much longer. and carcinogens, resistant

In heavy oils mineral the against skin measures. With modern hygiene and protective measures against skin contact and especially against inhalation, however, the risk of cancer in people from exposure to such fluids and oils is probably small.

1 Iversen OH. Tumorigenesis and carcinogenesis studies of a number of insulation oils and fluids on hairless and SENCAR mice with special reference to skin tumours and malignant lymphomas. *APMIS Suppl* (in press).

**Kidney cancer in utility workers exposed to polychlorinated biphenyls (PCBs)**

Sir,—On reading this paper (1989; 46:823–4) I found that the three case reports involved workers commonly exposed to several substances (of which PCBs were one group) and that there was absolutely no evidence offered (or found) which indicated that PCBs were any more responsible aetologically for the cancers than any of the other common exposures.

The title of the paper suggests to me that the authors have capitalised on the current PCB hysteria fostered by the popular press in North America—and perhaps in Europe? I am surprised that you let that title pass: it is misleading. Nowhere, other than in the title, do the authors infer a causal relation between the cancer and any of the substances to which the men were exposed. No evidence is presented even to suggest there might be a statistical association between the cancers and exposure to PCBs.

**Correspondence**

This conclusion is not justified for methodological reasons and because of limitations of both studies.

"The Michigan sample is described as ‘a probability sample of a large 9,000,000 population industrial state.’ But the sample was small and it cannot be concluded that it is representative. Firstly, the sampling was biased towards rural dwellers by taking different sampling rates for six geographical regions “to ensure that an adequate number of people would be selected in each area to justify establishing a clinic there.” No information is provided on the numbers of people selected. There were 4077 initial volunteers, of whom 2542 agreed to be examined. Of these, 1738 actually completed the examinations. So it is most unlikely that the participation rate was higher than 20%.

These numbers were whittled down further: others excluded were 507 children, 249 non-white adults, 159 obese people, 339 clinically abnormal, and 88 ex-smokers. This left just 190 men and 216 women. The prediction equations for lung function for Michigan women used in the Killburn paper were based on just the 216 non and current smokers aged 18 to 82. But even then a further 23 women were excluded from the calculations because the data “were identified as influential values.” Thus these 23 women must have had data which changed either the slope or position of the regression relations, so that their inclusion would have yielded a different regression line. It is impossible to conclude that these 193 white, non-obese, clinically non-abnormal, non-extreme women are representative of all Michigan women, let alone of all American women. It needs to be noted that the 23 additional exclusions were from all lung function analyses (FVC, FEV₁, FEV₁/FVC %, FEF₂⁰₋₅₀, FEF₅₀₋₇⁰, FEF₇⁰₋₉⁰, FEF₉⁰₋₇₀, and FEF₇₀₋₂₀), but it is not stated whether their extreme influence affected all relations or only one.

The Killburn paper, however, reports that "The entire Michigan sample of 486 white women which provided a representative sample of women in the United States was compared with white women in this paper. It appeared reasonable to compare them with a representative population for evidence of an occupational exposure rather than with a hand picked normal group selected for modelling.” Thus he is saying that he added back to the 193...
non and current smokers those with influential values, the ex-smokers, the obese, and the clinically abnormal. The number 486 agrees with the Miller paper, but the regression lines in table 2 and the figure in the Kilburn paper are those for the 193 subjects only. The Kilburn paper is positively misleading on this.

Before turning fully to the Kilburn paper, it is appropriate to comment further on the regression lines presented by Miller et al. The lines are linear relations of the lung function indices to age and height. They are based on women aged 18 to 82. For men, it is generally accepted that lung function continues to increase up to about age 25. Although the turning point may be lower for women, it will still probably be at least age 21. Thus the inclusion of younger women will bias the regression line to have a flatter age slope than it should be. Most influential data points will occur at the extremes of age or height, or both. This may have led to the exclusion of some of the youngest subjects but could also have excluded older subjects with relatively reduced lung function but still clinically normal for age. This again would have flattened the regression lines.

Kilburn studied histology technicians who attended four national conventions of the National Society of Histotechnology. The attendance rate varied between 22%, and 42%.

Kilburn argued that because "recruitment was directed at non-behavioural symptoms and testing a biased selection for pulmonary function testing seems unlikely." Under the circumstances of a series of national conventions, it must be assumed that volunteers (except perhaps the first few) were aware that lung function testing was included. With such poor response rates, it cannot be concluded that the selection was unbiased. Kilburn et al also make the implicit assumption that attendees at national conventions are representative of all histology technicians.

The comparisons in table 2 and the figure of the Kilburn paper are used to argue that the relations to age are steeper for the histology technicians and so the technicians must have an adverse occupational environment. It has already been pointed out above that the comparison Michigan relations are not based on all 486 comparison subjects. Also, the comparison regressions probably have too low age coefficients. Yet, for FVC for example, the Miller et al age coefficient is -0.0232 with standard error 0.0024. The slope for the histology technicians is -0.0273 well within the 95% confidence interval for the Michigan sample. For FEV1, the technicians age coefficient does lie outside that for the confidence interval for the Michigan group. But no standard error is given for the technicians, so it is impossible to determine what an appropriate statistical analysis would have shown. For FEF25-75, Kilburn et al have compared age coefficients when one relation includes height as a covariate and the other does not. It only requires a small correlation between age and height, as occurs commonly, to invalidate this comparison. It is incorrect to conclude that the histology technicians have a significantly steeper age coefficient. This part of the analysis was statistically unsatisfactory.

There is also another implicit assumption—that differences between people of varying age reflect the change in an individual with increasing age. This is generally not fully true, because of changes in nutrition—for example, between people born in the 1940s and the 1960s, and because of changing occupational exposure circumstances, if there is an exposure effect.

Finally, Kilburn et al conclude that the reduced lung function is caused by exposure to low doses of formaldehyde. To draw that conclusion, comparison must be made between those with known exposure to formaldehyde to those without, standardising for other exposures. Only a little information on exposure levels in the Los Angeles area is provided. Such information showed wide variability for all substances analysed (formaldehyde, xylene, toluene, and chloroform). No exposure data for other parts of the United States were provided. There is no justification in ascribing any occupational effect to formaldehyde, or indeed to any of the four substances.

In addition, in response to Rossiter's comment concerning lack of a height coefficient for FEF25-75 in the Miller equation, we have provided an equation from Morris et al7 with a height coefficient and calculated the FEF25-75 at the same five age intervals. As can be seen, they show an annual decrement of 31 ml which is much nearer to the Miller one of 36 ml than the histotech decrement of 57 ml a year.

In table 3 and thus in the figure he has correctly noted that the comparison was made with the Michigan model population of Miller et al, not with all Michigan women.

In addition, we note that the small difference for FEF25-75 1/sec in the first column under L Rock (60), is not statistically significant—the asterisk should be removed.

In modelling the Michigan women for pulmonary function values no increase or decrease with age was found to support the concept of a "turning point" between ages 21-25; thus the age slopes were linear from 18 to 82. This was confirmed by residual analyses which were clean. Thus inclusion of younger women did not bias the age slope. The exclusion of 23 women in modelling Michigan did not change the regression equations for FVC, FEV13, or FEF25-75 relied on in this paper.

The other issues raised by Rossiter are considered below.

(1) The comparison group is not a representative sample. The Michigan population probability sample studied for pulmonary function is one of the largest published probability samples. Age is normally distributed in the Michigan sample. The data are consistent with other published series as is shown in the table below for women adapted from Miller. Comparison of these age coefficients shows excellent agreement with Miller (Michigan), an average of the more recent non-smoking larger studies. If Crapo were adopted, or Morris, the results would not differ from those published in our paper. This agreement between series answers the question about bias by volunteers by showing great consistency in the pulmonary function behaviour of these population samples.

(2) The histology technicians are not representative of all histology technicians.

In the real world all samples are composed of volunteers as I am sure Rossiter realises. Perhaps one could
Pulmonary function in histology technicians compared with women from Michigan: effects of chronic low dose formaldehyde exposure on a national sample of women.

E Rossiter

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