Airway inflammation in cement production workers

Anne Kristin M Fell,1,2 Liv Ingunn B Sikkeland,3 Martin Veel Svendsen,1 Johny Kongerud2,4

ABSTRACT
Objective Cement aerosol exposure is associated with increased morbidity of airway disease among exposed workers. Our aim was to compare levels of inflammatory cells and soluble inflammatory markers in induced sputum samples from cement production workers between exposed and unexposed periods, and to compare these variables between cement workers and references.

Methods 35 healthy, non-smoking aerosol-exposed cement production workers from Norway provided a blood sample and performed induced sputum and spirometry after 5 days without exposure and during a period of exposure. These values were compared with those from an internal low-exposed reference group of 15 office workers and an external reference group of 39 non-exposed workers. Differential cell counts and inflammatory markers were assessed.

Results Median thoracic aerosol concentration over one work shift (8 h) was 0.6 mg/m³ (range 0.2–8.1) in maintenance workers and 1.75 mg/m³ (0.2–15.5) in furnace department workers. The median percentage of airway neutrophils in both groups combined was 51% (32–66) in the exposed period, which was significantly higher than in both the unexposed period (38%; 23–55) (p=0.04) and the external reference group (30%; 19–44) (p=0.001). Median interleukin-1β concentration was elevated compared with both office workers (p=0.05) and the external reference group (p=0.006).

Conclusions A significantly higher percentage of neutrophils was observed in cement production workers during the exposed period compared with both the non-exposed period and the external reference group, and corresponded with elevated IL-1β concentration. These data indicate that cement aerosol exposure in concentrations below the Norwegian occupational limits (respirable dust 5 mg/m³; total dust 10 mg/m³) may cause airway inflammation.

BACKGROUND
Cement particles are the major constituent of airborne dust in the cement production industry and are an important component of inorganic aerosols in the construction industry worldwide. Portland cement, the most commonly used cement, is a mixture of calcium oxide (60%–67%), silicon dioxide (17%–25%), aluminium trioxide (3%–8%) and ferric oxide (0%–5%).1 Published studies have shown that aerosol exposure during cement production and handling is associated with increased morbidity of airway diseases among workers in these industries.2–5 However, there is contradictory evidence of impairment of lung function in cement aerosol-exposed populations.6–17

Although the relationship between exposure to cement aerosol and respiratory diseases is unclear, there is strong evidence of an association between skin contact and the occurrence of allergic dermatitis, especially when water is added to cement.18 A similar mechanism could be suspected in the airways, because the alkaline properties of cement dust can cause irritation of the mucous membranes.11 8

What this paper adds
- No previous studies have reported on the use of biological materials (eg, bronchoalveolar lavage, biopsies or sputum) to detect early inflammation in cement production workers.
- A significantly higher percentage of neutrophils in sputum was observed in cement production workers during the exposed period compared with the non-exposed period and with the external reference group.
- Spirometric surveillance should be carried out at regular intervals until results from follow-up studies are completed and show if the increased percentage of neutrophils, as observed in our study, represents an early stage of respiratory disease.

MATERIALS AND METHODS
Subjects
Subjects were recruited from a cement plant in southern Norway that employs 78 production
workers in furnace and maintenance departments and 25 office workers. Only male workers were employed in these departments at the time of recruitment. All non-smoking, aerosol-exposed production workers were invited to participate. Never-smokers and ex-smokers who had stopped smoking at least 3 years before the examination were categorised as non-smokers. Aerosol-exposed workers were defined as workers who spent more than 50% of their working time in dusty areas. Eligible subjects were identified from the company registry of workers and were interviewed about their work tasks and aerosol exposure.

A total of 45 non-smoking males who worked more than 50% of their work shifts in dusty areas were eligible. Four cement workers were excluded because they left work during the study period (change of employer), two workers were excluded because of an inability to produce sputum of sufficient quality, and four workers did not wish to participate, leaving 35 workers who were included in the analyses. None of the workers not participating in the study reported respiratory disease, but one worker who left the company during the study period reported occasional wheezing and cough during the night.

The male office workers, who spent less than 10% of their working time in areas with dust exposure, were invited to participate as an internal reference group (office workers). All 15 non-smoking, healthy, male office workers were included. The external reference group comprised 39 non-smoking, non-exposed healthy students and hospital workers from a regional hospital.

All subjects received verbal and written information. Informed voluntary consent was obtained from each subject. The regional ethics committee approved the protocol.

The population characteristics and the lung function variables are shown in table 1.

Information on previous respiratory disease, respiratory symptoms, allergy and smoking habits was collected using a self-reported questionnaire on the day of the first consultation.

All subjects included in the study completed a Norwegian modification of the British Medical Research Council questionnaire on respiratory symptoms. None of the workers or references reported lower airway symptoms (cough more than 3 months during the past 3 years or attacks of wheezing or dyspnoea during the past 12 months). Twelve of the exposed workers (34%) and six of the office workers (40%) reported seasonal allergic symptoms (rhinitis and/or eye symptoms). The mean concentration of IgE in serum was 49 IU/ml (95% CI 10 to 120 IU/ml) as normal.

The study was designed to investigate changes in inflammatory cells and markers in cement production workers as a result of exposure. The workers were examined twice; these examinations were conducted at the same time of day. The first examination took place after a period of at least 5 days without work or aerosol exposure (T1). The second investigation was performed after a period of at least 2 weeks of regular work (T2). For the exposed workers, the order of the two examinations was determined by the shift plan for each worker. The two examinations were also performed in office workers to provide an internal reference group for comparing the responses of office workers and production workers. T1 was always the first of the two examinations for the office workers. We were able to examine the external reference subjects only once.

The furnace department workers were examined in 2005, and the maintenance and office workers in 2007. For the participants with known seasonal airway allergy, we avoided the time of year when their allergic symptoms appeared for all examinations. If a worker reported respiratory infection within 3 weeks of the planned sputum induction, the examination was postponed.

Blood samples were obtained before the spirometry and induced sputum measurements. Spirometry was performed using a dry-bellow spirometer (Vitalograph, Buckingham, UK). Norwegian reference values were used, and the manoeuvres were performed according to the American Thoracic Society guidelines.

### Sputum induction

Induced sputum was obtained and processed as described by Sikkeland et al using an ultrasonic DeVilbis 2000 nebuliser (DeVilbis, Somerset, Pennsylvania, USA) with an output of 1.5 ml/min. Aerosols of hypertonic saline solutions at concentrations of 3%, 4% and 5% were inhaled, each for 7 min, unless the forced expiratory volume in 1 s (FEV1) declined by more than 10% between inhalations. In subjects who exhibited a decline in FEV1 of more than 10%, the saline concentration remained the same for subsequent inhalations. If the FEV1 declined by more than 20% from the baseline value, the procedure was discontinued. Subjects were asked to expectorate sputum every 7 min. No bronchodilator was given before inhalation of the hypertonic saline solutions. The subjects were advised to blow their nose and rinse their mouth with water before coughing the sputum sample. The whole sample was processed within 2 h. Dithiothreitol (DTT) was used to dissolve the sputum plugs. At least 500 non-squamous cells were counted, and the cytopsin slides were stained with May Grünwald–Giemsa (Diff-Quik, Medion Diagnostics, Düdingen, Switzerland). 25

## Table 1 Characteristics of cement production workers, office workers and external reference workers

<table>
<thead>
<tr>
<th>Variable</th>
<th>Cement production workers (n=35)</th>
<th>Maintenance department (n=20)</th>
<th>Office workers (n=15)</th>
<th>ERG (n=39)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Furnace department</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Age (years)</td>
<td>37 (39 to 45)</td>
<td>39 (43 to 45)</td>
<td>51 (47 to 56)</td>
<td>40 (35 to 45)</td>
</tr>
<tr>
<td>Years employed</td>
<td>11 (5 to 17)</td>
<td>15 (10 to 20)</td>
<td>21 (16 to 26)</td>
<td></td>
</tr>
<tr>
<td>FEV1, % predicted</td>
<td>90 (84 to 96)</td>
<td>102 (95 to 108)</td>
<td>95 (88 to 102)</td>
<td>99 (95 to 103)</td>
</tr>
<tr>
<td>FVC, % predicted</td>
<td>92 (85 to 97)</td>
<td>108 (101 to 115)</td>
<td>99 (92 to 106)</td>
<td>105 (100 to 110)</td>
</tr>
<tr>
<td>FEV1/FVC, %</td>
<td>80 (77 to 84)</td>
<td>77 (74 to 80)</td>
<td>78 (75 to 81)</td>
<td>78 (76 to 80)</td>
</tr>
<tr>
<td>White blood cells, 10⁹/l</td>
<td>5.8 (5.3 to 6.3)</td>
<td>6.1 (5.3 to 6.9)</td>
<td>5.7 (5.2 to 6.1)</td>
<td></td>
</tr>
<tr>
<td>CRP, mg/l</td>
<td>1.2 (0.8 to 1.6)</td>
<td>3.0 (0.3 to 5.7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ECP, µg/l</td>
<td>8.7 (6.5 to 10.8)</td>
<td>8.7 (6.9 to 10.6)</td>
<td></td>
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</tbody>
</table>

Data are presented as means (95% CI) at baseline (T1). CRP and ECP levels were not measured for furnace department workers or external controls. White blood cells were not measured for furnace workers.

*Serum measurements.

CRP, C-reactive protein; ECP, eosinophil cationic protein; ERG, external reference group; FEV1, forced expiratory volume in 1 s; FVC, forced vital capacity; IgE, immunoglobulin E.
Germany). The supernatant was frozen at −80°C. The differential cell counts were performed by two blinded readers, and the average of the two observations was calculated and used as the result for each subject. The differential cell counts are presented as the percentages of the total non-squamous cell counts. The mean difference in the percentage of neutrophils (exposed period) between readers was 3% (SD 8%). All sputum samples had cell viability of >50% and squamous cell contamination of <40%. One of the exposed workers was unable to produce a sputum sample at T1 but managed to deliver a sample at T2.

**Biomarkers and blood samples**

The concentrations of the cytokines interleukin-1β (IL-1β), IL-6 and IL-8 in the sputum supernatant were measured in the same batch using DuoSet ELISA (enzyme-linked immunosorbent assay) kits (R&D Systems, Minneapolis, Minnesota, USA). The analyses were performed according to the manufacturer’s instructions.

Peripheral blood was sampled and analysed consecutively using standard procedures at the Fürst Medical Laboratory, Oslo, Norway (ISO/IEC 17025 certified). The concentrations of white blood cells, immunoglobulin E (IgE), C-reactive protein (CRP) and eosinophil cationic protein were measured.

**Aerosol measurements**

Cement production workers are exposed to aerosols with a wide particle size distribution, with some particles as small as 0.05 μm in aerodynamic diameter. The exposure varies in relation to location and work tasks, and the additives and alternative fuels used in the furnace (kiln). Respirable aerosol concentrations were measured in 2005, simultaneously with the sampling of sputum from furnace department workers, using an SKC 225-69 cyclone operated with SKC 224-PCEX7 pumps (SKC, Blandford Forum, Dorset, UK) with an airflow of 2.2 l/min. The personal thoracic aerosol concentration of exposure was measured for the maintenance workers in 2007 using a BGI 2.69 cyclone (BGI, Waltham, Massachusetts, USA) operated with SKC 224-PCXRS pumps with a flow of 1.6 l/min during the period of sputum induction. Thoracic aerosol samples were also collected in 2007 from the furnace department workers who had performed the sputum induction in 2005. All aerosol measurements were performed on 8 h shifts. Personal samples of x-quartz levels in worst-case situations had been measured in 2002 and showed non-detectable levels (detection limit 0.01 μg/m³) in two samples and 0.06 μg/m³ in the third sample compared with the Norwegian occupational exposure limit (OEL) of 0.1 μg/m³.

**Statistical analysis**

Statistical analysis was performed using SPSS V.15.0 (SPSS, Chicago, Illinois, USA). Because of the limited sample size, the two groups of exposed workers (from the furnace and maintenance departments) were combined into one group for the analysis of exposed production workers.

The Wilcoxon signed-rank test was used to compare differential cell counts and cytokine concentrations from before to after exposure within the same group. The Mann–Whitney test was used to compare sputum cell counts and cytokine concentrations between groups.

The percentage of neutrophils in sputum increases with increasing age. To adjust for age, multiple linear regression analysis was performed. In the regression model, exposure and age were used as independent variables and the two categorical variables for exposure were included (first variable: exposed=1 and non-exposed=0; second variable: internal controls=1 and exposed as well as external reference group=0). We used the percentage of neutrophils at T2 for exposed and office workers, and at T1 for the external reference group (the only test available for this group) as the dependent variable. The study was designed to include at least 15 participants in each group based on a power estimate of 80%, which assumed a 95% significance level to detect a true difference in the percentages of neutrophils between the two tests (before and after 5 days without exposure) of at least 16%.

**RESULTS**

**Sputum cell findings**

Table 2 shows the differential counts in induced sputum samples from the three exposure groups.

In cement production workers, the percentage of neutrophils was significantly higher during the exposed period than during the non-exposed period (p=0.04). Both the numbers and percentages of cells increased with increasing age. To adjust for age, multiple linear regression analysis was performed. In the regression model, exposure and age were used as independent variables and the two categorical variables for exposure were included (first variable: exposed=1 and non-exposed=0; second variable: internal controls=1 and exposed as well as external reference group=0). We used the percentage of neutrophils at T2 for exposed and office workers, and at T1 for the external reference group (the only test available for this group) as the dependent variable. The study was designed to include at least 15 participants in each group based on a power estimate of 80%, which assumed a 95% significance level to detect a true difference in the percentages of neutrophils between the two tests (before and after 5 days without exposure) of at least 16%.

**Table 2**: Differential cell counts in induced sputum from the cement aerosol exposed workers, office workers and unexposed external reference group.

<table>
<thead>
<tr>
<th></th>
<th>Exposed (n=35)</th>
<th>T1</th>
<th>T2</th>
<th>Office workers (n=15)</th>
<th>T1</th>
<th>T2</th>
<th>ERG (n=39)</th>
</tr>
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<tbody>
<tr>
<td><strong>Total cells/mg</strong></td>
<td></td>
<td></td>
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<tr>
<td>%</td>
<td></td>
<td>38 (23–55)</td>
<td>51 (32–66)*</td>
<td>39 (20–61)</td>
<td>43 (22–68)</td>
<td>30 (19–44) ***</td>
<td></td>
</tr>
<tr>
<td>Absolute numbers/mg sputum</td>
<td>657 (222–1386)</td>
<td>79 (351–1309)</td>
<td>283 (243–988)</td>
<td>408 (250–897)</td>
<td>324 (163–503) ***</td>
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<tr>
<td><strong>Macrophages</strong></td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td>%</td>
<td></td>
<td>59 (34–74)</td>
<td>47 (30–68)</td>
<td>57 (37–75)</td>
<td>56 (30–73)</td>
<td>70 (56–81) ***</td>
<td></td>
</tr>
<tr>
<td>Absolute numbers/mg sputum</td>
<td>1017 (504–1838)</td>
<td>825 (423–1026)</td>
<td>762 (410–1102)</td>
<td>711 (485–839)</td>
<td>570 (392–1364)</td>
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<tr>
<td><strong>Lymphocytes</strong></td>
<td></td>
<td></td>
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<tr>
<td>%</td>
<td></td>
<td>1.9 (1.0–3.9)</td>
<td>2.0 (1.4–4.3)</td>
<td>2.1 (1.7–3.8)</td>
<td>1.9 (1.1–2.6)</td>
<td>0 (0.0–0.7) ***</td>
<td></td>
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<tr>
<td>Absolute numbers/mg sputum</td>
<td>27 (13–80)</td>
<td>36 (12–75)</td>
<td>21 (16–94)</td>
<td>25 (11–47)</td>
<td>0 (0–7) ***</td>
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<tr>
<td><strong>Eosinophils</strong></td>
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<tr>
<td>%</td>
<td></td>
<td>0.2 (0.0–0.5)</td>
<td>0.0 (0.0–0.4)</td>
<td>0.1 (0.0–0.2)</td>
<td>0.2 (0.0–0.6)</td>
<td>0.0 (0–0.3)</td>
<td></td>
</tr>
<tr>
<td>Absolute numbers/mg sputum</td>
<td>0.9 (0.0–8.7)</td>
<td>0 (0–5)</td>
<td>1.1 (0–5)</td>
<td>0 (0–6)</td>
<td>0 (0–2)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Data are presented as median (25th–75th percentile) and percentages are calculated as the non-squamous cell %. *p<0.04, comparison between the non-exposed and the exposed sample among exposed workers; **p<0.01; ***p<0.001, comparison between exposed (exposed period) and the external reference group.

T1, sample from the non-exposed period; T2, sample from the exposed period.

ERG, external reference group.
percentages of neutrophils and lymphocytes were higher in the exposed workers than in the external reference group, but these values did not differ between exposed and office workers. The differences in neutrophil counts between the groups are illustrated in figure 1.

The multiple linear regression model with exposure (categorical variable) and age as independent variables showed that the percentage of neutrophils (dependent) at T2 was significantly associated with cement aerosol exposure. The mean percentage of neutrophils increased by 16.7 from T1 to T2 (β coefficient 16.7; p<0.001). Age was a significant factor in this analysis, and neutrophil count increased by 0.4% per year (β coefficient 0.4; p=0.02).

**Biomarkers in induced sputum**

The median IL-1β concentration was 28 pg/ml (25th–75th percentile, 21–36) in exposed workers, 17 pg/ml (13–20) in office workers, and 17 pg/ml (13–21) in the external reference group (figure 2).

In cement aerosol-exposed workers, the concentrations of IL-1β, IL-6 and IL-8 did not differ between the non-exposed and exposed periods. IL-6 and IL-8 concentrations did not differ between groups.

**Aerosol measurements**

The number of exposure measurements exceeds the number of included workers because some of the workers carrying samplers were smokers or did not want to participate in the health examinations. The median personal respirable aerosol concentration from six randomly chosen production workers measured on 2–3 separate days of exposed work was 0.5 mg/m³ (range 0.0–6.8). Three of the workers who carried respirable samplers (delivering 18 of the thoracic aerosol measurements) were included for sputum donation. One of the samples exceeded the Norwegian OEL of respirable dust (5 mg/m³).

All workers available on the 2 days of exposure measurements in 2007 carried thoracic aerosol samplers. The median thoracic aerosol concentration was 1.75 mg/m³ (0.2–15.5) in 18 furnace department workers and 0.6 mg/m³ (0.2–8.1) in 24 maintenance workers. Fourteen of the workers who carried thoracic samplers (delivering 18 of the thoracic aerosol measurements) were included for sputum donation. There is no established OEL for thoracic aerosol.

**DISCUSSION**

This study demonstrates a higher percentage of neutrophils in cement production workers during the exposed period than the non-exposed period and compared with external references. The concentration of IL-1β in sputum was higher in workers during the exposed period than in office workers and the external reference group. This seems to confirm our hypothesis that cement production aerosol stimulates inflammatory mechanisms in the airways of otherwise healthy workers.

The difference in the percentages of neutrophils between the two periods was observed only in cement production workers and was not detected in office workers. The lack of difference between the two sampling times in the office workers indicates that physical activity, climatic conditions or other unknown influences are probably not explanatory factors for the signs of inflammation observed in the exposed cement workers. Consequently, the signs of inflammation seen in the exposed cement workers may reflect exposure to cement production aerosol. This agrees with previous findings of neutrophilic inflammation after exposure to particles derived from tobacco smoke or air pollution, or occupational exposure.19 20

In addition to the higher percentage of neutrophils in the exposed period compared with the unexposed period, the cement production workers also had higher percentages of neutrophils and lymphocytes compared with the external reference group. However, the percentages of these cells did not differ at T2 between exposed workers and office workers. In contrast, after adjusting for age, the multivariate analysis showed that the percentage of neutrophils was related to exposure. Because we did not have exposure measurements for all included workers and because of interindividual day-to-day
variation in tasks and exposure, we used categorical variables for exposure. Age was an independent predictive factor of neutrophil percentage. This agrees with reports of increasing levels of neutrophils in sputum with increasing age.\(^{27}\) It is possible that some of the office workers were exposed to low levels of cement production aerosol in their working environment. One of the office workers reported a history of aerosol exposure during production work before becoming an office worker. Differences in age, low-level exposure and former exposure among the office workers could have caused us to underestimate the effects of exposure. The inclusion of the external reference group was considered useful for comparison.

In exposed workers, total cell counts and absolute numbers of inflammatory cells were similar in both periods and compared with values in office workers. This may reflect greater variance for these variables than for the percentage of neutrophils. Regardless, the absolute numbers of neutrophils and lymphocytes were significantly higher in workers than in the external reference group, indicating that longer avoidance of exposure to cement aerosol is needed to normalise the absolute number of neutrophils.

The elevated concentration of cytokine IL-1\(\beta\) in exposed workers compared with both office workers and the external reference group indicates that a cytokine response has taken place. This agrees with findings of elevated serum levels of IL-1\(\beta\) in American cement masons, whose major exposure is to cement aerosol.\(^{28}\) IL-1\(\beta\) upregulates the adhesion molecules on endothelial cells and neutrophils and thereby contributes to the accumulation of neutrophils in the airways.\(^{19}\) Even though the neutrophil counts decreased after 5 days without exposure, the IL-1\(\beta\) concentration did not decline during this time in the exposed workers. This could indicate that longer avoidance of exposure to cement aerosol is needed to normalise the sputum concentration of IL-1\(\beta\).

The similar concentrations of IL-6 and IL-8 in the three groups suggest a low response of these inflammatory markers. IL-6 is a common inflammatory marker that may be activated by several stimuli. IL-6 increases during exacerbation of chronic obstructive pulmonary disease (COPD) and appears to be useful in evaluating the intensity of the disease.\(^{29}\) and a low level of this cytokine is expected in healthy subjects. IL-8 has a chemotactic effect on neutrophils and is negatively correlated with lung function in patients with COPD.\(^{30}\) suggesting that the low IL-8 concentrations reflected relatively low-grade neutrophilic activation in these healthy subjects with normal spirometric values.

To our knowledge, no studies have reported on biological materials from the airways of cement aerosol-exposed workers. One report recently showed decreased phagocytic activity in blood neutrophils stimulated with a stimulant of reactive oxygen species in cement mill workers compared with controls.\(^{31}\) However, information about the exposure, inflammatory cells and soluble markers was not given, and it is difficult to compare our data with this other report. A study of healthy iron ore miners in Sweden found changes in inflammatory cells and soluble markers in induced sputum similar to those in our study.\(^{32}\) In these iron ore miners, increased levels of neutrophils, macrophages, fibronectin, metalloproteinase-9 and IL-10 were associated with exposure to dust and diesel exhaust. Although these variables did not differ between the exposed and non-exposed periods in the miners, the miners showed signs of airway inflammation compared with an external reference group.

When workers are used as their own controls, selection bias is probably less important.\(^{32}\) However, it is possible that individuals who are susceptible to adverse effects from cement aerosol could have departed the cement industry, leaving only robust subjects in the workforce to be included in the study. If so, we would have underestimated the inflammatory effects. Despite differences in the percentage of neutrophils between the exposed and unexposed periods within the same worker, it is possible that a greater decline would have occurred if avoidance of exposure had been sustained.

The exposed workers were included from 2005 to 2007. There were no reports of technical changes or differences in working routines, ventilation or use of protective equipment during this period. Thus, there is no reason to believe that the exposure had changed between sputum sampling and air measurement of the thoracic samples 2 years later. The same investigator performed sputum induction in both production workers and controls under similar conditions throughout the study period.

Confounders that may not be controlled adequately or adjusted for in the analysis could include unknown differences in socioeconomic factors or respiratory irritants outside the workplace, especially when comparing the exposed group and the external reference group.

DTT was used to dissolve the sputum plugs. DTT may change the native structure of the proteins because it reduces the protein disulfide bonds, and this may affect measurement of cytokine concentration in induced sputum. However, DTT was added to all samples as well as to the standard samples used to generate the standard curve, and all samples were processed similarly. Thus, the relative differences between periods and groups are unlikely to have been affected by inclusion of DTT.

As well as measuring respirable aerosol concentration, we also measured the thoracic fraction of airborne cement particles in exposed workers. The thoracic fraction represents the aerosol that reaches the airways below the larynx and includes the respirable fractions that contain particles small enough to reach the alveoli. Induced sputum contains cells and fluid from the large central respiratory sections below the larynx.\(^{33}\) Considering this, both fractions of the aerosol are of interest when studying changes in induced sputum samples.

Levels of inflammatory cells and markers from the exposed tests were thought to reflect recent exposure. The workers reported day-to-day variation in exposure as well as high peaks associated with special tasks. Monitoring of exposure each day over the whole 2-week period would have allowed us to correlate exposure with health outcomes, but this was not feasible in the present study. Nevertheless, we identified a group of eight subjects with an increase in neutrophil percentage of more than 20% (high responders, n = 8). Six of these workers (75%) regularly performed inspection rounds, which may include frequent peak exposures. Only seven (26%) of the other exposed workers reported this kind of exposure. This suggests that regular peak exposure is related to an increase in the percentage of sputum neutrophils.

The respirable aerosol level among the exposed workers in this study was well below the Norwegian OEL (5 mg/m\(^3\)). The thoracic fraction was also below this level. The increased levels of inflammatory cells and soluble inflammatory markers detectable in induced sputum samples from exposed workers suggests that the present Norwegian OEL is too high and should be reduced to avoid inflammatory changes in the airways of exposed workers.

Various types of work exposure can induce neutrophilic inflammation in sputum.\(^{34}\) and more pronounced neutrophilic inflammation is considered a component of the inflammatory pattern in COPD.\(^{19,20}\) It is not clear whether the increased...
percentage of neutrophils as observed in our study represents an early stage of respiratory disease or if it is only a marker of exposure without clinical consequences. Nevertheless, spirometric surveillance should be carried out at regular intervals until results from follow-up studies are completed and interpreted in relation to these questions.

To our knowledge, this is the first study to demonstrate a higher percentage of neutrophils in cement production workers during a period of exposure compared with a non-exposed period and with an external reference group. We found a higher IL-1β concentration in sputum from cement production workers during the exposed period compared with office workers and the external reference group. This could reflect the presence of underlying airway inflammation in healthy cement production workers with a normal FEV1/forced vital capacity (FVC) ratio after low-level exposure to aerosols. The long-term consequence of these acute changes in neutrophils and sputum inflammatory mediators are unknown, and the hypothesis that low-grade cement aerosol exposure causes airway disease should be tested in a 5–10-year follow-up study.

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Competing interests None.

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REFERENCES


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**Notes**

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