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. The analysis reported by Staessen et al. has this problem.
Their use of stepwise multiple regression methods to determine the impor-
tant 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 con-
found 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.13 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 statisti-
cal 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 rela-
tion. 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 pres-
sure. 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 car-
cinoma, 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.13 14 That their results are con-
try 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 stre-
tococcal infection in ten of fifteen
patients, but in most the exposure was
of short duration.13 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 glomerulo-
nephritis 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 conclu-
sions of their study are question-
able. It is elementary that occupa-
tional referents should represent the
general population. Community
based referents from the same socioe-
conomic 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 Laan1 that 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

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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


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, neurotoxicology, 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.


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. Participants 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

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