

Re: “Cardiovascular diseases and the work environment: a critical review of the epidemiologic literature on chemical factors” by TS Kristensen. *Scand J Work Environ Health* 1989;15:245—64

In his article on cardiovascular diseases and the work environment (1), Mr Kristensen briefly reviewed the epidemiologic literature on occupational chemical factors and cerebrovascular diseases. It is well known that epidemiologic studies can only show associations, but never prove causality. Yet, Mr Kristensen clearly stated in his first conclusion of the lead discussion that there is a causal relationship between lead exposure and blood pressure.

In a paper cited by Kristensen from *Environmental Health Perspectives* (2) Pocock et al stated that there is “no convincing epidemiologic evidence at present to support the claim that moderate elevations in body lead burden are of relevance to the risk of cardiovascular disease.” In the concluding paragraph of the conference discussion summary in the same issue of *Environmental Health Perspectives* (3), Schwartz stated that, although causal inference can be made from the animal studies on blood lead and blood pressure, causal interpretation cannot be taken from the epidemiologic studies. Since Mr Kristensen stated that he was reviewing epidemiologic studies, he should make a distinction between causality and association in his conclusions on lead.

Further clarification is needed on the discussion of the Cooper study (4). Mr Kristensen stated that Cooper found moderately elevated or normal standardized mortality ratios for cerebrovascular disease but failed to state that these figures were not significant. When proportionate mortality analyses were done in which race was taken into account, there were significant deficits in deaths from vascular lesions of the central nervous system for battery workers, and for production workers only “other hypertensive diseases” remained significant.

No data on blood lead exposure was presented in the Cooper study; however, Cooper stated that if the

cerebrovascular deaths from the Dingwall-Fordyce & Lane study (5) and the Malcolm & Barnett study (6), both heavily exposed populations, were combined, the results would be a nonsignificant standardized mortality ratio of 107. Cooper suggested that, if a heavily-exposed group could have been defined in his study, it might have duplicated the results from the studies from the United Kingdom.

Mr Kristensen would have done better to review fewer chemicals and to be more detailed on his study reviews so that all relevant facts necessary to draw the appropriate conclusions would have been included.

References

1. Kristensen TS. Cardiovascular diseases and the work environment: a critical review of the epidemiologic literature on chemical factors. *Scand J Work Environ Health* 1989;15:245—64.
2. Pocock SJ, Shaper AG, Ashby D, Delves HT, Clayton BE. The relationship between blood lead, blood pressure, stroke, and heart attacks in middle-age British men. *Environ Health Perspect* 1988;78:23—30.
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4. Cooper WC, Wong O, Kheifets L. Mortality among employees of lead battery plants and lead-producing plants, 1947—1980. *Scand J Work Environ Health* 1985;11:331—45.
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Rosalind A Volpe, DPH
Consultant, Environmental Health
International Lead Zinc Research Organization, Inc
PO Box 12036
Research Triangle Park, NC 27709-2036 USA

Author's reply

I welcome the opportunity to comment on a very central question in epidemiology — and in all empirical science for that matter: When is causality proved? Dr Volpe states: “It is well known that epidemiologic studies can only show associations, but never prove causality.” It is — implicitly — understood that studies employing other methods (experiments, I suppose) can

prove causality. This may be “well known,” but I still disagree. Causality can never be proved in the empirical sciences. All we can do is increase the quantity and quality (!) of our scientific investigations. By doing so, we can improve the scientific basis on which we form our judgments about the tenability of hypotheses. But we will never get final proof, and we will always have to live with some uncertainty.

In the last few years, there has been increasing interest among epidemiologists in the question of causal inference. One of the best discussions on the topic can be found in the book *Causal inference* (1). In this book Lanes writes: "Instead of asking what aspects of the data can establish causality, we should ask what other theories could explain the data [p 67]". Adopting this line, I would ask Dr Volpe that, if exposure to lead does not increase blood pressure and the risk of cerebrovascular diseases, how else can we explain the results of the empirical studies quoted in my review and the trend in table 1 on page 246 (2)? Attempting such an explanation would be much more fruitful than a discussion about the "significant" and "nonsignificant" standardized mortality values given in the few studies selected by Dr Volpe.

Dr Volpe writes that "Mr Kristensen would have done better to review fewer chemicals and to be more detailed on his study reviews so that all relevant facts necessary to draw the appropriate conclusions would have been included." As mentioned in my review, Sharp et al published (3) a very comprehensive and thorough review in 1987 on the very topic of lead exposure and hypertension. They concluded: "The scientific evidence in its totality strongly indicates a causal

relationship between lead exposure characteristics of the environment and elevation of blood pressure [p 228]." And added: "The biological plausibility of this relationship is well substantiated by animal experiments [p 228]" (3).

I might have "done better" to review fewer chemicals. However, I very much doubt that it would have changed my conclusions concerning lead.

References

1. Rothman KJ, ed. *Causal inference*. Chestnut Hill, MA: Epidemiology Resources Inc, 1988.
2. Kristensen TS. Cardiovascular diseases and the work environment: a critical review of the epidemiologic literature on chemical factors. *Scand J Work Environ Health* 1989;15:245-64.
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Tage S Kristensen, MSc
University of Copenhagen
Panum Institute
Blegdamsvej 3
DK-2200 Copenhagen N Denmark