# Asthma at work

## Part 2: diagnosis of occupational asthma

*In the second in a series of articles on asthma at work Lisa Bradshaw and Chris Barber give practical and evidence-based guidance on diagnosing occupational asthma.*

**THIS** is the second article in a series on occupational asthma (OA)[1]. The first article discussed the nature, extent and causes of OA; this article will explain how a diagnosis of OA is made. To recap, OA is asthma either caused by exposure to an inhaled agent at work when sensitisation or allergy to the specific agent takes place (occupational asthma due to sensitisation), or it is asthma that is caused by a high-dose exposure to an inhaled irritant within the workplace (acute irritant induced asthma, formerly referred to as reactive airways dysfunction syndrome). This article focuses on allergic OA.

Any working adult with new-onset asthma, a reoccurrence of childhood asthma or with any unexplained deterioration in their asthma symptoms, should have an occupational history taken to consider occupational asthma as a cause. Classically, OA is characterised by asthma symptoms that are considered by the individual to be worse on workdays, and/or improve on days away from work.

Occupational health or primary care health practitioners who suspect a worker has OA should refer the individual to an expert with an interest in this condition to try to minimise the time taken to make a diagnosis.

To make a diagnosis of OA the first step is to diagnose asthma. Secondly, a temporal relationship between the exposure in the workplace and episodes of asthma symptoms needs to be established. Finally, if possible, the sensitising agent or inhaled irritant needs to be identified. There are several ways to objectively measure the work-relatedness of asthma symptoms, and investigations are usually carried out in a stepwise approach. These investigations will be discussed in turn.

### HISTORY TAKING

Before any objective measures are taken, a detailed medical and occupational history needs to be gathered from the individual to try to confirm the cause–effect relationship between work and symptoms. Documenting a full and detailed history can be time consuming and can often take up to 60 minutes so this should be factored in to any new appointment. Box 1 (see p.28) shows the questions that should be asked when taking a detailed history.

The relationship with work should be questioned regarding all of the symptoms in box 1 (on p.28). It is important to understand whether the symptoms are worse on workdays and improve on holidays or days away from work. Some work-related symptoms, that is symptoms which are worse at work, may have a late response. For example, symptoms such as cough and chest tightness may occur in the evening of workdays only. It is important to investigate whether symptoms improve or deteriorate during the working week, and if the worker needs several days away from work before they feel symptom free on days off or holidays.

Any allergy-related symptoms should be documented, for example; allergic nasal or ocular symptoms. Occupational rhinitis can precede occupational asthma symptoms in some workers with IgE-mediated occupational asthma[2,3].

Workers should be allowed to talk freely about their job and any previous jobs they have had. This establishes whether any prior exposure or sensitisation to the same or similar agents may have occurred in other occupations. The health of work colleagues should be part of the enquiry, asking if colleagues have complained of respiratory or other work-related symptoms. Any time delay between commencing work and the onset of nasal or respiratory symptoms should be recorded; the length of this so-called latent period in OA can be as short as a few weeks or months, or as long as several years in some occupations.

Individuals working with respiratory sensitisers or with chemical or toxic substances should have access to material safety data sheets (MSDs). The worker should be asked to obtain these from their employer. Such sheets are extremely useful to identify which substances they are currently working with and whether these substances are known respiratory sensitisers or irritants.

Once a thorough medical and occupational history has been recorded, further objective testing needs to be carried out if OA is suspected. This is because a

## *Box 1: medical history prompts for occupational asthma diagnosis*

**Cough** – dry or productive? Does anything trigger the cough?
**Wheeze** – are there any precipitating factors and timing through the day?
**Chest tightness** – any precipitating factors and timing through the day?
**Shortness of breath** – graded using the Medical Research Council dyspnoea scale[4] definitions (see box 2 below)
**Eye and nasal symptoms** – specifically, rhino-conjunctivitis may precede or coincide with the onset of OA, and the risk of OA development is highest in the year following the onset of rhino-conjunctivitis
**Allergy** – previous history and family history of allergies and asthma
**Smoking history** – graded as pack years = (number of cigarettes per day/20 x years smoking)
**Symptoms** – are any of the above symptoms the same, better or worse at work? Are symptoms the same, better or worse on days away from work? Certain patients with occupational asthma complain of worse symptoms on the evenings of workdays only, and may not directly relate workplace exposures as relevant.

## *Box 2: Medical Research Council dyspnoea scale*

1 Not troubled by breathlessness except on strenuous exercise
2 Short of breath when hurrying or walking up a slight hill
3 Walks slower than contemporaries on the level because of breathlessness, or has to stop for breath when walking at own pace
4 Stops for breath after about 100 m or after a few minutes on the level
5 Too breathless to leave the house, or breathless when dressing or undressing

*Source: Medical Research Council[4].*

diagnosis of OA should not be based on a suggestive history alone, given the important impact of making such a diagnosis[3]. At this stage the worker should normally be referred to a specialist occupational lung disease clinic, a list of which are published online by the Health and Safety Laboratory[5].

The following investigations are usually carried out within the specialist centres to confirm or exclude the diagnosis of OA.

**Serial peak flow monitoring**

There is good evidence that peak expiratory flow (PEF) is a useful method for establishing a causal relationship between asthma and work exposures if good-quality measurements are taken both at work and at home[6]. Peak expiratory flow is measured as the maximum flow rate that can be achieved during a forced expiration when the individual starts the procedure from the level of maximum lung inflation.

Peak flow is measured with a highly portable device that can be taken into the workplace without causing too much disruption to the individual's working day. However, the worker needs to be motivated, have the ability to read the peak expiratory flow meter and be able to accurately record the readings onto a peak flow diary. With good coaching and explanation this can usually be achieved by most workers. Whilst carrying out peak flow monitoring it is important that the worker's medication is not altered unless their symptoms are so severe that to not increase medication would be unsafe. A change in medication could be associated with an improvement or deterioration in their asthma, which could wrongly mislead the interpreter to believe that this was work related.

There has been debate over how many peak flow readings the individual should be asked to record. Most clinicians ask workers to record these every two hours from waking to going to bed[7,8,9]. When four-times-a-day readings were compared with two-hourly readings, the latter had optimal sensitivity and specificity; however, four-times-a-day recordings are probably more reliable due to a higher compliance rate from the workers[10,11].

The length of time an individual should record peak expiratory flow has also been debated. Moscato, et al[12] concluded that periods of work should be long enough to allow informed evaluation of the pattern of response and to be able to avoid false-negative results, which may be from lack of exposure to the suspected offending agent. Time away from work during the period that the worker is monitoring their peak flow should be long enough to enable the healthcare professional to observe any recovery.

In summary, serial PEF should be recorded at least four times a day for at least three continuous weeks, with rest days or holidays included in this timeframe[3]. It is best to aim for readings every two hours, so that at least four good measures a day will be achieved.

**Serial peak flow analysis**

Whilst most hospital respiratory departments monitor peak flow data in suspected OA, computer-based analyses of PEF are helpful in the diagnosis and allow, for example, inter-department comparisons of serial PEF for clinical and research purposes.

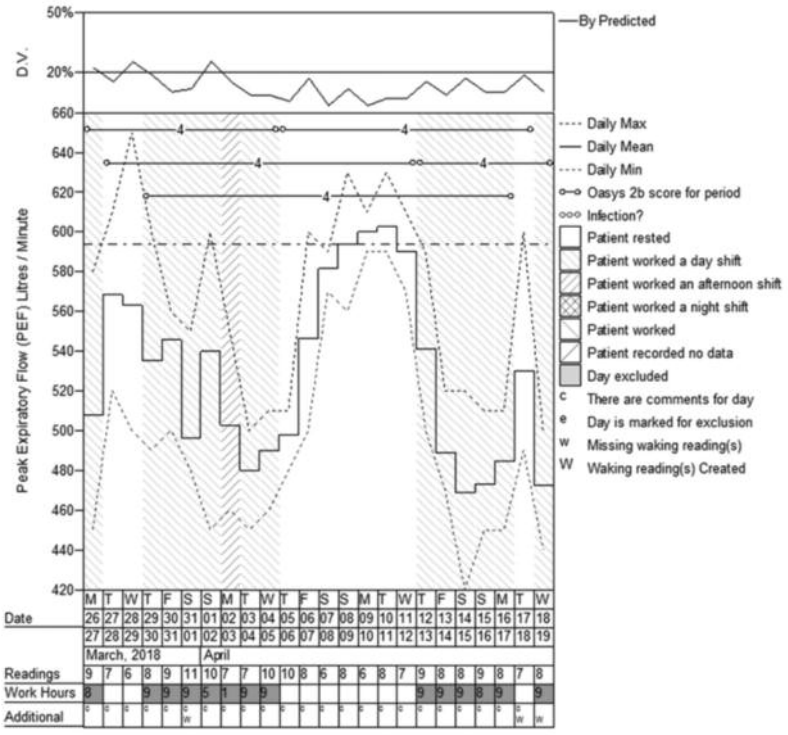
For example, the Oasys software program[13] calculates a work-effect index (from 0 to 4.0) from discriminant analysis based on pattern recognition. A positive chart (with a score above 2.51) has a reported sensitivity of approximately 75% and a specificity of 95% for a diagnosis of OA. Estimates are quality dependent, however, and pooled estimates suggest 64% sensitivity (95% confidence interval (CI) 43%–80%) and a specificity of 77% (CI 67%–85%)[6]. An example of a typical Oasys style serial PEF chart is shown in figure 1

(see p.29). Figure 2 (see p.30) shows the conclusion sheet with a calculated Oasys score.

As can be seen in figure 1, peak flows are plotted within the chart and diurnal variation (DV) is calculated as a percentage above the graph. There is a key at the side of the chart that shows clearly the work and rest days. As can be seen from the analysis and conclusion in figure 2 this was a positive peak flow analysis confirming a diagnosis of occupational asthma in this artisan baker.

The Oasys peak flow chart was generated by the free-to-download OASYS-2 program[14].

**Figure 1: a positive Oasys chart**




*Note: this is an output from an actual worker with occupational asthma using the Oasys program[14] to analyse their peak flow data.*

**Spirometry**

All workers suspected of having OA should have spirometry recorded and the results should be compared with the predicted value for their age height and gender. Reference to previous recorded values is essential to estimate the annual decline in forced expiratory volume in one second (FEV1) as this may itself be accelerated in OA. For example, Anees et al[15] found excessive FEV1 decline in workers with OA of an average of 100ml per year.

If airflow obstruction is observed – in other words if the FEV1/FVC (forced vital capacity) ratio is less then 70% or below the lower limit of normal – with reversibility, this would help to diagnose asthma. However, normal spirometry should not rule out a diagnosis of occupational asthma due to the variability of the disease.

The healthcare personnel performing the spirometry testing should be trained to national standards, which in the UK are set by the Association for Respiratory Technology and Physiology, and should follow relevant spirometry guidelines[16].

Sumner et al[17] reported significant errors in the estimation of lung function if only one (or the first two) technically acceptable blow(s) had been performed. For a FEV1 of 115.1ml, they calculated a mean underestimate of 35.4ml, and for a FVC of 143.4ml there would be an underestimate of 42.3ml if national standards were not adhered to.

**Immunological testing**

Skin prick testing or IgE testing to common aeroallergens (typically cat, grass and house dust-mite mix) can be carried out to define atopic status in workers with possible OA. Atopic workers are known to be at greater risk of developing IgE mediated occupational asthma caused by, for example, natural allergens such as latex[18] or laboratory animal dander[19].

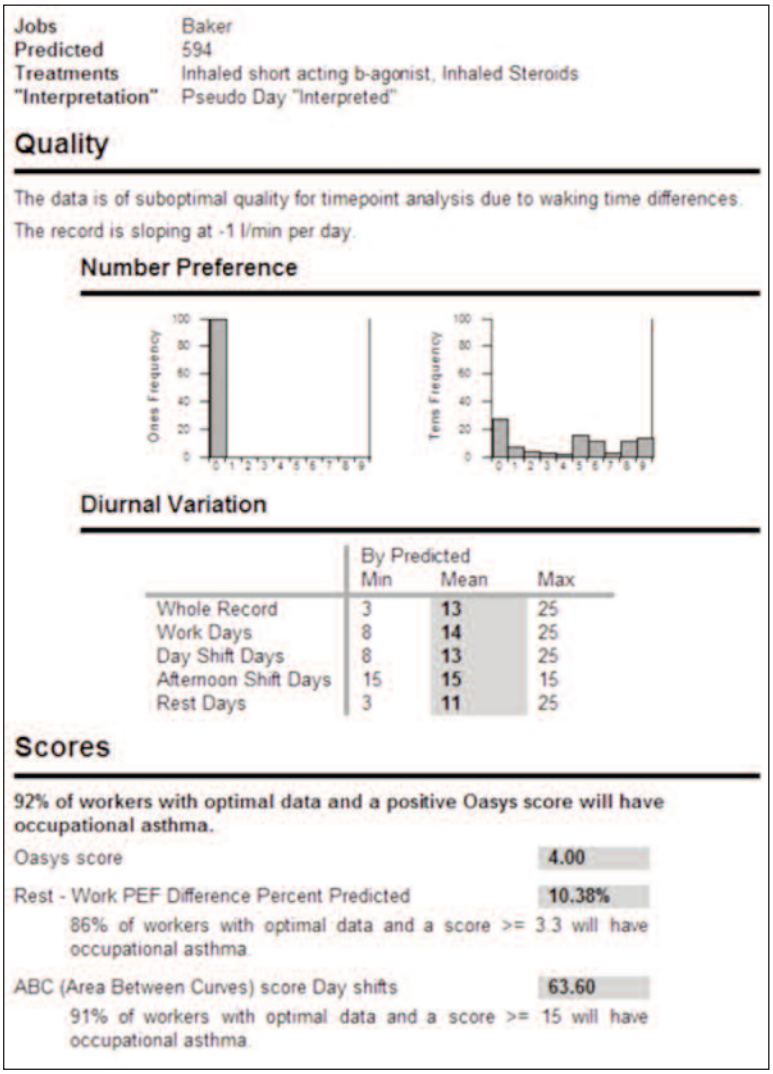
Specific immunological mechanisms are thought to play a large part in the pathogenesis of occupational asthma. Many exposures in the workplace have an allergic potential, and this is particularly true for exposures classed as high molecular weight (for example organic substances, proteins, and animal and plant products). It is believed that with predominantly IgE-mediated occupational asthma that sensitisation to the allergen occurs during the latent period between exposure and development of symptoms.

Flour, tea, coffee, castor beans and animal products have all shown immediate reactions on sensitised patients following skin prick testing[20]. A positive skin prick test to a workplace exposure would support a diagnosis of occupational asthma if it was also associated with a positive history and appropriate changes in pulmonary function[21]. However, a negative skin prick test of specific IgE would not rule out a diagnosis of OA[8,22]. One of the pitfalls of skin prick testing in occupational asthma is obtaining an occupational allergen extract that is well characterised and of suitable quality.

Low molecular weight exposures, such as chemicals, are thought to act as incomplete antigens (haptens) until they can combine with carrier proteins such as serum albumin to form complete antigens. As a consequence, IgE testing for low molecular weight allergens is generally less useful, although there are some exceptions.

Interpretation of immunology tests requires expertise. Specific IgE to an allergen can occur as a

Figure 2: Oasys conclusion sheet



Jobs Baker
Predicted 594
Treatments Inhaled short acting b-agonist, Inhaled Steroids
"Interpretation" Pseudo Day "Interpreted"

**Quality**

The data is of suboptimal quality for timepoint analysis due to waking time differences.
The record is sloping at -1 l/min per day.

**Number Preference**



**Diurnal Variation**

| | By Predicted Min | Mean | Max |
|---|---|---|---|
| Whole Record | 3 | **13** | 25 |
| Work Days | 8 | **14** | 25 |
| Day Shift Days | 8 | **13** | 25 |
| Afternoon Shift Days | 15 | **15** | 15 |
| Rest Days | 3 | **11** | 25 |

**Scores**

**92% of workers with optimal data and a positive Oasys score will have occupational asthma.**

Oasys score **4.00**

Rest - Work PEF Difference Percent Predicted **10.38%**
86% of workers with optimal data and a score >= 3.3 will have occupational asthma.

ABC (Area Between Curves) score Day shifts **63.60**
91% of workers with optimal data and a score >= 15 will have occupational asthma.

*Note: this is an output from an actual worker with occupational asthma using the Oasys program[14] to analyse their peak flow data.*

consequence of exposure to allergens alone, in workers who do not have any work-related asthma symptoms. Positive tests are thus not 100% specific with regards to a diagnosis of OA. Similarly, although variation between agents will be seen, these tests are also not 100% sensitive. Some workers with confirmed OA will have negative immunological tests.

**Non-specific bronchial challenge and occupational asthma**

Non-specific bronchial hyper-responsiveness is assessed by administering increasing concentrations of an irritant such as histamine, methacholine or mannitol. If the worker has a decrease in FEV1 from baseline of 15% (or 10% between doses) or greater following increasing concentrations of irritant inhalation, then this would be considered a positive test. Non-specific bronchial hyper-responsiveness is a feature of asthma (and hence of OA), although not always present in OA.

Changes in the degree of non-specific bronchial hyper-responsiveness can be assessed by measuring this when the worker has been away from the workplace for at least two weeks and then re-measuring when the worker is back at work for at least two weeks. If a significant increase in bronchial hyper-responsiveness is recorded when the worker returns to work, this again supports a diagnosis of OA.

Whilst assessment of non-specific bronchial responsiveness is a useful diagnostic investigation, single and serial measures have only moderate specificity and sensitivity for the validation of OA.

**Specific inhalation challenge**

Specific inhalation challenge (SIC) is generally regarded as the gold standard for the diagnosis, or exclusion, of occupational asthma. A control day is included within the challenge, during which a placebo is inhaled and lung function measured. This is usually followed by two active days, where the worker is exposed to increasing doses of the suspected agent and lung function again measured. The inhaled exposures are given in a controlled manner and the duration of exposure incrementally increased. The exposure can be stopped if lung function drops by more than 15% from baseline.

A positive SIC response is documented if FEV1 drops by 15% from baseline either soon after the test has commenced (early response) or a few hours later (late response). Some individuals may experience both early and late responses. Because of the potential of these biphasic (early and late) responses, the individual needs to be monitored in a specialist hospital environment. These tests should be performed only in specialised (tertiary) centres. A positive test can pinpoint the cause of OA, provided exposures received are equivalent to those in the workplace. A negative test does not exclude OA, as the exposure during the SIC may not have fully replicated workplace exposures and conditions.

SIC is not commonly carried out in the UK and is generally reserved for possible new causes of OA, for workers with conflicting results from other investigations and to identify the exact cause in a workplace when mixed exposures are potentially causative, and interventions are possible to reduce specific exposures.

**Fractional exhaled nitric oxide testing**

Fractional exhaled nitric oxide (FeNO) testing can be measured in the airway with a simple breath test. Its level may assist with a diagnosis of asthma, as airway inflammation is thought to produce nitric oxide. Measuring FeNO is thus a useful non-invasive biomarker in people with asthma[23]. This is a very quick

test to perform and the result is recorded in parts per billion (ppb). National Institute for Health and Care Excellence guidelines[24] published in 2017 recommend that a FeNO test should be offered as the first line of investigation for adults if a diagnosis of asthma is being considered. A result of 40 ppb or higher should be considered as a positive test; however, a low reading cannot rule out occupational asthma.

The utility of FeNO testing in the diagnosis of OA remains to be established. Lemiere et al[25] reported that an increase in FeNO after exposure to the agent that led to OA occurred more consistently in those individuals with OA triggered by high molecular weight allergens than in those with OA caused by low molecular weight allergens. Current British Thoracic Society (BTS) and Scottish Intercollegiate Guidelines Network (SIGN) guidance – based on the 2010 British Occupational Health Research Foundation guidance[26] – summarises that the role of exhaled nitric oxide measurements in the diagnosis of occupational asthma in this setting is not established[27].

**Sputum eosinophilia**

Sputum eosinophilia can also be helpful in the diagnosis of OA. To measure eosinophils in the sputum a non-invasive technique is used to induce sputum by inhalation of hypertonic saline for 10 to 20 minutes with an ultrasonic nebulizer. The induced sputum is then collected and processed with a mucolytic agent and a differential cell count is carried out. If eosinophils are present in the sputum this is a feature of airways inflammation and asthma, the upper limit of the normal range for sputum eosinophils is >2%. If a worker has sputum eosinophils greater than 2% then asthma should be suspected[28].

However, as with FeNO, a low percentage eosinophil count does not rule out asthma. Lemiere et al[28] reported a rapid decrease in eosinophilic inflammation after removal from the causative agent in OA, although individuals with a non-eosinophilic asthma phenotype seemed to have a poorer prognosis than those with eosinophilic airway inflammation at diagnosis.

Current BTS/SIGN guidance[27] states that: 'Sputum eosinophilia is not sufficiently sensitive or specific to help in the diagnosis of occupational asthma although it may help in the interpretation of equivocal SIC reactions. In the clinical setting the absence of sputum eosinophilia does not exclude a diagnosis of occupational asthma.'

## FOCUS ON DIAGNOSIS

Occupational asthma is an important disease to diagnose accurately. If the worker has occupational asthma their symptoms and prognosis can improve with early removal from the exposure that has caused the disease[4,28,29].

## *CONCLUSIONS*

- **Occupational asthma** (OA) is typically characterised by asthma symptoms that are considered by the individual to be worse on workdays, and/or improve on days away from work
- **OA** should be considered in all adults with new-onset asthma, deteriorating asthma control, or excessive decline in workplace spirometry
- **Prognosis** in OA is improved by early diagnosis
- **Workers** with possible OA should be referred to a specialist respiratory physician as soon as it is suspected
- **Diagnosis** of OA should not be based on history alone
- **In the UK**, the majority of cases of OA are diagnosed based on history, serial peak flow analysis and specific IgE testing
- **Spirometry** should always be performed by those who have been trained to national standards. In the UK, these are set by the Association for Respiratory Technology and Physiology
- **Immunology** can be helpful in the diagnosis but a negative test does not rule out OA
- **Fractional** exhaled nitric oxide (FeNO) and sputum eosinophilia are useful measures of airway inflammation and can be used to monitor deterioration at work and improvement away from work

Once all of the investigations relevant to the worker have been carried out, and results have been collated, a diagnosis of occupational asthma can normally be confirmed or excluded. The confirmation of a diagnosis remains a clinical judgement based on the results of multiple tests, and is best carried out in specialist centres.

If a diagnosis of occupational asthma is confirmed, then the worker will need continued support and advice from their specialist team, as a confirmed diagnosis is associated with adverse social, financial and psychosocial impacts[30,31].

These issues, along with management and compensation advice will be covered in the next article in this series. ■

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**Notes**
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*2 Newman Taylor AJ, Cullinan P et al. BOHRF guidelines for occupational asthma. Thorax 2005; 60(5): 364–366.*

*3 Fishwick D, Barber CM et al. Standards of care for occupational asthma: an update. Thorax 2012; 67(3): 278–280.*

*4 MRC dyspnoea scale/MRC breathlessness scale. Swindon: Medical Research Council. ohaw.co/MRCdyspnoea*

*5 Health and Safety laboratory Group of Occupational Respiratory Disease Specialists. Specialist occupational lung disease centres. ohaw.co/GORDSclinics*

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## *Further information*

- HSE online information on asthma: **www.hse.gov.uk/asthma**
- Work-related asthma statistics (2018): **ohaw.co/HSEasthma2018**
- Oasys and occupational asthma: **www.occupationalasthma.com**
- Updated standards of care for occupational asthma[3]: **ohaw.co/Fishwick2012**
- Canadian Centre for Occupational Health and Safety – includes a detailed list of potentially causative agents: **ohaw.co/CCOHSasthma**
- Health and Safety Laboratory Group of Occupational Respiratory Disease Specialists (GORDS): **ohaw.co/GORDS**
- British guideline on the management of asthma[27]: **ohaw.co/BTSasthma**
- NICE asthma guideline[24]: **nice.org.uk/guidance/ng80**