should be suspected in all adult-onset asthmatics whose asthma begins or worsens while they are working [71]. This is particularly important, since early removal from exposure may result in remission of symptoms and restoration of lung function. There is evidence, particularly for chemical sensitizers, but also for some protein allergens, that continuing exposure after the onset of asthma increases the risk of chronic asthma and airway hyper-responsiveness [72,73].

The defining characteristic of asthma is reversible airways narrowing. It can be difficult to identify when the results of lung function studies are normal or near normal between attacks [74]. Objective lung function tests are needed to document variable and reversible airflow obstruction. Improvement in FEV₁ and FVC after inhalation of bronchodilator is the most commonly used test to diagnose asthma. As with FEV₁, a 'positive' test is usually defined as a proportion, e.g. 15 or 20% improvement in FEV₁. However, a proportionate improvement is more readily achievable in those whose baseline FEV₁ is lower, e.g. 20% of 2.5 l is 500 ml, whereas 20% of 1 l is 200 ml. The prevalence of significant reversibility of FEV₁ defined as a proportion will therefore increase with decreasing baseline FEV₁. A statistically more valid measure of reversibility is the absolute difference in FEV₁ between two tests that is beyond the 95% confidence interval of between-test variability; this is some 200 ml. An increase in FEV₁ of >200 ml is unlikely to have occurred by chance and can therefore be described as a 'significant improvement in FEV₁'. A satisfactory compromise would be to define significant reversibility as a 15% improvement in FEV₁, provided this exceeds 200 ml.

Airway responsiveness to both non-specific (e.g. cold air, histamine and methacholine) and specific (e.g. low molecular weight chemical causes of asthma, such as isocyanates) agents can be investigated by inhalation challenge tests. These investigations are not usually needed to diagnose asthma or identify its cause. They should be undertaken only by those familiar with them and their potential hazards, and are beyond the scope of this review. Neither bronchodilator challenge nor airway responsiveness tests identify an occupational cause of asthma [75]. Specificity for occupational asthma is increased when significant reduction in function is temporally related to workplace exposure [16]. The most acceptable test is serial self-recorded PEF. The diagnostic value of this test depends on the reproducibility of the forced expiratory manoeuvres, as well as the compliance and honesty of the subject [16,72,76].

Standard spirometry at intervals can be used to corroborate the results of the worker's PEFr diary [16]. Serial PEFr should be recorded 2–3 hourly during waking hours, both at and away from work for up to 4 weeks, with recordings taken over two work periods and a rest period of at least 10 days [12,16,72,77]. However, there is no general agreement on what decrement of function over a work shift is necessary to make a diagnosis of occupational asthma [16,72]. Variability of 20–25% has been suggested for establishing significance of daily variability of PEFr measurements [12,16].

Serological tests, such as RAST or ELISA, to identify specific IgE serve as further confirmatory tests. Such tests provide a quantitative measure of the amount of circulating specific IgE. This can be useful in the serial evaluation of suspected cases of asthma, e.g. by measuring specific IgE on case presentation and subsequently after removal from exposure to enzymes. If symptomatic improvement follows removal from exposure and there is an associated significant fall in specific IgE, this is supportive of a diagnosis of occupational asthma. However, the demonstration of specific IgE, detected by any method, is not sufficient to conclude that the allergen is responsible for the employee's asthma. The presence of specific IgE is not unique to clinically symptomatic individuals, but reflects sufficient exposure to an allergen to stimulate an immune response [78,79].

In most cases, a confident diagnosis of occupational asthma can be made from the combined evidence of knowledge of the workplace, clinical history, physical examination, serial PEFr measurements assessed both during work and away from work, and immunological tests. For this reason, inhalation tests are usually not necessary for the investigation of enzyme-induced asthma, since diagnosis can be made by history, serial pulmonary function measurements and immunological tests [72,75,78].

Early specialist referral is recommended for the diagnosis of occupational asthma. Management strategies should include both general asthma management and workplace measures to avoid further exposure to enzymes [71,80]. Impairment evaluation should take place on at least two occasions. Temporary disability assessment should be made immediately after the time of diagnosis. Permanent disability should be assessed 2 years after avoidance of exposure, since improvement in symptoms, lung function and bronchial hyper-responsiveness plateau from this time [74,81]. Unless change in work practices can guarantee avoidance of exposure, the employee should be considered unfit for the work that caused the asthma and for any job that entails exposure to its cause [74].

Discussion

Both from an ethical perspective and following the

introduction of the Disability Discrimination Act 1995, a clear understanding of the implications of atopy and of pre-existing asthma in those who seek to work in the detergent industry is important

Atopy is a form of immunological reactivity in which specific IgE is readily produced in response to ordinary exposure to common environmental allergens [82]. Around 40% of the general population are atopic [23]. Atopy is a risk factor for sensitization and occupational asthma caused by many high molecular weight allergens [83], such as laboratory animal proteins [84] and bakery allergens [85–87], but there is no consistent relationship with low molecular weight chemicals [23]. Atopy has been associated with sensitization to enzymes in bakers [88–90] and in pharmaceutical workers [91], but collectively there is only weak evidence of an association among workers involved in enzyme production and detergent manufacture [92–99]. Although the risk of sensitization to enzymes and of asthma may be increased in atopics, atopy is not a major determinant of asthma in the workplace and few exposed atopics develop occupational asthma [100]. Since atopy discriminates poorly for asthma, it should not be used to screen out job applicants [23, 72,101].

It has usually been recommended that individuals with current asthma or asthma requiring treatment in the recent past should be excluded from employment that exposes them to respiratory sensitizers. The basis for this advice has been not because of an increased risk of sensitization ('susceptibility'), but because of the potential for increased severity of symptoms ('vulnerability') in those with existing asthma. In circumstances where allergen exposure is demonstrably well controlled and the risk of developing asthma low, such guidance is now probably inappropriate and asthma alone should not be regarded as sufficient reason to exclude an individual from employment. More appropriately, development of sensitization and/or occupational asthma are prevented by control of exposure, good hygiene practice and health surveillance [9,10,72]. Given the level of environmental control that is achievable in the detergent industry, the working environment can be made safe for all workers, including atopics [42] and most asthmatics.

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Appendix 1. Pre-employment respiratory questionnaire

	Yes	No	For medical use only
1. Does your chest ever feel tight or your breathing become difficult?			
2. Have you ever had an attack of wheezing or whistling in your chest?			
3. Have you ever had an attack of shortness of breath that came on during the day when you were not doing anything strenuous?			
4. Have you ever had an attack of shortness of breath that came on with exercise?			
5. Have you ever been woken at night by an attack of shortness of breath or coughing?			
6. Have you ever woken up with a feeling of tightness in your chest first thing in the morning?			
7. Which of the following statements best describes your breathing?			
a. I never or only rarely get trouble with my breathing.			
b. I get regular trouble with my breathing, but it always gets completely better.			
c. My breathing is never quite right.			
8. Has a doctor ever told you that you have asthma?			
9. Have you ever had an attack of asthma?			
10. Have you had an attack of asthma any time in the last 12 months?			
11. Are you currently taking any medicines, tablets or inhalers for asthma?			
12. Other than when you have a cold, have you ever had:			
a. Sneezing, running or blockage of the nose?			
b. Itching or watering of the eyes?			
c. Are you currently taking any medicines or tablets for these symptoms?			
13. Have any of the problems described in question 12 occurred at any time in the last 12 months?			
14. a. Have you ever smoked cigarettes?			
If yes, how many did you smoke a day?			
For how many years?			
b. Do you currently smoke cigarettes?			
If yes, how many cigarettes do you smoke a day?			

Appendix 2. Periodic respiratory questionnaire

	Yes	No	For medical use only
1. Since your last examination, has your chest ever felt tight or your breathing become difficult?			
2. Since your last examination, have you had wheezing or whistling in your chest?			
3. Since your last examination, have you had an attack of shortness of breath that came on during the day when you were not doing anything strenuous?			
4. Since your last examination, have you had an attack of shortness of breath that came on with exercise?			
5. Since your last examination, have you been woken at night by an attack of shortness of breath or coughing?			
6. Since your last examination, have you woken up with a feeling of tightness in your chest first thing in the morning?			
7. Which of the following statements best describes your breathing?			
a. I never or only rarely get trouble with my breathing.			
b. I get regular trouble with my breathing, but it always gets completely better.			
c. My breathing is never quite right.			
8. Since your last examination, has a doctor told you that you have asthma?			
9. Since your last examination, have you had an attack of asthma?			
10. Are you currently taking any medicines, tablets or inhalers for asthma?			
11. Since your last examination, other than when you have a cold, have you had:			
a. Sneezing, running or blockage of the nose?			
b. Any itching or watering of the eyes?			
c. Are you currently taking any medicines or tablets for these symptoms?			
12. Have any of the problems described in question 11 occurred at any time in the last 12 months?			
13. Since your last examination:			
a. Have you ever smoked cigarettes?			
If yes, how many did you smoke a day?			
b. Do you currently smoke cigarettes?			
If yes, how many cigarettes do you smoke a day?			