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## CASE BASED DISCUSSION

# Metalworking fluids: a new cause of occupational non-asthmatic eosinophilic bronchitis

R E Wiggans,<sup>1,2</sup> C M Barber<sup>2,3</sup>

**Ruth E Wiggans (REW):** A 52-year-old man was referred with chronic cough of increasing severity over the last 4 years. The cough was productive of green sputum and he experienced coughing attacks weekly. He reported no other respiratory symptoms. He had a sore throat following coughing bouts but denied other upper airway complaints. He was otherwise well with no systemic symptoms. His cough had improved following a 2-week summer holiday, and subsequently deteriorated following his return to work.

A chest X-ray organised in primary care was normal. Three years earlier, his general practitioner increased his lansoprazole from 15 to 30 mg once daily for cough. This had not helped although treatment continued. His past medical history included treated obstructive sleep apnoea and hypertension for which he took bendroflumethiazide and losartan; the latter substituted for his ACE inhibitor 3 years earlier. He recalled no personal or family history of asthma or atopy and was a lifelong non-smoker. He had kept budgerigars until 6 months previously when the last bird died.

He had worked for 12 years as a computer numerical control (CNC) machine setter and operator, machining metal parts used to make tools for woodworking. He machined bronze, brass, leaded mild steel, high-speed steel and aluminium pieces to the desired specification. He operated five machines in a single area of the factory, adjacent to where ash handles were turned. He was the sole CNC operator turning metal components in the factory and was not aware of any colleagues reporting respiratory symptoms.

Water-based metalworking fluids (MWFs) were used on all five machines. Each machine collected and recirculated MWFs via its own sump. For the last 4 years, the fluids had occasionally become 'foul smelling' and sometimes changed colour from a translucent blue to a chocolate brown. The work-site did not perform dip-slide fluid analysis or use biocide contrary to agreed industry practice. The patient reported exposure to MWF mist when opening the machine doors and cleaning with compressed air. He wore a non-fit tested disposable paper mask for respiratory protective equipment.

Physical examination of the patient was normal. Spirometry revealed an FEV<sub>1</sub> of 3.17 L (83% predicted), FVC of 3.9 L (81%) and a FEV<sub>1</sub>/FVC ratio of 104%. FE<sub>NO</sub> was 92 parts per billion (ppb). TL<sub>CO</sub> was 12.4 (116%) mmol/min/kPa and K<sub>CO</sub> 2.29 (160%) mmol/min/kPa/L. Total IgE was raised at 122 KU/L, peripheral eosinophils normal at  $0.13 \times 10^9/L$  and specific IgG to aspergillus,

budgerigar and pigeon within normal limits. A high resolution CT (HRCT) performed midway through a normal working week revealed mild gas trapping on expiratory views.

**Chris M Barber (CMB):** A priority in this case is to understand whether the cough is being aggravated by a workplace exposure, or is a symptom of an occupational lung disease. This distinction is important as occupational conditions commonly deteriorate with ongoing exposure to the offending agent, and prognosis is better with early recognition and exposure modification. An accurate diagnosis is important to avoid unnecessary change in a patient's work. In addition, any diagnosis of an occupational lung disease has potential implications for other exposed workers who are also at risk.

His exposure to MWFs is highly relevant. They are a common cause of occupational asthma (OA) in Britain and the leading cause of occupational extrinsic allergic alveolitis (EAA).<sup>1</sup> Occupational respiratory diseases associated with water-containing MWFs have increased in incidence since MWFs have widely replaced neat oil coolants. Used MWFs are recirculated via stand-alone or shared-sump reservoirs, with those containing water at risk of microbial contamination. These microbes and their constituents are aerosolised in MWF mist, which workers may then inhale. In addition to bioaerosols, previous challenge studies have established chemical constituents of MWFs including ethanalamine and biocides to be causes of OA.<sup>2</sup> Metals dissolved in MWFs have also been reported to cause asthma, but none used in this case were known causes. Thus, although exact mechanisms are not fully understood, inhalation of both chemical and biological allergens in MWF mist is thought to cause OA in susceptible workers.

MWF-related occupational lung diseases may occur in outbreaks. Such outbreaks are logistically challenging to manage, as although hundreds of workers may report work-related symptoms, the majority do not have an occupational disease. Work-related cough has been common among past outbreaks, being attributed to conditions including EAA, OA, work-aggravated asthma, bronchitis and rhinitis. The cause of MWF-related disease can be difficult to ascertain, as exposures may have changed before a worker is assessed, for example by relocation to another area or indeed if an individual loses their job. It is vital to obtain a detailed history from patients to understand as precisely as possible the timing of their symptoms, their relationship with work, the details of their working



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environment and exposures, and the implications of a change in work circumstances.

His work-related cough and high FE<sub>NO</sub> suggests work-related asthma. An OASYS serial peak flow analysis was requested to examine this further. OASYS measurements are typically made over a period of 3–4 weeks, and any change in working practices or medication over this time may affect the results. Decisions delaying treatment are made on a case-by-case basis, being determined by the symptoms and stability of the patient.

**REW:** Two months later, his OASYS demonstrated minimal diurnal variation (DV) at and away from work (5.6% and 6.5%, respectively), with a maximal DV of 13%. The work-effect index (WEI) was negative at 1.64. As the WEI was negative but DV borderline, a mannitol challenge was requested to look for further evidence of airway hyperresponsiveness.

The test was performed during a routine working week on no inhaled corticosteroids (ICS). The maximum % change in FEV<sub>1</sub> was 2.8 following the complete dose of 635 mg osmohale, with a maximum FEV<sub>1</sub> change between doses of –1.4%. A repeat FE<sub>NO</sub> taken midway through the working week was 94 ppb. An induced sputum sample done at the same time contained 14% eosinophils. Occupational eosinophilic bronchitis was suspected, and the patient returned following a week off work for a repeat FE<sub>NO</sub>. At this point, FE<sub>NO</sub> had dropped to 11 ppb. A diagnosis of occupational non-asthmatic eosinophilic bronchitis (NAEB) was made and the patient commenced on ICS. He was provided with written confirmation of the diagnosis and recommendations about how to reduce further MWF exposures. Work provided fit-tested half-face disposable masks and the patient reduced his use of compressed air. At his next appointment, a midweek FE<sub>NO</sub> on ICS was 18 ppb and his cough had almost disappeared.

**CMB:** In the absence of significant peak expiratory flow rate (PEFR) variation, DV and measurable airway responsiveness classical asthma is unlikely. The WEI is negative, suggesting work-related changes in airway calibre do not explain his symptoms. EAA is also unlikely to be the cause of his cough, given his HRCT and lung function. In the absence of classical asthma, the very high FE<sub>NO</sub> and sputum eosinophilia are suggestive of NAEB. The work-related change in FE<sub>NO</sub> confirms that this is occupational NAEB, further reinforced by the response to inhaled steroid and reduced exposure.

To our knowledge, this is the first case of NAEB caused by MWF exposure. NAEB is defined as a chronic productive cough without symptomatic or physiological evidence of variable airflow obstruction, normal airway responsiveness and sputum eosinophilia >3%. It accounts for between 10% and 30% of cases of chronic cough referred for specialist assessment and tends to be more common in non-smokers. The condition has been reported to have been caused by a small number of occupational agents also recognised to cause OA including acrylates, isocyanates, flour,  $\alpha$  amylase, chloramine, styrene, formaldehyde, latex and stainless steel welding.<sup>3</sup> Since a number of

agents present in MWFs can cause OA, it is plausible that they cause NAEB.

Asthma and NAEB share common pathological features. High levels of eosinophils have been observed in sputum, bronchoalveolar lavage and biopsy in both conditions. However, NAEB is associated with increased superficial airway mast cell infiltration, unlike the smooth muscle infiltration associated with asthma. This superficial airway infiltration may explain the prominence of cough in NAEB and the absence of airway remodelling and hyperresponsiveness.<sup>4</sup> Furthermore, this superficial airway infiltration and subsequent inflammation may expose afferent nerve fibres involved in the cough reflex, increasing symptoms and aggravating the inflammatory response.

There are no long-term follow-up studies investigating outcomes in occupational NAEB. Evidence from the few follow-up studies in non-occupational NAEB suggests that over two-thirds of affected individuals continue to be symptomatic 1 year after diagnosis, with around 10% going on to develop more classical features of asthma.<sup>5</sup> For this patient, removal from exposures would be ideal to present the best outcome for symptom control. Unfortunately, relocation is not always possible as employment opportunities carrying the same skill level, payment and job satisfaction may not be available. Though employers have a responsibility to relocate workers wherever possible, they are not always able or willing to do this. Occupational NAEB should be considered in patients with chronic cough who work with fumes, dusts, gases or vapours, particularly if the cough improves on rest days or holidays.

**Twitter** Follow Ruth Wiggins at @wigruth

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