Diesel exhaust causing low-dose irritant asthma with latency?

Femi Adewole1,2, Vicky C. Moore2, Alastair S. Robertson2 and P. S. Burge2

Background Diesel exhaust exposure may cause acute irritant-induced asthma and potentiate allergen-induced asthma. There are no previous reports of occupational asthma due to diesel exhaust.

Aims To describe occupational asthma with latency in workers exposed to diesel exhaust in bus garages.

Methods The Shield database of occupational asthma notifications in the West Midlands, UK, was searched between 1990 and 2006 for workers where diesel exhaust exposure was thought to be the cause of the occupational asthma. Those without other confounding exposures whose occupational asthma was validated by serial peak expiratory flow (PEF) analysis using Oasys software were included.

Results Fifteen workers were identified with occupational asthma attributed to diesel exhaust. Three had validated new-onset asthma with latency. All worked in bus garages where diesel exhaust exposure was the only likely cause of their occupational asthma. Occupational asthma was confirmed by measures of non-specific reactivity and serial measurements of PEF with Oasys scores of 2.9, 3.73 and 4 (positive score > 2.5).

Conclusions The known non-specific irritant effects of diesel exhaust suggest that this is an example of low-dose irritant-induced asthma and that exposures to diesel exhaust in at least some bus garages are at a sufficient level to cause this.

Key words Diesel exhaust; Oasys; occupational asthma; serial peak flows.

Introduction Diesel exhaust has caused acute irritant-induced asthma following a single large exposure from a diesel railway engine [1]. It has also acted as an adjuvant for sensitization to aeroallergens [2]. In vitro exposure to diesel exhaust results in release of interleukin (IL)-4 and histamine from basophils [3]. Exposure to diesel exhaust particles at 200 µg/m3 can cause sputum neutrophilia without changes in forced expiratory volume in 1 s (FEV1) in healthy volunteers [4]. Exposure to 300 µg/m3 in asthmatics, however, has resulted in a minor increase in methacholine reactivity [5]. Occupational asthma from diesel exhaust exposure has not been previously described [6].

Some of the highest exposures to diesel exhaust occur in bus garages in cold climates, where the buses are warmed up with running engines for some time before leaving. There have been growing concerns about adverse health effects of exposure to diesel exhaust. These include various effects on the respiratory system, cardiovascular and coagulation profile as well as possible carcinogenicity [7].

Methods The SHIELD database, a surveillance scheme for occupational asthma in the West Midlands, UK [8], identified 15 workers with occupational asthma attributed to diesel exhaust since the database started in 1990. In three of them, there was objective confirmation of occupational asthma from non-specific reactivity and serial peak expiratory flow (PEF) measurements and no other identified exposures apart from diesel exhaust. They form the basis of this report. Each carried out 2 hourly serial measurements of PEF from waking to sleeping including periods at and away from work. These were analysed with the Oasys software, an Oasys score > 2.5 or an area between the curves of ≥15 l/min/h is indicative of a significant occupational effect [9]. Non-specific reactivity to methacholine was measured by the Yan method at presentation and follow-up.

Results All the three workers reported worked in bus garages where diesel buses were run indoors, engine tuning

1Department of Medicine, Obafemi Awolowo University/Teaching Hospitals Complex, Ile-Ife, Nigeria.

2Occupational Lung Disease Unit, Birmingham Heartlands Hospital, Birmingham, UK.

Correspondence to: Femi Adewole, Department of Medicine, Obafemi Awolowo University, Ile-Ife, Nigeria. Tel: +234 8034074930; e-mail: adewolef@yahoo.co.uk

© The Author 2009. Published by Oxford University Press on behalf of the Society of Occupational Medicine. All rights reserved. For Permissions, please email: journals.permissions@oxfordjournals.org
was done in the main garage and rolling roads were present for servicing and testing running buses. All had wheezing and breathlessness, which started for the first time while working on buses indoors, with improvement on days off and on holidays; all took inhaled corticosteroids. Their details are shown in the Table 1.

Worker 1: a mechanic who serviced running diesel engines and emission tested running buses (on rollers) in the garage without exhaust extraction and with exhaust extraction in the service bay. He improved when recovering broken down buses outside. He is now on long-term sick leave as permanent relocation has not been possible.

Worker 2: a tyre fitter and inspector working inside the bus garage while engines were running. He eventually retired from work. His garage and buses were particularly old.

Worker 3: a coachbuilder working next to a roller test bed where eight buses were run for emission tests twice weekly (Figure 1). He continued to have night-time symptoms and eventually resigned to avoid further exposure.

Discussion
We have reported three workers with good evidence of occupational asthma from their history supported by serial

<table>
<thead>
<tr>
<th>Worker</th>
<th>Description</th>
<th>Details</th>
<th>Improvement</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Mechanic servicing running diesel engines and emission tested running buses</td>
<td>Improved when recovering broken down buses outside. He is now on long-term sick leave.</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Tyre fitter and inspector working inside the garage while engines were running</td>
<td>Eventually retired from work.</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Coachbuilder working next to a roller test bed where eight buses were run</td>
<td>Continued to have night-time symptoms and eventually resigned.</td>
<td></td>
</tr>
</tbody>
</table>

Table 1. Clinical and occupational characteristics of the workers

<table>
<thead>
<tr>
<th>Latency (years)</th>
<th>Age</th>
<th>Atopic</th>
<th>Smoking</th>
<th>Methacholine PD$_{20}$ ($\mu$g)$^a$</th>
<th>Peak flow record</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>5</td>
<td>+</td>
<td>Never smoker</td>
<td>2772</td>
<td>Exposed 3000</td>
</tr>
<tr>
<td>2</td>
<td>1.5</td>
<td>-</td>
<td>Ex-smoker</td>
<td>178</td>
<td>Unexposed 375</td>
</tr>
<tr>
<td>3</td>
<td>54</td>
<td>+</td>
<td>Never smoker</td>
<td>881</td>
<td>Oasys score 52</td>
</tr>
</tbody>
</table>

PD$_{20}$, dose of methacholine producing a 20% fall in FEV1.

$^a$Normal PD$_{20} > 2000 \mu$g methacholine.

Figure 1. Maximum, minimum and mean daily Oasys plot of Worker 3. The top part of the chart shows the mean diurnal variation (DV) for each day. The middle of the chart shows the maximum, mean and minimum peak flow for each day. The work periods are the shaded areas and the rest periods are blank. The lines containing numbers in this part of the chart are scores for complexes (seven complexes in total for this record). The black continuous line is the mean PEF, the upper line the maximum PEF and lower line the minimum PEF for each day. At the bottom of the record are the days and dates of the record. The dotted line across the middle of the record is the workers’ predicted PEF. The record shows deterioration in 5/5 workweeks and improvement in 4/4 weekends. His Oasys score is 4.00 in this record.
measurements of PEF and positive Oasys analysis, where diesel exhaust was the only identified exposure. All had new-onset asthma with long latent intervals from first exposure to first symptom, without any large acute exposure. They therefore do not fulfil the criteria for acute irritant-induced asthma. Work-aggravated asthma is a term that is often loosely used but implies that the asthma would have occurred anyway without the specific exposure and that the mechanism of aggravation is not allergic. It is usually identified in a worker with current asthma whose asthma deteriorates regularly on first exposure to an irritant exposure i.e. without latency, and without sufficient irritant exposure to precipitate asthma in previously normal workers. It could also result from a similar irritant mechanism in a worker who develops asthma for another reason during exposure to a low-level irritant. This requires the identification of a non-occupational cause of adult-onset asthma. This may include drugs such as beta blockers and salicylates, severe bronchial infection, acute irritant exposures away from work and hormone-associated asthma in females. If the adult-onset asthma is cryptogenic, any attribution to a cryptogenic aetiology has to be made on statistical rather than clinical grounds. In practice, most exposures occurring for the first time in adult life are encountered at work, as environmental causes encountered in childhood usually cause asthma before starting work. The incidence of adult-onset asthma in the general population is 0.9/1000/year [10]; this includes asthma due to work exposures that are the commonest identified cause of adult-onset asthma.

The three workers reported here were selected from a group of 15 whose asthma was probably caused by diesel exhaust. All the other 12 had other possible (but less likely) causes of their asthma. The three selected were not exposed to any other cause of recognized occupational asthma and did not have any evidence of childhood asthma.

Most occupational asthma with latency is thought to be due to sensitization, but low-level irritation has been proposed as a mechanism for occupational asthma with latency [11], in a similar manner to irritant-induced contact dermatitis. The least confounded example of low-dose irritant-induced asthma is in athletes doing endurance events in cold weather, where inhalation of cold dry air is the only identified exposure. Around 50% of elite cross-country skiers develop new-onset asthma while training. Bronchial biopsy studies show bronchial inflammation with severe basement membrane thickening similar to (but more extensive than) seen in allergic asthma [12]. Diesel exhaust has been shown to cause bronchial inflammation in volunteers [3,4], whether the mechanism in our patients is allergic, irritant or a combination awaits methods of differentiating between low-dose irritation and sensitization, but on current evidence would best be classified as occupational asthma due to chronic low-dose irritation.

Individual susceptibility is likely to be involved in low-dose irritant-induced asthma, as well as asthma due to sensitization. In the original report by Brooks et al. [11], atopy was found to be a predisposing factor; two of the current workers were atopic in terms of positive skin prick tests to common environmental antigens (present in 30–50% of the general population). The latent intervals in the present study were much longer than in Brooks’ report, which (arbitrarily) excluded workers with >4 months exposure to the irritant before symptoms developed. A cross-sectional study of bus garage workers has shown more cough and sputum and wheezing than blue-collar workers but no relationship between FEV1 and length of employment [13]. If individual susceptibility was important, there is unlikely to be any consistent relationship between the length of exposure and disease: those with the longest exposures are likely to be those least susceptible.

The control of diesel exhaust exposure in bus garages poses problems. Many older diesel engines take some time to warm-up sufficient for safe running in cold weather. Local exhaust extract fitted to the vehicle exhaust is ideal, but cannot be used during emission testing, a feature in all the workers reported. Bus garages are rarely designed so that fixed extract systems are close to parked vehicles. The identification of diesel exhaust as a cause of asthma should result in much tighter control of emissions in the workplace, and particularly in bus garages and underground car parks or mines where diesel engines are run.

### Key points

- Diesel exhaust in bus garages can cause new-onset occupational asthma with latency.
- Occupational asthma with latency may be due to low-dose irritant effects as well as hypersensitivity.
- Levels of exposure to diesel exhaust in at least some bus garages are sufficient to cause occupational asthma.

### Conflicts of interest

None declared.

### References

3. Devouassoux G, Saxon A, Metcalfe DD et al. Chemical constituents of diesel exhaust particles induce IL-4


