

## CORRESPONDENCE

### Exposure to benzene and mortality from leukaemia: results from coke oven and other coal product workers

Sir,—There has been continuing widespread interest, reflected in the paper by Swaen and Meijers (1989; 46:826-30),<sup>1</sup> in mortality from leukaemia after occupational exposure to benzene. Subsequent correspondence\* noted that excess mortality had not been identified among byproduct workers exposed to benzene and other aromatic hydrocarbons in the North American coke oven industry.<sup>2</sup> A further publication<sup>3</sup> reported no indication of an increased risk of leukaemia in a group of former benzene plant workers. Preliminary results from analyses in progress on the mortality of two cohorts of coke oven workers in Britain may, therefore, be of interest.

#### The study groups

The two cohorts consist of male industrial workers employed in 1967 in self contained coke works or coke departments of the then National Smokeless Fuels Ltd (NSF) and British Steel Corporation (BSC) (now Coal Products Ltd and British Steel plc respectively). Details of the cohorts, data collection, methods of follow up etc have been reported previously.<sup>4</sup> After further data validation the present analyses, over a roughly 20 year mortality follow up from 1967, are based on 3812 NSF workers from 13 plants and 2708 BSC workers from 14 plants.

In considering exposure to benzene, three subgroups of NSF workers have been identified: men with any recorded experience in by products work, men with any recorded coke oven (battery) work experience, and men known to have ever worked in maintenance jobs before 1967. For BSC, two subgroups only were considered: byproduct workers and coke oven workers. The BSC maintenance workers were not considered as a subgroup as the original definition of the study cohort had excluded BSC men who were in maintenance jobs in 1967. The occupational subgroups are not mutually exclusive because of job mobility within the industry.

### Environmental benzene concentrations

Hygiene measurements taken during the 1980s indicate the airborne concentrations of environmental benzene to which the workers may have been exposed. Published data suggest that the sphere of influence of coke works on its surroundings may be 1300 m; that is, up to that distance, benzene concentrations higher than those present in the general atmosphere from other sources are likely to be found.<sup>5</sup> It is likely, therefore, that all coke plant workers are exposed to benzene concentrations somewhat higher than those of the general population. Results from personal sampling of 49 men at two CPL coke plants showed mean time weighted average exposure concentrations for benzene workers in the byproducts plants of 1.32 ppm benzene compared with 0.31 ppm in battery men.<sup>6</sup> More extensive published<sup>6</sup> and unpublished data from both companies support these figures as order of magnitude concentrations of airborne benzene in coke works in Britain in the 1980s. Table 1 summarises some of these data.

Each column refers to measurements at various works, and there are important works specific variations in the concentrations recorded. Also, men in the two cohorts worked in the coke plants for various durations, in several instances dating from prewar years. No measurements of environmental benzene are available for these

periods. The likelihood of works and time specific variations in benzene concentrations makes it difficult to generalise, but we assume that concentrations in earlier decades were in general higher rather than lower than those experienced in the 1980s.

### Statistical methods

Death rates specific to age group and geographical region were applied to person-years at risk at plants in England and Wales. Scottish rates were applied to the two Scottish plants.

### Results

Three NSF men (who had worked in different plants) died from leukaemia during the 20 year follow up period. The deaths occurred in 1973, 1983, and 1984 at ages 59, 43, and 76 respectively. Two were recorded as International Classification of Diseases (8th revision) 205.0, the third as 205.1. Two BSC men died from this cause in 1977 and 1982 at ages 56 and 78 respectively. These men had also worked at different plants. Primary cause of death was recorded as 204.0 and 204.1 respectively.

Table 2 gives numbers of expected deaths in various occupational subgroups.

Note that the single observed death in each of the three subgroups of NSF men actually refers to only one man, who had work experience in general jobs, possibly involving some ex-

Table 1 Numbers of personal samples in various concentration ranges by occupations of men sampled

| Benzene conc (ppm) | Occupations                |                         |                            |                         |
|--------------------|----------------------------|-------------------------|----------------------------|-------------------------|
|                    | BSC benzole workers No (%) | BSC w en workers No (%) | NSF benzole workers No (%) | NSF w en workers No (%) |
| 0.00-0.19          | 15 (17.9)                  | 29 (61.7)               | 45 (14.7)                  | 16 (43.2)               |
| 0.20-0.39          | 18 (21.4)                  | 14 (29.8)               | 61 (19.9)                  | 9 (24.3)                |
| 0.40-0.59          | 10 (11.9)                  | — (—)                   | 36 (11.7)                  | 5 (13.5)                |
| 0.60-0.79          | 7 (8.3)                    | 1 (2.1)                 | 29 (9.4)                   | 4 (10.8)                |
| 0.80-0.99          | 5 (6.0)                    | — (—)                   | 17 (5.5)                   | 2 (5.4)                 |
| 1.00-1.49          | 11 (13.1)                  | — (—)                   | 28 (9.1)                   | — (—)                   |
| 1.50-1.99          | 7 (8.3)                    | 1 (2.1)                 | 32 (10.4)                  | 1 (2.7)                 |
| 2.00-2.99          | 6 (7.1)                    | — (—)                   | 23 (7.5)                   | — (—)                   |
| 3.00-3.99          | 2 (2.4)                    | — (—)                   | 19 (6.2)                   | — (—)                   |
| 4.00-4.99          | 1 (1.2)                    | — (—)                   | 5 (1.6)                    | — (—)                   |
| 5.00-5.99          | 1 (1.2)                    | — (—)                   | 4 (1.3)                    | — (—)                   |
| 6.00-6.99          | 1 (1.2)                    | — (—)                   | 4 (1.3)                    | — (—)                   |
| 7.00-7.99          | — (—)                      | 1 (2.1)                 | 1 (0.3)                    | — (—)                   |
| 8.00-8.99          | — (—)                      | — (—)                   | 1 (0.3)                    | — (—)                   |
| 9.00-9.99          | — (—)                      | — (—)                   | — (—)                      | — (—)                   |
| 10.00-10.99        | — (—)                      | — (—)                   | — (—)                      | — (—)                   |
| 11.00-11.99        | — (—)                      | — (—)                   | 1 (0.3)                    | — (—)                   |
| Total              | 84 (100.0)                 | 47 (100.0)              | 307 (100.0)                | 37 (100.0)              |

Table 2 Summary of subgroups

| Cohort | Subgroup                                         |
|--------|--------------------------------------------------|
| NSF    | All men<br>Byproduct<br>Coke oven<br>Maintenance |
| BSC    | All men<br>Byproduct<br>Coke oven                |

\*The total amount

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### Discussion

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Table 2 Summary results on leukaemia mortality in both cohorts and in selected subgroups

| Cohort | Subgroup    | No of Men | Person-years* | Obs | Exp | SMR (95% CI)      |
|--------|-------------|-----------|---------------|-----|-----|-------------------|
| NSF    | All men     | 3812      | 66742         | 3   | 7.1 | 0.42 (0.09, 1.23) |
|        | Byproducts  | 662       | 11167         | 1   | 1.3 | 0.76 (0.02, 4.29) |
|        | Coke ovens  | 1661      | 28476         | 1   | 3.0 | 0.34 (0.00, 1.86) |
|        | Maintenance | 1061      | 18510         | 1   | 1.7 | 0.58 (0.01, 3.28) |
| BSC    | All men     | 2708      | 46969         | 2   | 4.9 | 0.41 (0.05, 1.47) |
|        | Byproducts  | 631       | 10384         | 1   | 1.0 | 0.98 (0.02, 5.57) |
|        | Coke ovens  | 1688      | 27840         | 1   | 2.9 | 0.35 (0.01, 1.92) |

\*The total amount of observation time accumulated during the follow up period.

posure to coke oven fumes. Of the two BSC men who died from leukaemia, one had some byproducts experience, and the other had worked in coke oven jobs.

We have also reviewed unpublished tabulations of leukaemia mortality over 17 years (1967 to the end of 1983) in an associated study of 287 male industrial workers employed on 1 January 1967 at four tar distillation plants and one benzene refinery. Results showed no deaths from leukaemia. Expected deaths were not calculated, but are likely to be about 0.5. Details of the cohort and mortality from other causes 1967-83, have been reported.<sup>7</sup>

### Discussion

The experience of the combined cohort over 20 years amounted to a reasonably large scale study of men occupationally exposed to low concentrations of benzene. No evidence was found for excess mortality from leukaemia in either the NSF or BSC cohort overall (standardised mortality ratio (SMR) 42 and 41 respectively), or among men known to have worked in the coke oven battery jobs in particular (SMR 34 and 35 respectively). The SMRs for byproduct workers, though somewhat higher, did not suggest excess mortality from leukaemia (SMR 76 and 98 respectively), but were based on only 2.3 expected deaths.

The results are therefore consistent with the other evidence reviewed recently: whereas excess leukaemia mortality has been shown in relation to high exposure to benzene, several large scale studies of men exposed at concentrations below 10 ppm have shown negative results. Furthermore, these preliminary analyses by exposure group, together with the available, albeit recent, hygiene

measurements, go some way towards overcoming the two limitations of the available low exposure studies highlighted in that review, that is, the lack of quantitative exposure data, and the possibility that a proportion of the 'exposed cohort' has not been exposed to benzene at all.

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- 1 Swaen GMH, Meijers JMM. Risk assessment of leukaemia and occupational exposure to benzene. *Br J Ind Med* 1989;46:826-30.
- 2 Brunekreef B, Swaen GMH, Meijers JMM. Correspondence. *Br J Ind Med* 1990;47:717-8.
- 3 Redmond CK, Strobino BR, Cypress RH. Cancer experience among coke by-product workers. *A m NY Acad Sci* 1976;217:102-15.
- 4 Swaen GMH, Slangen JJM, Volovics A, Hayes RB, Scheffers T, Sturmans F. Mortality of coke plant workers in the Netherlands. *Br J Ind Med* 1991;48:130-5.
- 5 Hurley JF, Archibald RMCL, Collings PL, Fanning DM, Jacobsen M, Steele RC. The mortality of coke workers in Britain. *Am J Ind Med* 1983;4:691-704.
- 6 National Smokeless Fuels Ltd. *Pollution at coke works*. National Smokeless Fuels Ltd, 1986. (Final report on ECSC project NO 7257-14/340/08.)
- 7 Drummond L, Luck R, Afacan AS, Wilson HK. Biological monitoring of workers exposed to benzene in the coke oven industry. *Br J Ind Med* 1988;45:256-61.
- 8 MacLaren WM, Hurley JF. Mortality of tar distillation workers. *Scand J Work Environ Health* 1988;13:404-11.

### Bootstrap estimate of the variance and confidence interval of kappa

Sir,—Methodological research in clinical medicine and epidemiology is often concerned with measuring the extent of agreement between two methods or observers for rating an outcome, or the reproducibility of a method or observer for rating an outcome on two different occasions. The kappa coefficient, as originally described by Cohen,<sup>1</sup> quantifies agreement or reproducibility when the outcome is dichotomous. The coefficient was subsequently extended to nominal and ordinal outcome variables with three or more categories.<sup>2,3</sup>

The computation of kappa, including a test of null hypothesis and an estimation of confidence interval based on normal distribution theory, is summarised by Fleiss.<sup>4</sup> Although the normal theory procedure is reliable for testing of null hypotheses, the procedure is often not reliable for constructing a confidence interval. As the kappa coefficient is bounded by 1 (perfect agreement), its sampling distribution is highly skewed when strong agreement or reproducibility exists. (Note that kappa can also be negative (observed agreement less than chance expected agreement) in which case it is bounded by -1). A better alternative to determine the confidence interval of kappa is therefore based on the empirical sampling distribution generated by the computer intensive bootstrap resampling method.<sup>5</sup>

We have written a computer program in the BASIC language (compiled by Microsoft's QBASIC version 4.5) to carry out the bootstrap estimate of the variance and confidence interval of kappa. The program works on the IBM compatible PC with or without a math coprocessor and it supports CGA, EGA, and VGA. Because the program is entirely menu driven, it is easy to run. The user types "KAPPA" as a DOS command and then simply responds to a series of question prompts by the program. One question asks the user to state C, the number of categories in the outcome variable. If C is greater than 2 the user is then asked to state whether the outcome variable is nominal or ordinal.

The ordinary kappa coefficient is computed when C is 2. If C is greater