Correspondence

relative risk for lung cancer of 1:7 (95% CI 0-7-4)1. This increased value, however, was not confirmed by a second follow up as the CI was reduced to 1.2 (95% CI 0.6-2.2).4 The results remained unchanged after adjustments for smoking.5 Moreover, with an external reference, the lung cancer SMR of SS welders was lower (1.1; 95% CI 0.7-1.6).3

The case-control study by Hull et al in Los Angeles county showed ORs of 0.9 (95% CI 0.5-1.8) for SS welders and 1.3 (95% CI 0.6-2.3) for SS welders predominantly exposed to welding fume and nickel (manual metal arc welders), whereas the OR was 1.6 (95% CI 0.8-3.1) for MS welders. Adjustments for smoking made little difference.6

The European mortality study included 11 092 welders from eight countries.11 This large study provided no consistent difference between MS welders, for which the SMR was 1.78 (95% CI 1.77-2.43, statistically different) and predominantly SS welders whose SMR was 1.23 (95% CI 0.75-1.90). The results of this study for cancer incidence provided the same pattern as those for mortality as the standardised incidence ratio (SIR) for lung cancer was 1.75 (95% CI 1.22-2.42) for MS welders and 1.39 (95% CI 0.74-2.38) for predominantly SS welders.12

In conclusion, it seems to me that although SS welders are potentially exposed to chromium and nickel compounds, epidemiological studies focused on the risk of lung cancer of SS welders do not provide clear evidence to suggest that SS welders are at higher risk of lung cancer than MS welders. Therefore, the cause of the excess lung cancers found among MS and SS welders is an unanswered issue.1 A recent study by Jockel et al supports the hypothesis that some of the excess risk of lung cancer among welders could be due to exposure to asbestos.13 Further investigations that controlled for smoking, exposure to asbestos, and possible different healthy worker effects among MS vs SS welders1 are needed.

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Urinary N-acetyl-β-D-glucosaminidase (NAG) and exposure to inorganic lead

Editor—Urinary activity of N-acetyl-β-D-glucosaminidase (NAG) has been reported to be one of the earliest markers to be increased in workers exposed to lead.1 2 The underlying mechanism for an increase in NAG activity is unknown. It was suggested that the increase in NAG activity may be due to stimulation of exocytosis.3 In a recent publication4 based on workers from a lead smelting plant, it was further suggested that increase in NAG activity among workers exposed to lead was due to contaminant "albeit slight cadmium exposure". Their conclusion was based on the finding that urinary cadmium concentration (CdB) was the only significant variable in explaining the variation in NAG activity through stepwise regression analysis. Furthermore, the correlation coefficient (r) between NAG and CdB, was 0.41 in the non-exposed and 0.35 among workers exposed.5

Our data from exposed workers in a polyvinyl chloride lead stabiliser plant did not support this hypothesis. The increases in NAG, the heat lability isoenzyme (NAG-A), and the heat stable isoenzyme (NAG-B) were all highly associated with the recent change in blood lead (PbB) concentration over the past six months (PbBA).6 Among several exposure indices derived from serial PbB concentrations, PbBA was the only significant variable to account for the variation in NAG, NAG-B, and NAG-A. Furthermore, CdB and blood cadmium (CdB) did not correlate well with NAG and its isoenzymes. When they were forced into the regression model, CdB was in fact negatively correlated (table). Activity of NAG is also increased when other xenobiotics affect the proximal tubules,7 8 and it is indeed very unlikely that NAG is a specific marker for cadmium. As inorganic lead is known to cause proximal tubular dysfunction, it is therefore not surprising to see an association between lead exposure and NAG.

Among lead smelters, it is possible that there may be significant concomitant exposure to cadmium. This is evident by the fairly wide range of CdB results (0.3-5 μg/l) and the significantly higher CdB and CdB concentrations among the workers exposed to lead.9 Our cohort of PVC lead stabiliser workers had never been exposed to cadmium. Their geometric mean (range) CdB and CdB were much lower than those of the lead smelters (CdB: 0.56 (0.10 to 1.92) μg/l, CdB 0.41 (0.12 to 2.07) μg/l creatinine). We have also previously reported that NAG activity was better correlated with CdB and about 40% of the workers exposed to cadmium with a CdB of less than 3 μg/l had increased NAG concentrations.10

It is possible that where there is significant cadmium exposure, cadmium plays a greater part in increasing NAG activity than does lead, and perhaps even masks the contribution of lead. Our data show that lead does increase NAG activity in the absence of cadmium exposure.

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Contribution of PbBA, CdB, and CdB to variation in NAG*

<table>
<thead>
<tr>
<th>Independent variables</th>
<th>Partial regression coefficients (β) (95% CI)</th>
<th>Unit free β r</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total NAG:</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>PbBA</td>
<td>0.42 (2.22 to 6.01)</td>
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<td>0.05</td>
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<tr>
<td>CdB</td>
<td>0.6 (-0.08 to 0.40)</td>
<td>0.10</td>
<td>0.05</td>
</tr>
<tr>
<td>CdBU</td>
<td>-0.04 (-0.31 to 0.04)</td>
<td>0.22</td>
<td>0.05</td>
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<tr>
<td>NAG-B:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PbBA</td>
<td>1.11 (-5.96 to 16.43)</td>
<td>0.66</td>
<td>0.43</td>
</tr>
<tr>
<td>CdB</td>
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<td></td>
</tr>
<tr>
<td>CdBU</td>
<td>-0.03 (-0.39 to 0.34)</td>
<td>0.02</td>
<td></td>
</tr>
</tbody>
</table>

Multiple linear regression analysis with log transformed data.

*Correlation coefficient (r) between NAG and CdB and CdB was 0.41 in the non-exposed and 0.35 among workers exposed.
an enzyme (β-galactosidase) exposure population. In a study on workers exposed to Pb from a Pb acid battery factory in which all subjects had a CdU below 2 μg Cd/g creatinine (mean 0.36 μg Cd/g creatinine in both the control and exposed groups) we could not find any difference in NAG between the control and exposed groups. The mean PbB in the battery workers (510 μg Pb/B) was, however, 50% higher than that of the Pb stabiliser workers examined by Chia et al. The hypothesis that NAG represents a specific renal marker associated with an early stage of tubulotoxication of Pb exposure is also not supported by other independent studies performed in our laboratory and by the findings of other authors. In the study by Gerhardsson et al on moderately exposed Pb smelter workers,4 NAG did not correlate with variables that reflected current (PbB) or time-integrated Pb concentration. Moreover, a PbB index or Pb concentration in bone. Our recent study on Pb smelter workers corroborates this conclusion,20 as a stepwise multiple regression analysis indicated the lack of a direct association between NAG and the concentration of Pb in blood, urine, or tibia. The only predictor variable that was found to be significantly correlated with NAG irrespective of whether the correlation was examined for the total population or for the Pb smelter workers was CdU (the slopes of NAG v CdU were similar in both groups). The concomitant Cd exposure in these Pb smelter workers was low as shown by the CdB and CdU values that were still within the limits of distributions usually found for the population from large areas in Belgium. It is interesting to note, however, that the current exposure to Cd (reflected as CdB) did not influence the correlation (reflected as CdU) in the control group (geometric mean (range) CdB 0.6 (0.1 to 2.6) μg Cd/g creatinine; 0.53 (0.16 to 1.51) μg Cd/g creatinine) are similar to those reported in Chia et al's PbB-stabilised workers (CdB 0.56 (0.10 to 1.92) μg Cd/g). CdU 0.41 (0.12 to 2.07) μg Cd/g creatinine. Taken together, the results suggest that the direct relation between Pb exposure and NAG is still questionable, and it seems more likely that the renal burden of Cd, even at very low concentrations, may play a predominant part in the alterations of tubular lysosomolysis and release of renal NAG in the urine. This hypothesis is supported by our previous findings from cohorts of different populations such as another group of Pb smelter workers,19 pregnant women,17 and the general population.1 In none of these studies did Pb exposure emerge as a determinant of NAG, but in all of them NAG positively correlated with CdU that reflected a low exposure to Cd. In two of these studies the subjects' CdU did not even exceed 2 μg Cd/g creatinine.14,15 Furthermore, a recent study from our laboratory may provide some insight into the basis of the lack of correlation of this association.16 A dose related increase in the urinary activity of NAG-B (considered as the lesonal form of NAG) with CdU has been found that is already significant in a subgroup that excreted 0.5 to 2 μg Cd/g creatinine. The existence of a specific association between NAG-B and CdU with no detectable Cd threshold suggests that Cd may produce cellular changes in the kidney at urinary Cd concentrations presently considered as the normal range 0.5 to 5 μg Cd/g creatinine with no low environmental exposure to Cd. All these results reinforce the interpretation that the alleged association between renal NAG activity and moderate exposure to Pb may be insufficiently demonstrated by the findings of this and other studies. The finding, however, is frequently due to the fact that these authors have neglected to take into account the slightly increased body burden of Cd that is a frequent finding in workers exposed to Pb.

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