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Increased incidence of renal cell tumours in a cohort of cardboard workers exposed to trichloroethylene

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Sir:

Recently an article was published describing the incidence of renal cell tumors in a cohort of cardboard workers exposed to trichloroethylene (Henschler et al. 1995). This article describes a retrospective cohort study of 169 workeen exposed to trichloroethylene (TRI).

There are several remarks to be made about lhis study. First, the original exposed cohort consisted *of* 183 male workers, but 14 subjects were excluded because they refused or were too ill io participate or could not be traced by the closing day *of* the study. Subjects *who* are lost to follow-up *and* whose vital status cannot be determined at the end-date of the follow-up should *never* be excluded from the analysis of a retrospective cohort study, but should remain in the cohort until the dale that they were lost from follow-up. A similar methodological error is indicated by Table I (description of the TRI-exposed and control cohorts). In this table it is stated that the median time of entry for the exposed group is 1956, with a minimum of 1918 and a maximum *of* 1972. This means that *subjects* were already regarded as being at risk in 1918, which conflicts with the exposed cohort definition, *which* demands exposure to have take place between 1956 and 1975. Probably 1918 is the earliest date of birth. However. the person-years at risk generation does not start at birth. but after 1 year *of* exposure starting from I January 1956.

Secondly. no exposure information is available. The authors merely speculate that the exposures must have been high, but they present no evidence, except some cases of acute toxicity. These cases occurred during repair and maintenance and should not be seen as representative for the general working conditions. Although there are no exposure data, from the description of the cases in Table 3 only two of the renal cell cancer patients held jobs associated with a high degree of exposure (job in board machine area).

Thirdly, far the workers who had died the causes of death were obtained from hospital medical records or from the physician who last treated the patient. This information was compared to mortality rates of *the* general male population. The information from the hospital records and treating physicians may be *of* a better quality, which makes a comparison with the general population mortality rates incorrect.

Fourthly. the cancer incidence section of the paper is very peculiar. in a normal retrospective cancer incidence study one expects to find the usual range of cancer lypes, including some lung cancers, digestive tract cancers, skin cancers etc. However, in this cancer incidence study only *renal* cancers are reported. From this observation, it can *be* deduced that no general inventory of cancer incidence was performed. in a consistent reproducible fashion, similar for both cohorts. It *is* not clear how the cases *of* renal cancer were detected. The only logical explanation is that the cases of renal cancer had already been observed prior to the initiation of the actual study and even worse. that the cases of renal cancer triggered the *conduct* of the *study. If* this is true, then we are merely dealing with a cluster investigation, dressed up with some additional data collection to mimic a poorly conducted retrospective cohort study. In the case of a prior cluster of renal cancer, followed by a poorly conducted study, it comes as no surprise that more cases of renal cancer were found than expected. In this setting, it is inevitable to find an increased incidence of renal cancer. If there was a prior cluster of renal cancer in the cardboard workers that triggered the epidemiological investigation, this should have been clearly described in the report, because it puts the results in a completely different perspective. The omission of this information in the article is a serious violation *of* epidemiologic conventions.

The occurrence of disease is not evenly distributed across the total population. Chance is an important factor. There will always be clusters of diseases. If these *fall in a*

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certain exposed group, they may appear to be causally linked with the exposure, but in reality it is just a coincidence. Epidemiologists agree that the investigation of a cluster has a limited significance for *the* detection of risk factors for diseases. *Rothman (1990)* refers to this phenomenon as the Texas sharpshooter procedure. The Texas sharpshooter first fires some shots and then draws the target where the *shots* have hit the wall.

The uneven distribution of diseases in human populations is clearly demonstrated in this study. The only statistically significant finding of the SMR analysis in this study (Table 5) is a nearly tenfold increase of brain tumor mortality in the non-exposed group. The three deaths from a brain tumor are about half as likely to occur as the two deaths from kidney *cancer*.

Finally, Henschler downplays the relevance of the negative retrospective cohort mortality studies with the argument that these studies may have missed a kidney cancer risk, because kidney cancer has a *good* survival rate. Cases of kidney cancer would not be picked up in mortality studies. This argument is not correct. The survival rate is indirectly relevant for detectability in mortality studies. If a disease has a relatively high incidence, despite the good prognosis, changes in the mortality rates will be *detected* in mortality studies. The background mortality rate is crucial for the statistical power of a mortality study, given a certain relative risk. The age adjusted mortality rates for kidney cancer in the general population are in the same order of magnitude as for brain tumor mortality or leukemia (kidney cancer mortality = 5.8 per 100000; brain tumor mortality = 5.1 per 100000; leukemia = 5.5 per 100000: CBS 1992). Given a certain relative risk, a cohort mortality study is just as capable of detecting a kidney cancer risk as a brain tumor risk or a leukemia risk.

It is quite clear that the study presented by Henschler is seriously biased by the a priori presence of a cluster of renal cell tumors. By withholding information on the a priori presence of a cluster of renal cell cancer, the authors incorrectly pretend to have carried out a proper cohort study, which is not the case. It is obvious that this study cannot be used in support of a causal association between exposure to TRI and renal cell cancer.

References

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