a confusing problem in controlling for factors such as alcohol when it is unclear whether one is controlling for a true confounder or a factor in the chain of causality.[7] The analysis reported by Staessen *et al* has this problem. Their use of stepwise multiple regression methods to determine the important independent predictors of blood pressure is suspect; the method is fraught with inferential hazards due to the vagaries of statistical model assumptions, multicollinearity, measurement error, and construct validity.[8-10]

Lastly, recent studies suggest that use of tobacco may negatively confound a relation between blood pressure and concentration of lead in blood.[11 12] Tobacco users tend to have higher blood lead concentrations, but lower blood pressures. Indeed, it may be necessary to not only take into account usual smoking habits, but also smoking behaviour proximate to collection of data.[11] With such a strong relation between concentration of lead in blood and use of tobacco in their data, what is the joint relation with blood pressure?

With respect to attributable risk, the North Americans suffer from too narrow a perspective. One of the difficulties in interpreting data from epidemiological studies examining this relation is that designs and statistical analyses have ignored the results of experimental research pointing to a biological mechanism by which lead probably exerts its effect. This mechanism suggests that lead acts as a potentiator, or effect modifier, of a causal relation between a triggering agent and the blood pressure response.[13 14]

If true, then relations described by large cross sectional population studies are probably the wrong design to disentangle the nature of this relation. Indeed, they may even lead to a false impression as to the public health importance of lead as a causal factor in the development of raised blood pressure. This is due to the failure of such methods to take into account the effects of these triggering agents, and particularly a failure to distinguish between the acute and the chronic effects of such triggers.

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Glomerulonephritis, renal carcinoma, and solvent exposure: bias from choice of referents

Sir,—Harrington *et al* (1989;**46**:643–50) claim that their case-referent study of renal disease and exposure to organic solvents is superior to previous studies; they consider their study methodologically relevant, whereas previous ones (concerning glomerulonephritis) almost without exception, they argue, had serious methodological flaws.

With their phrase "almost without exception" Harrington *et al* mean five of seven, but to reach this number they have ignored two strong case-referent studies.[1 2] That their results are contrary to eight of nine previous studies does not bother them because they obviously think that studies, the designs of which are open to bias, are automatically wrong. The claimed superiority of their work is open to discussion, however.

Firstly, although not stated directly, it apparently concerned only acute glomerulonephritis as they excluded non-acute cases. There is only one such study previously. In that, the exposure was time related to a streptococcal infection in ten of fifteen patients, but in most the exposure was of short duration.[3] Bearing its rareness in mind I doubt that Harrington *et al* have collected 50 patients with acute poststreptococcal glomerulonephritis; neither was it mentioned in the paper. Thus what they have found is that *acute* non-streptococcal glomerulonephritis is not associated with *long term* exposure to solvent, a finding of dubious value for excluding a causal association.

Even if we assume that patients with chronic glomerulonephritis were included, the design and the conclusions of their study are questionable. It is elementary that occupational referents should represent the general population. Community based referents from the same socioeconomic group and the same geographic location may automatically include many people with the same occupation and thus with a similar degree of exposure as the cases, especially in an area with an industrial bias such as the West Midlands. The presence of this bias is suggestive judged from the high degree of exposure in the referent group. Thus an exposure index of greater than 1–100 in 60% of the referents by far exceeds the degree of exposure of the referents in previous studies. An exception is the unblinded study of van der Laan[4] who found that 54% of the referents had had moderate to severe exposure to organic solvents for 400 hours or more. Anyone familiar with the working conditions

of the general population of a western society will know that a serious bias must have been introduced.

The high degree of exposure in the referent group of Harrington *et al* may possibly reflect the average exposure of the working population in the West Midlands, but probably not the exposure of the general population; certainly not of the general population in other areas. The study of Harrington *et al* has confirmed that patients with glomerulonephritis are frequently exposed to organic solvents, but due to their choice of controls their finding is not conclusive.

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Author's reply

Ravnskov raises some interesting issues concerning our paper. He is, of course correct in pointing out, as we do, that our findings are inconclusive due to power considerations in the case-referent design. Unfortunately, however, he does not write from a totally unbiased position, given the fact that his studies are among those commented on in our discussion.

We did not "ignore" any of the relevant studies—indeed his work is cited as important and relevant. But it is too simplistic merely to add up studies and weigh them in some numeral balance of for or against. All published studies need to be assessed for their epidemiological strengths and weaknesses. When this more logical approach is used, most are found wanting, including ours.

The point about streptococcal and non-streptococcal glomerulonephritis is valid. The use of community referents may be "elementary" but it is methodologically difficult which is perhaps why most other studies eschew the device. That alone weakens such studies. Hospital based controls are universally recognised as inherently more biased than community based controls. In our paper we go to considerable lengths to point out that our results are inconclusive, an aspect which needs no further emphasis by Ravnskov. Nevertheless, it is clear to any unbiased observer that most of the published studies are seriously flawed. Ours may have low power but at least it avoids most of the weaknesses inherent in most of the other studies.

NOTICES

3rd Meeting of the International Neurotoxicology Association, Salsomaggiore Terme (Parma), Italy, 1–5 July, 1991.

The 3rd INA meeting will provide a forum for interdisciplinary exchanges between scientists involved in different areas of neurotoxicology, including experimental, clinical and epidemiological aspects, and covering a wide range of relevant information from neuropathology, neurochemistry, neurophysiology, neuroteratology, and neurobehavioural toxicology. Four symposia based on invited lectures will be arranged by the scientific committee. Unsolicited contributions will be presented as posters, which will be discussed during special sessions. Workshops on specific issues will also be organised. The preliminary programme includes subcellular and cellular mechanisms of neurotoxicity; neurotoxicity and ageing; developmental neurotoxicity; and screening for neurotoxicity in humans. For further information, contact: Dr A Mutti, Organising Secretary 3rd INA Meeting, Laboratory of Industrial Toxicology, University of Parma—Via Gramsci 14, I-43100 PARMA Italy.

International Symposium on Future Trends in the Changing Working Life, Finlandia Hall, Helsinki, Finland, 13–15 August 1991.

Many factors, including internationalisation, automation, raised level of education and training, aging of the population, and changes in values and attitudes will drastically change the nature of work in the next decade and into the 21st Century. The general objective of the Symposium is to facilitate the transfer of research to benefit the development of work and the quality of the working life in the future. To achieve this four major themes will be considered in plenary sessions—namely, work in an international environment, the quality of working life, work in the future, and human resources in work in the future. Particpants are welcome to present oral free communications or posters, or to participate in formal and informal discussions. The official language of the Symposium is English, with simultaneous translation into Finnish. For further information contact: Work in the 1990s International Symposium on Future Trends in the Changing Working Life, c/o Institute of Occupational Health, Suvi Lehtinen, Topeliuksenkatu 41 aA, SF-00250 Helsinki, Finland.

Correction

On talc, tremolite, and tergiversation (1990;**47**:505–507).

Owing to a copy editing error lines 3–5 second column page 505 are incorrect. They should read " . . . various forms of asbestos, fibrous glass, and the fibrous earths including attapulgite and sepiolite.[5]"