

PostScript

LETTERS

Neurobehavioural testing in workers occupationally exposed to lead

Whether or not low to modest levels of exposure to lead have a detrimental effect on cognition is an important issue given the growing attention, for example, in the United States, that has recently been paid towards potentially revising downward the levels of lead exposure allowed in the workplace. Thus, we read with interest the meta-analysis of studies on this topic that appeared in this journal by Goodman and colleagues.¹ Unfortunately, we believe that the authors' conclusions are not valid. Specifically, the authors state that "the data available to date are inconsistent and are unable to provide adequate information on the neurobehavioural effects of exposure to moderate blood concentrations of lead". We found no direct support for this conclusion in the publication. Moreover, numerous flaws in their method limit any specific inferences that can be made. In general, we found that the meta-analysis combined evidence from studies of widely varying quality and did not account for significant confounding within and between studies. Given these and other flaws, it was predictable that the authors did not find an association between blood lead levels and neurobehavioural test scores.

Specific concerns that we had with the methods include: (1) The authors offer no evaluation of the quality of the evidence from available studies based on study design and analytical method. (2) The authors combine data from poorly done studies with data from well done studies, clouding any effects that are observable from the better conducted studies. (3) Although age and education adjustment within studies is assessed, six studies were included that did not adjust for age, and another three studies did not adjust for education. These are the two most well established predictors of neurobehavioural test scores and the most important potentially confounding variables. (4) Even among the remaining studies that did adjust for age and education, the authors do not address the confounding in the meta-analysis that is caused by variation in age and education across study populations. (5) The authors' main effect measure is an exposed versus control comparison. Among the options that could have been pursued, this is the effect measure with the lowest power. It is unable to assess a dose-effect relation, and it is also the one most prone to selection bias. (6) Relatively few of the 22 studies listed in table 2 contribute to the estimate of the effect size for each neurobehavioural outcome. Moreover, the authors do not state which studies contributed to the effect estimate.

It is important to note that several recent studies, all published before this article was accepted for publication, reported that blood lead was associated with neurobehavioural test scores in multiple cognitive domains. One study of 803 Korean lead workers is the largest study reported to date and observed consistent associations of blood lead with test scores in the domains of executive abilities,

If you have a burning desire to respond to a paper published in *Occupational and Environmental Medicine*, why not make use of our "rapid response" option?

Log on to our website (www.occenvmed.com), find the paper that interests you, and send your response via email by clicking on the "eletters" option in the box at the top right hand corner.

Providing it isn't libellous or obscene, it will be posted within seven days. You can retrieve it by clicking on "read eletters" on our homepage.

The editors will decide as before whether to also publish it in a future paper issue.

manual dexterity, and peripheral motor strength at blood lead levels as low as 18 µg/dl.² In another study of former organolead manufacturing workers, tibia lead was associated with test scores at cross section and with longitudinal declines in test scores.³ These findings suggest that lead may have both short term and progressive influences on neurobehavioural performance.

We elaborate on our main concerns, below.

(1) No evaluation of the quality of the evidence available from studies, and (2) Data from poorly done studies were combined with data from well done studies. It is traditional in meta-analysis to establish a priori criteria for what defines acceptable evidence from studies. The authors only had three inclusion criteria, none of which refer to the quality of the study designs, analytical method, adjustment for confounding, evaluation of bias in selection of exposed and non-exposed subjects, and other such methodological factors. There is apparently no consideration for this arguably single most important step in meta-analysis. The meta-analytical results could simply reflect wide heterogeneity in the quality of the evidence that was combined. This factor alone could account for the overall conclusion of no association.

(3) Inclusion of studies that did not control for age and education. Age and education are the two most important predictors of neurobehavioural test scores in working populations. In the absence of adjustment for these confounders there should be convincing evidence that the two groups being compared were equivalent in age and education. Eight of the included studies did not adjust for age and/or education. The authors offer no explanation for why these studies should be included in the meta-analysis.

(4) No adjustment for age, education, or lead dose differences across studies. By not adjusting for age and education differences across studies, the authors make an implicit assumption that age and education do not modify the relation between blood lead and neurobehavioural test scores. This may or may not be true. In the meta-analysis, the authors also implicitly assume a fixed difference in blood lead levels between exposed and non-exposed groups. Table 1 clearly indicates that this assumption does not hold.

(5) Reliance on exposed versus control comparisons. This is a weak test and a test

that is not germane to the conclusions that the authors make. The authors conclude that blood lead levels, that are described as "moderate" in one location in the manuscript and "low" in another, are not associated with neurobehavioural test scores. All studies included exposed workers with a range of blood lead levels, from very low to high. More appropriate approaches could have been considered, for example, only including studies that reported beta coefficients for the blood lead versus test score relation, or adjusting for mean blood lead levels in exposed and non-exposed groups.

(6) Reliance on a small number of unspecified studies for effect estimates. Table 2 of the meta-analysis reports the number of studies that were combined to derive effect estimates, but does not specify which studies were combined. This omission does not allow the reader to determine whether solid evidence was combined with more questionable evidence, or to evaluate whether any of the issues described above were germane to the effect estimates reported.

Two more concerns exist regarding the authors' treatment of the issue of cumulative versus ongoing lead exposure, as well as the identification of the source of funding for this study. In their introduction, the authors quote the review by Balbus-Kornfeld *et al*, which noted that "the current scientific evidence is flawed because of inadequate estimation of cumulative exposure to or absorption of lead ..." but fail to acknowledge this issue in the interpretation of their own meta-analysis. In fact, as has been widely reported in the literature, methods are now available to non-invasively measure bone lead levels as a reliable and accurate measure of cumulative lead dose. Several studies³⁻⁵ suggest that cumulative lead dose, as measured by tibia lead levels, is a very important biological marker that may be related to cognitive decrements not predicted by blood lead levels. With regard to funding, the authors note that they are mainly from the Exponent Health Group in Alexandria, Virginia, and Menlo Park, California; however, they fail to describe what motivated the study or sources of funding for the study. We believe this information would be of interest to scientists and policy makers engaged in work on this topic.

B S Schwartz

Professor and Director, Division of Occupational and Environmental Health, Johns Hopkins Bloomberg School of Public Health; bschwartz@jhsph.edu

W Stewart

Adjunct Professor, Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health

H Hu

Associate Professor and Director, Occupational/Environmental Medicine, Department of Environmental Health, Harvard School of Public Health

References

- 1 Goodman M, LaVerda N, Clarke C, *et al*. Neurobehavioural testing in workers occupationally exposed to lead: systematic review and meta-analysis of publications. *Occup Environ Med* 2002;59:217-23.

- 2 **Schwartz BS**, Lee BK, Lee GS, *et al.* Associations of blood lead, dimercaptosuccinic acid-chelatable lead, and tibia lead with neurobehavioral test scores in South Korean lead workers. *Am J Epidemiol* 2001;**153**:453–64.
- 3 **Stewart WF**, Schwartz BS, Simon D, *et al.* Neurobehavioral function and tibial and chelatable lead levels in 543 former organolead workers. *Neurology* 1999;**52**:1610–17.
- 4 **Schwartz BS**, Stewart WF, Bolla KI, *et al.* Past adult lead exposure is associated with longitudinal decline in cognitive function. *Neurology* 2000;**55**:1144–50.
- 5 **Payton M**, Riggs KM, Spiro A III, *et al.* Relations of bone and blood lead to cognitive function: the VA Normative Aging Study. *Neurotoxicol Teratol* 1998;**20**:19–27.

Suicide mortality among electricians

Järholm and Stenberg¹ evaluated suicide mortality rates among electricians (“exposed to electromagnetic fields (EMFs)”) and glass and wood workers (“unexposed to EMFs”) in the Swedish construction industry. Standard mortality rates were lower for the two job groups compared to the Swedish general population. This is likely to be due to the healthy worker effect. The internal cohort analysis showed that electricians had a lower suicide mortality rate than glass and wood workers.

As the authors rightfully point out, these results should not be seen as evidence against the association between exposure to EMFs and suicide, in particular because no quantitative estimates of exposure were obtained to directly evaluate this association. Järholm and Stenberg cited a small measurement survey in the Swedish construction industry, which indicated that exposure levels were low and comparable between the two occupational groups. Therefore, one would not expect to see an EMF mediated increase in suicide risk among electricians compared to glass and wood workers, if an association between EMF exposure and suicide truly exists.

Järholm and Stenberg suggested that the difference in suicide rate between the two job groups was unlikely to be due to differences in socioeconomic factors, but they did not provide an alternative explanation. One possible explanation may be a healthy worker survivor effect related to employment status (for example, at time of death) within this cohort. That is, active workers may be more physically and mentally fit than those who left the industry or are unemployed, and may therefore be at lower risk of committing suicide.² A large body of literature suggests that unemployment and suicide are positively related,^{3,4} and being out of work was positively associated with suicide in the electric utility industry.⁵ Since cessation of work also leads to cessation of work related exposures, employment status may be an important potential confounder (or perhaps effect modifier) for the association between work related exposures and suicide. The lower suicide rate among electricians compared to glass and wood workers may be explained by a larger proportion of glass and wood workers with an inactive employment status at the time of death.

Although it is unlikely that consideration of employment status, if possible, would greatly alter the conclusions reached by Järholm

and Stenberg,¹ it would be informative to see its influence on the rate ratio.

E van Wijngaarden

Department of Epidemiology, School of Public Health, University of North Carolina at Chapel Hill, Chapel Hill, NC 27599-7435, USA; edwin@unc.edu

References

- 1 **Järholm B**, Stenberg A. Suicide mortality among electricians in the Swedish construction industry. *Occup Environ Med* 2002;**59**:199–200.
- 2 **van Wijngaarden E**, Savitz DA, Kleckner RC, *et al.* Exposure to electromagnetic fields and suicide among electric utility workers: a nested case-control study. *Occup Environ Med* 2000;**57**:258–63.
- 3 **Dooley D**, Fielding J, Levi L. Health and unemployment. *Annu Rev Public Health* 1996;**17**:449–65.
- 4 **Kposowa AJ**. Suicide mortality in the United States: differentials by industrial and occupational groups. *Am J Ind Med* 1999;**36**:645–52.

Authors' reply

We appreciate Dr Wijngaarden's interest in our report and his suggestion for understanding the differences in risk. Dr Wijngaarden suggests that difference in unemployment rate between electricians and glass worker and wood workers could be an explanation.

We have no data on employment status at time of death and can therefore not test this hypothesis. However, if employment status is an important predictor, this could explain some of the difference, as the wood workers had a different employment structure to the other groups. Electricians and glass workers have had permanent positions for a long time, while wood workers were employed for a certain project, for example, building a house, before the 1990s. When the project was finished they had to find another employer. Today, most construction workers have permanent positions in Sweden.

In our search of the literature in an attempt to understand differences in suicide rates between occupations, we found little information. This might be an important area of research in the future.

B Jarvholm, A Stenberg

Dept of Public Health and Clinical Medicine, Occupational Medicine, Umeå University, S-901 87 Umeå, Sweden; bengt.jarvholm@envmed.umu.se

Are incinerator workers exposed to PCDDs and PCDFs?

Kumagai and his colleagues¹ have reported that incinerator workers employed at intermittently burning incineration plants were not necessarily exposed to high concentrations of polychlorinated dibenzo-*p*-dioxins (PCDDs) and polychlorinated dibenzofurans (PCDFs). The authors' conclusions were based on concentrations of PCDDs and PCDFs in serum samples of the workers.

I have deep concerns regarding the study methodology and results which do not consider the accumulation of PCDDs and PCDFs in the adipose tissue. PCDDs and PCDFs are organochlorines with different degrees and positions of chlorination, which determine their persistence and toxicity. They are lipophilic and difficult to metabolise, and any environmental exposure of living organisms to them results in their accumulation and persistence in fat tissues.² Meanwhile, it is feasible to use blood sera to obtain and

analyse PCDDs and PCDFs. Adipose tissue organochlorines levels have been regarded as a preferred indicator of human exposure. Levels in adipose tissue are known to be higher and more representative of the cumulative internal exposure.^{2,3} Previously, Archibeque-Engle and colleagues⁴ did not find a significant relation between serum concentration and tissue residues for organochlorine compounds. Based on the lack of correlation between adipose tissue and serum, as well as an absence of some compound residues in serum, the authors emphasised that adipose tissue should be analysed in addition to serum.

Finally, I would like to acknowledge the authors for such original subject study, which enables us to raise the profile of and discuss new hypotheses in environmental and occupational health.

M F Allam

Department of Preventive Medicine and Public Health, University of Cordoba, Spain; fm2faahm@uco.es

References

- 1 **Kumagai S**, Koda S, Miyakita T, *et al.* Polychlorinated dibenzo-*p*-dioxin and dibenzofuran concentrations in serum samples of workers at intermittently burning municipal waste incinerators in Japan. *Occup Environ Med* 2002;**59**:362–8.
- 2 **Angulo R**, Martinez P, Jodral ML. PCB congeners transferred by human milk, with an estimate of their daily intake. *Food Chem Toxicol* 1999;**37**:11081–8.
- 3 **Lopez-Carrillo L**, Torres-Sanchez L, Lopez-Cervantes M, *et al.* The adipose tissue to serum dichlorodiphenyldichloroethane (DDE) ratio: some methodological considerations. *Environ Res* 1999;**81**:142–5.
- 4 **Archibeque-Engle SL**, Tessari JD, Winn DT, *et al.* Comparison of organochlorine pesticide and polychlorinated biphenyl residues in human breast adipose tissue and serum. *J Toxicol Environ Health* 1997;**52**:285–93.

Importance of work intensity on respiratory problems in hairdressers

We read the report by Hollund *et al* with great interest.¹ We agree that there is limited information about the prevalence of airway symptoms caused by highly reactive chemicals in hairdressing salons. In this well designed study, authors focused on age as a risk factor and observed an increased prevalence of respiratory symptoms among the oldest and youngest hairdressers and observed more symptoms among hairdressers over 40 years of age.

Work intensity, work duration, working conditions, and job titles (master, and fellow hairdresser) should also be considered as risk factors for occupational asthma and respiratory symptoms. With the exception of work intensity, these features have been reported as risk factors in previous studies.^{2–4} Work intensity is an objective parameter for evaluating occupational exposures. In our study, we calculated work intensity from the average number of chemical applications per week (bleaching, dye, and permanent wave) and observed a 3.6 times higher risk of occupational asthma among hairdressers with high work intensity (95% CI 1.2 to 10.9) with a significant trend (χ^2_{trend} 4.9, $p = 0.027$).⁵ However, we did not observe any excess by work duration, which probably is a result of the healthy worker effect. Hollund *et al* stated that the older hairdressers had more customers than the younger ones, which may be