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Occupational eosinophilic cough conditions

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Occupational eosinophilic cough conditions

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This project was to improve understanding of emerging occupational respiratory conditions typified by chronic cough and airway eosinophilia. Chronic cough is associated with impaired quality of life and eosinophilic airway disorders may be associated with accelerated lung function decline. It is clear from the case reports that workplace allergens may induce cough-variant asthma and non-asthmatic eosinophilic bronchitis. These conditions may be more difficult to recognise as being occupational in nature given that by definition they lack some of the classical symptoms of asthma and the most common diagnostic tests may be normal. Patients with these conditions usually present with an isolated chronic and work-related cough. Cough-variant asthma may be confirmed with work-related changes in airway responsiveness. Eosinophilic bronchitis can only be confirmed by measuring sputum eosinophils. In the UK access to this type of physiological testing is limited to a small number of specialist centres. These tests may not form part of the routine diagnostic protocol and reliance on peak flow testing is likely to miss patients with cough-variant asthma and eosinophilic bronchitis. The recognition of these diseases may offer an opportunity to modify allergen exposures early, which is likely to improve prognosis for affected workers.

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EXECUTIVE SUMMARY

Objectives: To improve understanding of emerging occupational respiratory conditions typified by chronic cough and airway eosinophilia.

Main Points: Classical occupational asthma has been recognised for many centuries. An increasing number of reports of workers developing chronic occupational respiratory symptoms due to other variants of allergic airway disease have more recently emerged.

Cough-variant asthma and non-asthmatic eosinophilic bronchitis vary from classical occupational asthma in some important ways, both in terms of the symptoms reported, and in the diagnostic tests required. Objective confirmation of these conditions predominantly relies on serial measurements of eosinophils in induced sputum, tests that are not routinely performed in British patients with suspected occupational asthma. Accurate diagnosis is key, in order to differentiate occupational from non-occupational disease, and to allow appropriate occupational advice to be given. Diagnosis of these conditions may offer an earlier opportunity to identify occupational respiratory allergies and modify allergen exposures, in order to improve prognosis for affected workers.

Recommendations: Further longitudinal studies are required, to build on the current case report evidence-base, in order to better understand the relationship between occupational exposures, eosinophilic airway inflammation, and the risk of accelerated lung function decline.

1 INTRODUCTION

Occupational asthma is a preventable airway disease, which usually develops due to an allergy to an agent inhaled in the workplace [1]. It is estimated that this accounts for somewhere in the region of 9-15% of all new adult cases of asthma [2,3], making it the most frequently reported work-related airway disease in Britain [4]. In 2007 this equated to just over 300 new cases of occupational asthma reported by British respiratory and occupational physicians, although the true incidence is likely to be much higher [4].

Workers developing this condition often do so within the first 1-2 years of exposure [1,5], although longer latent periods do occur, particularly in workers exposed to bakery allergens [6]. Typical symptoms of occupational asthma include episodic wheezing, breathlessness, chest tightness and coughing, all of which may occur at or after work. Such work-related symptoms may be associated with allergic eye or nasal symptoms, and typically are less marked on rest days and holidays [1,5]. If the condition remains unrecognised, ongoing allergen exposure is associated with accelerated lung function decline [7], and chronic persistent asthma may develop. This form of chronic respiratory ill health may persist even after allergen exposure has ceased, requiring long-term medication, and health service utilisation. Occupational asthma is therefore associated with increased sickness absence rates, on average an estimated extra 2-10 work-days per year [8], and affected workers may also be forced to relocate or leave employment with subsequent loss of income, and benefit requirements [9-11]. These factors combine to produce a huge burden on society which has been estimated to cost between £121,000 – £176,000 over the lifetime of each male worker developing occupational asthma (based on figures from 2003) [8]. The Health and Safety Executive (HSE) has estimated that the over all costs to society from new cases of occupational asthma may be as high as £1.1 billion over a ten-year period [4].

Recent published guidelines have served to highlight the importance of rapid accurate diagnosis of occupational asthma, linked with removal from further allergen exposure [1,5], in terms of improving the prognosis for these patients. Accurate diagnosis is also critical in symptomatic workers who do not have occupational asthma, in order to avoid inappropriate employment advice, and subsequent adverse economic outcomes. Health surveillance and worker education are methods aimed at early recognition of possible cases in the workplace, and are legal requirements for allergen-exposed workers [13]. Many cases of occupational asthma however are not diagnosed via this route, presenting to primary [14,15] and secondary care [5]. The results of British studies suggest that occupational asthma remains under recognised, leading to delays in diagnosis [16]. The diagnostic process for such patients may also be complex [17], as

no single test is suitable for all cases [18], and access to specialist centres varies within the UK [19].

HSE has invested a great deal of effort in to reducing the incidence of occupational asthma, by increasing awareness, reducing exposures, and attempting to improve the diagnostic process for symptomatic workers. Although classical occupational asthma has been recognised for many centuries, an increasing number of reports of workers developing chronic occupational cough due to other types of allergic airway disease have more recently emerged [20-30]. The aim of this project is to review the published evidence relating to these conditions, in terms of causes, diagnosis, and prognosis for affected workers.

2 METHODS

Table 1 below shows the search terms utilised to identify possible relevant articles in Pubmed.

Table 1. Search terms and phrases utilised in literature review.

Search terms and phrases
Eosinophilic bronchitis
Cough variant asthma
Occupational eosinophilic bronchitis
Occupational cough variant asthma
Occupational eosinophilic cough

Three hundred and fifteen references articles were identified by the search, and the titles and abstracts were reviewed for relevance. The relevant articles were then reviewed by two respiratory clinicians and entered in to web based reference management too to aid tracking of references. In total there were one hundred and nine articles entered in to the reference management tool for review and potential inclusion in the final report.

3 EOSINOPHILIC AIRWAY CONDITIONS: DEFINITIONS

Classical asthma is a common respiratory disease in Britain, with approximately 6% of the adult population self-reporting this condition [31]. Patients with asthma often present with recurrent episodes of coughing, wheezing, shortness of breath and chest tightness, which may be precipitated by contact with allergens or irritants. These symptoms in part relate to changes in airway calibre, and hyper-responsive airways [32], which form the basis of established diagnostic tests for asthma. These tests include demonstrating variable airflow obstruction by examining serial peak flow records, documenting airway reversibility to inhaled bronchodilators, and measuring the level of airway responsiveness to non-specific inhaled irritants such as histamine and methacholine. Chronic inflammation is also present in asthmatic airways, with an associated increase in eosinophils, mast cells, and Th2 lymphocytes [33]. Untreated, this may lead to airway remodelling with goblet cell hyperplasia, reticular basement membrane thickening, vascular proliferation, and smooth muscle hypertrophy [32]. The resulting eosinophilic bronchial inflammation may be demonstrated by higher than normal numbers of eosinophils in the sputum of patients with active asthma [34], with a level of greater than 3% of sputum eosinophils being taken as an objective marker of poor asthma control [35].

In 1979, a new variant of asthma was described in which a chronic bronchodilator-responsive cough was the only presenting symptom [36]. In this condition, termed cough-variant asthma, sputum eosinophilia and bronchial hyper-responsiveness are still present, but the variable airway calibre (as measured by serial peak flows) of classical asthma is absent. Following this, a decade later, a further variant was also described, a condition termed eosinophilic bronchitis (without asthma) [37]. In this variant, again typified by chronic cough, sputum eosinophilia (percentage of sputum eosinophils greater than 3%) is present, but both bronchial hyper-responsiveness and variation in airway calibre are absent [38]. Shortly after this, a further eosinophilic airway variant, termed atopic cough, was also described [39]. This condition is reported to be one of the commonest causes of chronic cough in Japan [40], and shares many of the features of eosinophilic bronchitis, such as a bronchodilator-resistant dry cough with eosinophilic tracheobronchitis, in the absence of bronchial hyper-responsiveness or variable airflow obstruction [41,42]. There are however some important differences between the clinical features of these two related conditions, as atopic cough (unlike eosinophilic bronchitis) does not involve bronchoalveolar eosinophilia or airway remodelling, is less likely to progresses to classical asthma, and responds to treatment with antihistamines [42].

The recognition of these related but different eosinophilic airway conditions has led to a wide range of research aimed at a better understanding of the pathophysiology of asthma in general.

Studies of immune cells and cytokines in bronchial biopsy, sputum and lavage samples have demonstrated important similarities and differences between some of these conditions, particularly in the type and site of the inflammatory response [41,42].

4 EOSINOPHILIC AIRWAY CONDITIONS: PROGNOSIS

The symptoms of eosinophilic airway conditions usually respond well to inhaled corticosteroids, with an associated reduction in sputum eosinophil counts [43,44]. In eosinophilic bronchitis, where cough is usually the predominant symptom, inhaled steroids also result in a reduction in subjective cough severity scores, and cough reflex sensitivity to inhaled capsaicin [43].

In terms of prognosis, there is good evidence from longitudinal studies that over a third of patients with cough-variant asthma will develop clinical features of classical asthma when followed-up over a period of several years [45-47]. Small studies have also suggested that whilst inhaled steroids may reduce the risk of this transformation, classical asthma may still occur despite therapy [47].

Similar longitudinal studies have also investigated the prognosis of eosinophilic bronchitis, demonstrating that symptoms and sputum eosinophilia often recur within a few months if inhaled steroid therapy is not continued long term [48]. Classical asthma may also develop in these patients [49], and recurrent episodes of eosinophilic bronchitis may be associated with accelerated decline in lung function [48,49]. In some rare instances, the eosinophilic inflammation may be resistant to standard therapy, and progressive chronic airway obstruction may develop in the absence of airway responsiveness [50].

The prognosis for patients with atopic cough may be better, and although classical asthma may develop, this appears to occur much less frequently than in patients with cough-variant asthma. In a study of 82 patients with atopic cough followed for an average of just under 5 years, only one patient developed classical asthma. In the comparison group of 55 patients with cough-variant asthma however, classical asthma developed in 8 patients [47].

It is likely therefore that a continuum of eosinophilic airway disorders exists, ranging between non-asthmatic eosinophilic bronchitis and atopic cough at the milder end, with cough-variant asthma in the middle, and classical asthma at the more severe end of the range. Patients with milder forms of disease may develop all of the features of classical asthma over time, and early recognition of these conditions is heavily dependant on the demonstration of sputum eosinophilia.

5 OCCUPATIONAL EXPOSURES AND EOSINOPHILIC AIRWAY DISEASE

As far back as the early 1990s, it was suggested in Poland that occupational allergies in the baking industry could present as isolated attacks of coughing [20]. This followed interviews with a small series of patients with Baker's asthma, who reported attacks of coughing without wheezing, for 0.5-3 years prior to the development of typical asthma attacks. A longitudinal study was then carried out of a further 17 bakers with isolated work-related cough, who all had airway responsiveness, but did not report wheezing, and had no evidence of airflow obstruction. Over the two-year period of follow-up, 4 developed the full clinical picture of asthma, and coughing remained the only symptom for the remaining 13 workers. Although sputum eosinophil counts were not measured, it is likely that this was an early report of occupational cough-variant asthma, recognising the potential for this condition to progress to classical occupational asthma. More recently a further longitudinal study has been performed by the same group, using specific inhalation challenges and sputum examination to confirm that apprentice bakers may develop cough-variant baker's asthma in response to inhaled bakery allergens [51].

Over the last fifteen years, examining induced sputum for work/challenge-related increases in eosinophil counts has become routine practice in some centres, with a 1-2% increase in sputum eosinophilia being suggested as an additional useful diagnostic test for occupational asthma [52]. Over this period, a number of case reports (summarised in Table 2) have emerged of patients reporting work-related respiratory symptoms associated with isolated increases in sputum eosinophil counts, confirming the existence of a new occupational condition, known as (non-asthmatic) occupational eosinophilic bronchitis.

5.1 CASE REPORTS

5.1.1 ACRYLATE GLUE [22]

A 50 year-old female developed work-related shortness of breath, chest tightness, wheeze, dry cough and nasal symptoms, three months after starting a new job. She worked with glue containing cyanoacrylate and methacrylate, at a company manufacturing weather strips for cars. She had a 15-pack year smoking history, but had stopped smoking 20 years previously. There was no family history of atopy. Physical examination, chest X-ray and skin prick testing were all normal. A symptom questionnaire, spirometry, methacholine challenge, induced sputum and

bloods were completed whilst the patient was at work. Spirometry and methacholine challenge were normal, but she had 13% eosinophils in her sputum, and a blood eosinophilia. After a 3-week period off work, the patient's symptoms were much improved, and the eosinophil levels in her blood and sputum had returned to normal. After remaining off work for 3 months she underwent a specific inhalation challenge. Following the control day exposure she had no eosinophils in her sputum, but this increased to 5.8% eosinophilia 7 hours after a 30 minute exposure to the glue, associated with a recurrence of her respiratory symptoms.

5.1.2 BAKERY ALLERGENS

CASE 1 [25]

A 54 year-old male ex-smoker reported a four-year history of chronic cough and wheeze. He had worked as a baker for 36 years, and noticed that his symptoms were worse at work, and better during holidays. His lung function was normal, serial peak flows showed no diurnal variation, there was no airway responsiveness to methacholine, and the cough did not improve with inhaled bronchodilators. A specific inhalation challenge to lysozyme, an egg white protein, was associated with an increase in sputum eosinophils from 0% to 8%, without any associated change in lung function or airway responsiveness.

CASE 2 [28]

A 41 year-old non-smoker reported a three-year history of non-productive cough, with no wheeze or shortness of breath. He had worked as a baker for ten years, and noticed that the cough was worse at work and better on his rest days. Examination, chest x ray and routine bloods were normal. Skin testing was negative to common allergens, rye, oat, corn and soy flour but positive to wheat flour. Total IgE was raised (190kU/l) and serum IgE to wheat was positive. Spirometry was normal and there was <20% variability in peak flow. Provocation testing, sinus sinography, and 24 hr gastric monitoring were all negative. Induced sputum after a work shift showed raised eosinophils at 40%. He continued to work but was treated with inhaled steroids leading to a marked improvement in symptoms. After one month of treatment he was asymptomatic. At this time his sputum eosinophilia had reduced to 2%. He then left work, the steroid inhaler was stopped, he had no symptoms and his sputum showed 0% eosinophils. After a flour bronchial challenge he developed a non-productive cough, no change in FEV_1, but an increase in his sputum eosinophils to 54%.

CASE 3 [30]

A 51-year-old non-smoking female baker, presented with an 8-year history of work-related chronic cough, without wheezing or dyspnea. Examination, spirometry, and radiology were all normal. There was no evidence of airway responsiveness to methacholine, or significant daily variability in peak flow. Specific IgE to fungal α-amylase and to wheat flour were positive. Specific inhalation challenge with fungal α-amylase and with wheat flour precipitated a dry cough during the challenges, but no fall in lung function or increase in airway responsiveness were observed a day after the challenge. Differential cell counts in induced sputum samples demonstrated work-related increases in sputum eosinophils. These were measured at 1% after 2 weeks off work, and 4% at work. Further challenge testing confirmed this, with baseline sputum eosinophils of less than 2% increasing to 33% 24 hours after the α-amylase challenge, and to 12% 24 hours after the wheat flour challenge. The cough settled within three months of therapy with inhaled steroids.

5.1.3 DISINFECTANT (CHLORAMINE T) [26]

A 61 year-old non-smoking non-atopic female nurse developed a non-productive cough following ten years of exposure to a chloramine T containing disinfectant. A specific inhalation challenge was performed, which involved a placebo challenge with nebulised saline, which was not associated with any significant change in sputum eosinophilia. A week later the patient was exposed to the disinfectant by painting it on to a surface for 15 minutes. This exposure was associated with an increase in sputum eosinophilia from 1% at baseline, to 8% at 6 hours, and 11 % at 24 hours. There was however no associated increase in airway responsiveness or change in serial peak flow. In addition to the positive challenge, the patient demonstrated specific IgE to chloramines, and improved markedly following discontinuation of further chloramines T exposure.

5.1.4 EPOXY RESIN [21]

A 31 year-old non-smoking male reported finger eczema within a month of commencing work making reinforced plastics, with exposures to an epoxy resin hardening system. Over the next two-years the eczema progressed, affecting his eyelids, and he also developed cough and rhinitis which were clearly work-related. Investigations demonstrated normal lung function, a normal chest X-ray, a raised total IgE level, a mildly increased blood eosinophil count, and an increase in sputum eosinophilia. The patient was diagnosed with allergic rhinitis, and also suspected of

having asthma. He was therefore treated with a combination of theophylline, a bronchodilator (procaterol hydrochloride), and an antihistamine (repirinast). The cough initially improved with treatment, and resolved with a change to a different job. The allergic rhinitis also improved, and the cough did not recur when the anti-asthma medication was stopped.

Although the title of the case report suggests that this was a case of eosinophilic bronchitis due to epoxy resin, the authors actually concluded that this patient might have represented a case of occupational asthma. Without measurements of airway responsiveness, serial peak flows, or a specific inhalation challenge, it is not possible to assess which condition actually caused the occupational cough and sputum eosinophilia seen. The differential diagnosis for this case therefore includes classical asthma, cough-variant asthma, and non-asthmatic eosinophilic bronchitis. A further possible diagnosis is that the patient may simply have had occupational allergic rhinitis, a recognised cause both of chronic cough [53] and sputum eosinophilia [54], which improved initially with antihistamine therapy, and resolved with work relocation. Whilst this case report therefore confirms that anhydride epoxy resin exposures are a cause of occupational cough and sputum eosinophilia, it did not clearly establish that this was by inducing non-asthmatic eosinophilic bronchitis.

5.1.5 FORMALDEHYDE [27]

A 38 year-old woman who had worked in a laboratory for 10 years, developed cough and chest tightness after 9 years of work. She was found to have baseline increased sputum eosinophilia of 19%, which decreased after a two-week break from work to 11%. To confirm the diagnosis, she underwent a specific inhalation challenge to formaldehyde, following a nine-week break from work. On separate days, sputum eosinophilis were 3% following the control exposure, 4% after 30 minutes of formaldehyde exposure, and 22% after 120 minutes exposure. There was however no significant change in lung function or airway responsiveness following the specific challenge.

5.1.6 ISOCYANATES

CASE 1 [28]

A 44 year-old man reported a 6-month history of a work related dry cough, not associated with wheeze or shortness of breath. He had worked in a foundry for 8 years making cores, which involved exposure to methylene diphenyl isocyanate (MDI). He smoked 10 cigarettes a day, was not atopic, and had not previously suffered from any respiratory disease. Examination,

chests x-ray, routine bloods tests, spirometry and peak flow recordings were all normal. Induced sputum showed an eosinophil count of 35% after a work shift, and 0% while asymptomatic and not exposed at work. A specific bronchial challenge with MDI (up to a maximum concentration of 20 ppm for 30 minutes) led to a marked increase in the percentage of his sputum eosinophils up to 60%, with no associated change in FEV_1 or airway responsiveness to methacholine.

CASES 2 and 3 [29]

MDI has since been confirmed as a cause of occupational eosinophilic bronchitis in a Korean study of fifty-eight MDI-exposed workers in a car upholstery factory. This recorded symptoms, serum specific IgE, and performed MDI inhalation challenges. Two non-atopic workers were found with work-related symptoms, who had an increase in sputum eosinophils with MDI challenge, but showed no evidence of airway responsiveness, or fall in lung function with the challenge. The first of these workers was male, aged 54, with 6.6 years of exposure, whose sputum eosinophils increased from 1% to 46% with the challenge. The second was female, aged 50, with 4.3 years exposure, whose sputum eosinophils increased from 6% to 15% with the MDI exposure.

5.1.7 MUSHROOMS [24]

In 2002, a cross-sectional investigation of 69 Japanese mushroom farm workers was performed, aimed at identifying the aetiology of the work-related chronic cough reported in this workplace. Workers with work related respiratory symptoms on questionnaire underwent detailed clinical investigations, including skin prick testing, chest x-ray, pulmonary function tests, serology, bronchial hyper-responsiveness by methacholine challenge and sputum eosinophil count. Airborne endotoxin levels were also measured and found to be high in the harvesting and packing rooms. Two-thirds of workers reported work-related chronic cough, after excluding 2 workers who were diagnosed with extrinsic allergic alveolitis (EAA). Of these, 15 of the 42 workers were diagnosed with cough-variant asthma, and 3 more workers were diagnosed with eosinophilic bronchitis. The remainder of the workers were diagnosed with either postnasal drip (18 workers), or organic dust toxic syndrome (6 workers).

5.1.8 RUBBER LATEX [23]

A 31 year-old female nurse on a thoracic surgery ward developed a work- related chronic cough and urticaria associated with latex gloves. There was no associated wheeze or dyspnea. Examination, chest and sinus radiography, 24hr oesophageal manometry, pH monitoring, methacholine challenge, serial peak flow, and spirometry were all normal. Her induced sputum showed 80% eosinophils, and immunological tests confirmed latex allergy. A subsequent sixty-minute specific inhalation challenge with latex gloves was associated with severe rhino-conjunctivitis, and a non-productive cough. There was however no change in FEV_1, but a significant increase in sputum eosinophils. With one-month treatment of inhaled corticosteroid, her cough had improved markedly, and there were no detectable eosinophils in the sputum.

5.1.9 WELDING FUME [28]

A 48 year-old man developed a chronic cough, breathlessness and wheeze, three years after commencing employment as a welder, with exposures to aluminium and stainless steel. Despite the cough, he had remained at work for a further nine years, with inhaled corticosteroid therapy over the last two years. A diagnosis of occupational asthma was suspected, but a specific inhalation challenge in the laboratory, and in the workplace showed no significant changes in lung function or airway responsiveness. He therefore returned to work, and a month later was found to have sputum eosinophilia of 39%. He was therefore removed from work, which was associated with a reduction in sputum eosinophils to 26% at one month, and 14% at three months. In order to confirm the diagnosis, he had a further specific challenge, welding stainless steel for 30 minutes. Baseline sputum eosinophils were 13%, which increased to 51% by the end of the challenge day. A week later off work, the sputum eosinophil count fell to 7%, and rose markedly to 67% (associated with a return of his symptoms) when he went back to work.

Table 2. Case reports of occupational eosinophilic bronchitis.

Case	WR symptoms (duration)	Occupation (agent)	Diagnostic method	Sputum eosinophil count
50 F	Cough/wheeze/chest tightness/dyspnoea (1.75 years)	Car weather strip manufacturer (acrylate glue)	WR change SIC	At work =13% Off work =0% Increased: 5.8% (7 hours) 5% (24 hours)
54 M	Cough/wheeze (4 years)	Baker (lysozyme)	SIC	Increased 0% to 8%
41 M	Cough (3 years)	Baker (flour)	WR change SIC	At work =40% Off work =2% Increased to 54%
51 F	Cough (8 years)	Baker (wheat and alpha-amylase)	WR change SIC (wheat flour) SIC (α-amylase)	At work =4% Off work =1% Increased to 12% Increased 2% to 33%
61 F	Cough (not specified)	Nurse (disinfectant - chloramine T)	SIC	Increased: 1% (baseline) 8% (6 hours) 11% (24 hours)
38 F	Cough/chest tightness (1 year)	Laboratory worker (formaldehyde)	WR change SIC	At work =19% Off work =11% Increased: 3% (baseline) 4% (30 mins exposure) 22% (120 mins exposure)
44 M	Cough (6 months)	Foundry (MDI)	WR change SIC	At work =35% Off work =0% Increased to 60%
54 M	Chronic cough (not specified)	Car upholstery (MDI)	SIC	Increased 1% to 46%
50 F	Chronic cough (not specified)	Car upholstery (MDI)	SIC	Increased 6% to 15%
31 F	Cough (5 years)	Theatre nurse (latex)	WR change SIC	At work =80% Off work =0% Increased
48 M	Cough/chest tightness (9 years)	Welder (stainless steel)	WR change SIC	At work =39% Off work 1 month =26% Off work 3 months =14% Return to work = 67% Increased 7% to 51%

M = male
F = female
WR = work-related
SIC = specific inhalation challenge
MDI = methylene diphenyl diisocyanate

6 DISCUSSION

It is clear from these published case reports that the same high and low molecular weight workplace allergens, which have long been accepted as causing classical asthma, may also induce both cough-variant asthma and non-asthmatic eosinophilic bronchitis. These conditions may be more difficult to recognise as being occupational in nature given that by definition they lack some of the classical symptoms of asthma (such as wheeze and chest tightness), and the most commonly utilised confirmatory diagnostic tests (such as measurements of serial peak flow, or airway responsiveness to histamine/methacholine) may be normal. Although patients with these conditions usually present with an isolated chronic and work-related cough [21,23,26,28,30], this is not always the case, and other symptoms suggestive of classical asthma may be present [22,25,27,28]. Although cough-variant asthma may be confirmed with work-related changes in airway responsiveness, eosinophilic bronchitis can only be objectively confirmed with measurements of sputum eosinophils. It should be noted however, that sputum eosinophilia is not specific for asthma variant conditions, as it may also occur in a number of other conditions including allergic rhinitis and chronic obstructive pulmonary disease [54].

In the UK, access to the full range of this type of physiological testing, particularly specific inhalation challenges, is limited to a small number of specialist centres [19]. These tests may not therefore form part of the routine diagnostic protocol for workers with possible occupational asthma [18], and reliance on serial peak flow testing is likely to miss patients with occupational cough-variant asthma and eosinophilic bronchitis. A lack of work effect in serial peak flow, absent airway responsiveness, and a lack of reduction in FEV_1 after specific or workplace challenge, may all be taken as falsely reassuring, leading to this group of workers being given inappropriate occupational and compensation advice.

Chronic cough is associated with impaired quality of life [55], and eosinophilic airway disorders may be associated with accelerated lung function decline [7,48-50]. The recognition of occupational cough-variant asthma and eosinophilic bronchitis may therefore offer an opportunity to modify allergen exposures early, which is likely to improve prognosis for affected workers. If the condition is driven by a workplace allergen, it seems inherently likely that avoiding further exposures will prevent the development of occupational asthma in some cases. It seems reasonable therefore to advise that these conditions be considered in symptomatic allergen exposed workers, and to develop referral pathways with adequately equipped specialist centres for affected workers. As with classical occupational asthma, objective confirmation to ensure accurate diagnosis is vital, to differentiate work-related respiratory symptoms due to allergy, from those that reflect irritant responses to non-specific

dusts, gases, vapours and fumes [56-57]. A good example of this is in baking industry, where, in cross-sectional surveys, work-related respiratory symptoms are reported by 3-19% of exposed workers, but only approximately a third to a half of these can be attributed to sensitisation to bakery allergens [58].

In a relatively recent publication [18], UK specialist occupational respiratory experts ranked the diagnostic tests that should be available for patients with suspected occupational asthma. Assessment of sputum eosinophils was at that time felt to be purely a research tool, and did not routinely need to be available. It is highly likely therefore that there will need to be a change in the diagnostic protocols for UK workers, with an increased availability of sputum cell counts.

RECOMMENDATIONS

- To develop referral pathways with adequately equipped specialist centres for affected workers
- Further longitudinal studies are required, to build on the current case report evidence-base, in order to better understand the relationship between occupational exposures, eosinophilic airway inflammation, and the risk of accelerated lung function decline.

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Occupational eosinophilic cough conditions

This project was to improve understanding of emerging occupational respiratory conditions typified by chronic cough and airway eosinophilia. Chronic cough is associated with impaired quality of life and eosinophilic airway disorders may be associated with accelerated lung function decline. It is clear from the case reports that workplace allergens may induce cough-variant asthma and non-asthmatic eosinophilic bronchitis. These conditions may be more difficult to recognise as being occupational in nature given that by definition they lack some of the classical symptoms of asthma and the most common diagnostic tests may be normal. Patients with these conditions usually present with an isolated chronic and work-related cough. Cough-variant asthma may be confirmed with work-related changes in airway responsiveness. Eosinophilic bronchitis can only be confirmed by measuring sputum eosinophils. In the UK access to this type of physiological testing is limited to a small number of specialist centres. These tests may not form part of the routine diagnostic protocol and reliance on peak flow testing is likely to miss patients with cough-variant asthma and eosinophilic bronchitis. The recognition of these diseases may offer an opportunity to modify allergen exposures early, which is likely to improve prognosis for affected workers.

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