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**Key terms:** [eosinophil cationic protein](#); [inflammation](#); [myeloperoxidase](#); [nasal lavage](#); [prevention](#); [saccharin test](#)

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## Improved nasal clearance among pulp-mill workers after the reduction of lime dust

by Kjell Torén, MD,<sup>1</sup> Jonas Brisman, MD,<sup>1</sup> Stig Hagberg, MSc,<sup>1</sup> Göran Karlsson, MD<sup>2,3</sup>

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**Objectives** The purpose of this study was to investigate nasal symptoms and function among workers exposed to lime dust and to determine if a reconstruction of the workplace improved the worker's nasal health.

**Methods** In 1992, pulp-mill workers (N = 15) exposed to lime dust and an equal number of matched unexposed referents were examined by questionnaires, nasal peak expiratory flow, the saccharin test, nasal lavage, and a clinical examination of the upper airways. The study was repeated one year later, after the pulp mill had been rebuilt. Dust levels were measured on both occasions with stationary and personal samplings.

**Results** In 1992 the total dust level was  $1.2 \text{ mg} \cdot \text{m}^{-3}$ . The saccharin test showed a significantly increased nasal transit time for the exposed workers in comparison with that of the unexposed referents (difference 3.5 min, 95% confidence interval 0.1 — 6.9 min). One year later the dust levels had decreased to  $0.1 \text{ mg} \cdot \text{m}^{-3}$ , and the difference in nasal transit time had decreased (difference -0.8 min, 95% confidence interval -4.8—3.3 min).

**Conclusions** Workers exposed to lime dust have an impaired mucociliary function. This impairment is probably due to the alkalinity of the lime. When dust levels are reduced, mucociliary function improves; therefore renovating a workplace to reduce dust levels has a positive effect.

**Key terms** eosinophilic cationic protein, inflammation, myeloperoxidase, nasal lavage, prevention, saccharin test.

Exposure to burnt lime (calcium oxide) has been associated with an increase in the prevalence of upper airway symptoms (1). In pulp mills using the sulfate process, there is a lime kiln in which calcium carbonate is decomposed to calcium oxide and carbon dioxide during heating. The calcium oxide is subsequently reused in the pulping process. The kiln workers are exposed to burnt lime, and they often complain of irritation of their eyes, nose, and throat.

In 1991 efforts to improve the work environment began in one of the largest pulp mills in Sweden by reconstructing the lime kiln to minimize leakages of burnt lime from the kiln and increase the recirculation of lime. This reconstruction gave us an opportunity to study the respiratory health effects of exposure to lime dust and also to evaluate the health effects of the reconstruction.

The study design was interventional. Exposed workers and unexposed referents were investigated in February 1992, just before the reconstruction and one year

later, in February 1993. The reconstruction took two months, after which the workers returned to their earlier tasks. The study included dust sampling, assessment of respiratory symptoms and lung function, and a clinical examination of the nose.

### Subjects and methods

#### Exposure

Stationary samples of the total amount of dust were taken at the same nine places before and after the reconstruction. Personal samples of the total amount of dust were taken for six workers before the reconstruction and for four workers after the reconstruction. The dust was collected on 37 mm cellulose acetate filters at a flow rate of  $2 \text{ l} \cdot \text{min}^{-1}$ .

Four samples of burnt lime from the kiln were obtained before and after the reconstruction. They were

<sup>1</sup> Occupational Medicine, Sahlgrenska University Hospital, Göteborg, Sweden.

<sup>2</sup> Department of Otorhinolaryngology, Sahlgrenska University Hospital, Göteborg, Sweden.

<sup>3</sup> Department of Allergy, Sahlgrenska University Hospital, Göteborg, Sweden.

Reprint requests to: Dr Kjell Torén, Department of Occupational Medicine, St Sigfridsgatan 85b, S-412 66 Göteborg, Sweden.

analyzed by means of X-ray diffraction to measure the concentrations of heavy metals.

The temperature was measured with a globe thermometer at two places before and after the reconstruction.

### Subjects

The exposed group included all the workers ( $N = 17$ ), all men, from the lime kiln department. All of them were exposed to lime dust. The study was performed with 15 of them, as two subjects were excluded because of on-going infectious rhinitis. For each worker, one unexposed referent was matched for age ( $\pm 5$  years), gender and smoking habits (smoker, ex-smoker, never smoker). The 15 referents were selected from a group of about 50 workers from the transportation and office departments. Because of the matching criteria (gender, age, and smoking habits) this was the total sample. The mean age of the exposed workers was 45.2 years and that of the referents was 46.6 years. There were eight pairs of smokers, two pairs of ex-smokers, and five pairs of never smokers.

Twelve of the original 15 pairs participated in the second part of the study, in 1993. Two exposed and one unexposed subject were excluded because of on-going rhinitis, and the incomplete pairs were excluded.

### Methods

The exposed workers and the referents were examined by the same physician on two occasions, in February 1992 and in February 1993. The same equipment, operators, and procedures were used on both occasions. The exposed workers and the referents were mixed, but total blindness was impossible to obtain.

The subjects answered a questionnaire at home before attending the clinical part of the study. The questionnaire focused on symptoms from the upper airways, such as nose bleedings, crusts in the nose, nasal blockage, and nasal secretion. In addition there were questions about occupational history and smoking habits. Each subject's nose and throat were inspected by an ear, nose and throat specialist (GK). Visible inflammation was semi-quantitatively defined as an occurrence of crusts or a red and swollen mucous membrane on a scale from 0 to 3.

The mucociliary function of the nasal mucosa was tested according to Andersen et al (2). The investigation was made at room temperature, after an adjustment period of 20 min. A small particle of saccharin was placed on the superior surface of the inferior turbinate about 4 cm from the nasal tip with the use of a nasal speculum and headlight. A timer was started and the subject was instructed to swallow every 30 s. When the subject noticed a strong sensation of sweetness, the timer was stopped. The mucociliary clearance was expressed as the transit time in minutes. The nasal cycle was not specifically recorded, but the nose examinations were performed at

the same time of day on both occasions, and in the same nasal cavity, which happened to be the most patent one. There was no restriction regarding smoking before the investigation.

Nasal peak expiratory flow (PEF) was measured with a mini-Wright peak flow meter equipped with an anesthetic face mask. The highest of three readings was used.

Nasal lavage was carried out according to the Baltimore method (3). The lavage fluid was centrifuged, and the supernatant was frozen immediately at  $-20^{\circ}\text{C}$ , and about 10 h later it was frozen at  $-80^{\circ}\text{C}$ . Preparations for cell counting were made from the sediments of the lavage fluid. The cells were, however, impossible to count due to artifacts, probably because the transportation time from the mill to the laboratory was too long.

In April 1993, the frozen lavage fluid specimens from both study occasions, 1992 and 1993, were analyzed according to the content of eosinophilic cationic protein (ECP), myeloperoxidase (MPO), and hyaluronic acid (Pharmacia Diagnostics, Uppsala, Sweden). The investigation from 1993 contained serum samples obtained for the analyses of ECP, MPO and Phadiatop<sup>TM</sup>.

The lung function of the subjects [forced expiratory volume in 1 s ( $\text{FEV}_{1.0}$ ), forced vital capacity (FVC) and  $\text{FEV}\%$  ( $100 \times \text{FEV}_{1.0}/\text{FVC}$ )] was investigated with a dry spirometer (Vitalograph<sup>®</sup>). The spirometric maneuvers were judged according to the ATS statement (4). The values were expressed as the percentage of the predicted (5).

### Statistical methods

The statistical analyses were performed with intact pairs. For the 1992 and 1993 studies the results are presented as the differences between the exposed and unexposed subjects.

In the attempt to assess the effect of the rebuilding, the material was analyzed in two ways. First, the following algorithm has been used: [(exposed 1992 – exposed 1993) – (unexposed 1992 – unexposed 1993)]. Second, the improvements of the exposed (exposed 1992 – exposed 1993) and the unexposed (unexposed 1992 – unexposed 1993) have been analyzed separately. In both situations, for the noncontinuous variables, the number of pairs in which the exposed had a “positive” test was compared with the number of pairs in which the unexposed had a “positive” test. The pairs in which both members are either “positive” or “negative” were dismissed. For nasal transit time and nasal PEF the correlations between the results from 1992 on one hand and the improvement in 1992–1993 and the results from 1993 on the other were calculated with Spearman's correlation coefficient ( $r_s$ ).

The level of significance for the continuous variables was tested with Student's *t*-test for paired samples and with Fisher's exact test for proportions. For continuous

variables the 95% confidence intervals (95% CI) for the differences were estimated based on the t-test. When evaluating the change between 1992 and 1993, a one-tailed test was used, as improvement was expected.

## Results

### Exposure

The area samples showed a reduction in the dust levels after the reconstruction. The geometric mean of the total dust level decreased from 1.2 (range 0.1 to 7.7)  $\text{mg} \cdot \text{m}^{-3}$  to 0.1 (range 0.1 to 0.2)  $\text{mg} \cdot \text{m}^{-3}$ . The reduction was most pronounced in the two sample areas close to the kiln, for which the geometric means decreased from 7.7 to 0.2  $\text{mg} \cdot \text{m}^{-3}$ .

The personal samples of total dust indicated decreased exposure. The geometric means decreased from 1.2 (range 0.4–5.8)  $\text{mg} \cdot \text{m}^{-3}$  to 0.2, (range 0.1–0.6)  $\text{mg} \cdot \text{m}^{-3}$ .

The reconstruction resulted in a temperature decrease, from 42 to 28°C.

Before the reconstruction the concentrations of lead, cadmium, nickel, and chromium in the lime were < 5, < 0.5, 4.8, and 3.9  $\text{mg} \cdot \text{kg}^{-1}$ , respectively. After the reconstruction the metal levels increased, the concentrations of lead, cadmium, nickel and chromium being 94, 3.9, 11, and 91  $\text{mg} \cdot \text{kg}^{-1}$ , respectively. Before the reconstruction 40 kg of limestone per ton of produced pulp was added to the process; after the reconstruction the amount was 7 kg per ton.

### Health effects

**1992 study.** There were no significant differences regarding reported symptoms when the analysis was made

**Table 1.** Group mean values for lung function, nasal transit time, nasal peak expiratory flow (PEF), eosinophilic cationic protein (ECP), myeloperoxidase (MPO) and hyaluronic acid (HA) in nasal lavage in 1992. [SE = standard error of the mean,  $\text{FEV}_{1.0}$  = forced expiratory volume in 1 s, FVC = forced volume capacity,  $\text{FEV}\% = (100 \times \text{FEV}_{1.0})/\text{FVC}$ ]

Variable	Exposed subjects (N = 15)		Unexposed subjects (N = 15)	
	Mean	SE	Mean	SE
$\text{FEV}_{1.0}^a$	105	2.4	108	3.5
FVC <sup>a</sup>	101	2.8	101	2.8
$\text{FEV}\%^a$	79	1.3	80	1.3
Nasal transit time (min)	13.4	1.3	10.0	1.2
PEF ( $\text{l} \cdot \text{min}^{-1}$ )	442	26.3	470	13.3
ECP ( $\mu\text{g} \cdot \text{l}^{-1}$ )	2.7	1.0	3.1	1.0
MPO ( $\mu\text{g} \cdot \text{l}^{-1}$ )	106	37.7	149	45.0
HA ( $\mu\text{g} \cdot \text{l}^{-1}$ )	42.4	6.2	47.8	5.6

<sup>a</sup> Percent of predicted value.

with matched subjects. Nasal bleeding was reported by the exposed worker of four pairs and by the unexposed worker of three pairs. In five pairs the exposed worker reported crusts in the nose, and in one pair the unexposed worker reported this symptom. Nasal blockage was reported by the exposed worker in one pair and by the unexposed worker of three pairs. Nasal secretion was reported by the exposed worker of two pairs and by the unexposed worker of one pair. In the remaining pairs the exposed and unexposed subjects gave the same answer.

The clinical nose examination indicated (without statistical significance) more inflammation among the exposed subjects. Nasal inflammation was found in the exposed member of eight pairs (seven classified as "1" and one as "2") and in the unexposed member of two pairs (both classified as "1"). In the remaining five pairs both subjects were classified as "0". A septal deviation was noted in five subjects, four unexposed and one exposed. Actually, one of the unexposed subjects with a septal deviation and the one exposed subject were from the same pair. No structural abnormalities involving the turbinates were observed.

The saccharin test showed a significantly increased nasal transit time among the exposed workers, the mean difference between the exposed and unexposed subjects was 3.5 min (95% CI 0.1–6.9). Among the exposed subjects the mean transit time was 13.4 (range 6.0–26) min. Among the unexposed subjects it was 10.0 (range 4–20) min.

The nasal PEF was lower among the exposed subjects than among the unexposed,  $-39 \text{ l} \cdot \text{min}^{-1}$ , but the difference was not significant (95% CI 1.7–74). There were no significant differences with regard to ECP ( $-0.3 \mu\text{g} \cdot \text{l}^{-1}$ , 95% CI 1.0–1.6), MPO ( $41.3 \mu\text{g} \cdot \text{l}^{-1}$ , 95% CI 1.0–108.0) or hyaluronic acid ( $5.5 \mu\text{g/l}$ , 95% CI 9.6–0.10) in the lavage fluid of the exposed and the unexposed subjects.

Table 1 shows the group mean values (ie, matching dissolved) for lung function, nasal transit time, PEF, ECP, MPO, and hyaluronic acid.

**1993 study.** There were no significant differences regarding the reported symptoms when the analysis was made for the matched pairs. Nose bleeding and nasal blocking was reported among the same numbers of exposed and unexposed subjects. Nasal crusts and nasal secretion were reported for the exposed subjects in three pairs and for the unexposed subject in one pair.

The clinical nose examination showed no differences between the exposed and unexposed subjects. Nasal inflammation was found in the exposed member of three pairs (two classified as "1" and one classified as "2"). Among the unexposed subjects nasal inflammation was found in three, all classified as "1".

The saccharin test did not show any apparent difference between the exposed and unexposed subjects, the mean difference being  $-0.8$  min (95% CI  $-4.8$ — $3.3$ ). For the exposed workers the mean transit time was 8.6 (range 1.4—15) min. For the unexposed workers it was 10.2 (range 5.5—20) min.

The nasal PEF was still slightly lower among the exposed subjects, the difference being  $-27$  l · min<sup>-1</sup> (95% CI 18—72). There were no significant differences between the exposed and unexposed subjects with regard to the concentrations of ECP, MPO, and hyaluronic acid in the lavage fluid, as well as ECP and MPO in serum or with regard to lung function. Three of the exposed and two of the unexposed subjects had a positive Phadiatop™ test, indicating atopy.

#### *Differences between the investigations made in 1992 and 1993*

If the degree of improvement was calculated according to [(exposed 1992 – exposed 1993) – (unexposed 1992 – unexposed 1993)], the nasal transit time decreased (difference 4.7 min, 95% CI  $-1.0$ — $10.3$ ) and the nasal PEF increased (difference  $-25.8$  l · min<sup>-1</sup>, 95% CI  $-51.5$ — $0.1$ ). There were no significant differences regarding the other variables, including the noncontinuous ones.

If the groups were analyzed separately as (exposed 1992 – exposed 1993) and (unexposed 1992 – unexposed 1993) the exposed group showed significant improvement in the nasal transit time (difference 4.9 min, 95% CI 0.3—9.5) and a nonsignificant improvement in the nasal PEF (difference  $-21.6$  l · min<sup>-1</sup>, 95% CI  $-52.9$ — $9.7$ ). Among the unexposed subjects there was also a slight improvement in the nasal transit time (0.53 min, 95% CI  $-2.2$ — $3.2$ ) and a slight impairment (decrease) in the nasal PEF (4.2 l · min<sup>-1</sup>, 95% CI  $-6.0$ — $22.4$ ).

The results for the nasal transit time are plotted in figure 1. Within the exposed group, the correlation coefficient between the results from 1992 on one hand and

those from 1993 and the improvement in 1992—1993 on the other were  $-0.40$  ( $P = 0.19$ ) and  $0.90$  ( $P = 0.001$ ), respectively. Within the unexposed group the corresponding correlation coefficients were  $0.35$  ( $P = 0.25$ ) and  $0.63$  ( $P = 0.03$ ).

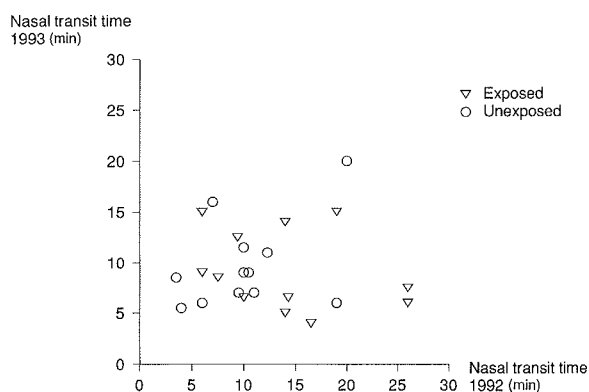
The results for the nasal PEF are plotted in figure 2. Within the exposed group, the correlation coefficients between the results from 1992 on one hand and the results from 1993 and the improvement in 1992—1993 on the other were  $0.67$  ( $P = 0.02$ ) and  $0.76$  ( $P = 0.004$ ), respectively. Within the unexposed group the corresponding correlation coefficients were  $0.91$  ( $P = 0.0001$ ) and  $0.69$  ( $P = 0.01$ ).

#### **Discussion**

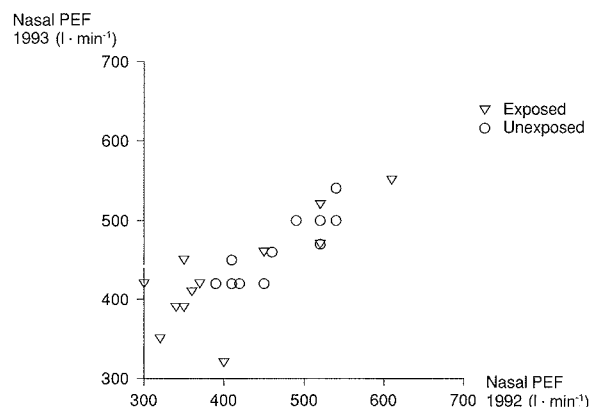
The present study showed that rebuilding the lime kiln in a pulp mill resulted in lower dust levels. An increased nasal transit time, indicating impaired nasal clearance, was found among the exposed workers before the reconstruction. The difference in nasal transit time disappeared after the reconstruction, and the improvement was statistically significant. The concentrations of inflammatory markers in the nasal lavage fluid did not differ significantly between the groups either before or after the reconstruction.

The precision of the study is low, due to the small number of exposed workers. The precision could have been increased if lime kiln workers from other mills had been included, but, as the aim was to study the effects of reconstruction, this was not done.

The exposed subjects were compared with matched unexposed referents. In the analyses of the change (improvement) due to the rebuilding, two models for analyzing the data were applied. In the first model the improvement among the exposed subjects was analyzed as [(ex-



**Figure 1.** Correlation between nasal transit time in 1992 and 1993 (after rebuilding of the lime kiln) for 12 pulp-mill workers exposed to lime dust.



**Figure 2.** Correlation between the nasal peak expiratory flow (PEF) in 1992 and 1993 (after rebuilding of the lime kiln) for 12 pulp-mill workers exposed to lime dust. Note that the axes begin at 300 l · s<sup>-1</sup>.

posed 1992 – exposed 1993) – (unexposed 1992 – unexposed 1993)]. This model compensates for a possible trend in the accuracy of the methods. On the other hand, the results may be blurred by possible improvement for the referents, and therefore the data were also analyzed as (exposed 1992 – exposed 1993) and as (unexposed 1992 – unexposed 1993). Regarding the nasal transit time, this last model resulted in statistically significant results for the exposed subjects, as both the exposed and unexposed subjects improved between 1992 and 1993.

The examination was formally blinded (ie, the staff was not informed of whether the worker was exposed or not). However, the workers' appearance made it possible to guess their exposure status. This factor may have introduced some bias into the clinical examination of the nose. To minimize shifts in the accuracy of the methods, the investigations were performed by the same operators, with the same equipment, and at the same time of the year. All the analyses of the blood and lavage fluid were performed on the same occasion, after the follow-up in 1993.

Smoking and age were regarded as potential confounders, but with the matched design the influence of these factors was diminished. The influence of the nasal cycle was minimized by performing the saccharin test at the same time of day on both occasions. A septal deviation was noted in five subjects (one exposed and four unexposed subjects). For these subjects the nasal transit time in the 1992 investigation was 12.3 min for the unexposed subjects and 6 min for the exposed subjects. As the mean transit time for all the unexposed subjects was 10.0 min and for all the exposed it was 13.4 min, inclusion of the subjects with septal deviation diminished the differences between the exposed and unexposed groups.

This study included a small number of subjects, and there were only minor measurable differences between the groups. Hence the results must be judged with caution. The most obvious change observed was the impaired mucociliary activity among subjects exposed to the lime dust. Decreased mucociliary clearance had been observed earlier among workers exposed to wood dust (2) and formaldehyde (6) and among hairdressers exposed to hair spray (7). Workers exposed to lime dust had not been studied in this respect. The exposed workers also displayed an insignificantly decreased nasal PEF. This finding may indicate swollen mucous membranes in the nose, a finding which, to some extent, was also supported by the clinical examination. Taken together, these observations indicate that exposure to burnt lime may have a toxic effect on nasal mucosa. This effect is plausible, as burnt lime is a strongly alkaline substance.

In the second examination, after the reconstruction, the differences between the groups regarding mucociliary clearance and nasal PEF had disappeared or dimin-

ished. If the change among the referents is not compensated for, the impairment of the nasal transit time was significant. Among the exposed subjects the improvement of the nasal transit time was the most prominent among those with the slowest clearance in 1992. This finding is plausible, since the most affected persons improved the most. However, there was also some improvement among the unexposed subjects, and this result may reflect a shift in the accuracy of the method.

However there had not only been a decrease in the dust levels, but the temperature had decreased from 42 to 28°C. It has been reported that subjects in hot wet Malaysia and the hot dry desert of Israel do not differ in their mucociliary function when compared with subjects from temperate climate zones (8). Furthermore, experiments in a climate chamber shifting temperature from 23 to 15°C and from 23 to 31°C did not significantly influence mucociliary function (8). However, there was an initial fall in the clearance when the temperature in the chamber was raised to 39°C. To our knowledge there are no studies reporting the influence on mucociliary function when ambient temperatures in the range of those reported in this study are lowered. We think, however, that the improved nasal clearance after the reconstruction was mainly an effect of the reduced lime dust levels, but some influence of reduced temperature cannot be excluded.

The analyses of the inflammatory markers (ECP, MPO, and hyaluronic acid) did not show any significant differences between the exposed and unexposed subjects, nor were there any significant differences after the reconstruction. This finding may indicate that these markers are of less value when nonallergic inflammation is being studied, but this possibility is something that needs to be evaluated by further research.

The reconstruction of the kiln resulted in an accumulation of some metals in the lime, due to the increased recirculation. There is no obvious reason to believe that increased exposure to these metals would decrease nasal transit time (increase the nasal clearance). However, the increase in chromium exposure may be of importance since contact dermatitis caused by chromium has been reported among lime kiln workers (9).

In summary, workers exposed to lime dust showed impaired mucociliary clearance, which improved after the reduction of the dust levels. This finding indicates a positive health effect of the reconstruction of the lime kiln.

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