Original article
Scand J Work Environ Health 1988;14(3):153-160
doi:10.5271/sjweh.1937

A mortality study of vinyl chloride monomer workers employed in the United Kingdom in 1940-1974.
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This article in PubMed: www.ncbi.nlm.nih.gov/pubmed/3393850
A mortality study of vinyl chloride monomer workers employed in the United Kingdom in 1940—1974

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JONES RD, SMITH DM, THOMAS PG. A mortality study of vinyl chloride monomer workers employed in the United Kingdom in 1940—1974. Scand J Work Environ Health 14 (1988) 153—160. The mortality experience of 5 498 male workers employed for at least one year during 1940—1974 in the vinyl chloride industry of the United Kingdom was followed through to 31 December 1984. There was a significant excess of nonsecondary liver tumors with 11 deaths, of which seven were angiosarcomas. All the angiosarcoma deaths occurred in autoclave workers with a median latency of 25 years from date of first exposure. A strong healthy worker effect was seen. Other than that for liver cancer, no increased incidence of cancer deaths attributable to vinyl chloride monomer exposure was found. There was no evidence of increased mortality from chronic liver disease. The incidence of death from respiratory disease was low and was not affected by polyvinyl chloride dust exposure.

Key terms: angiosarcoma of the liver, cohort study, epidemiology, occupational exposure, vinyl chloride.

Following the early reports of an association between angiosarcoma of the liver and exposure to vinyl chloride monomer (VCM) (5, 8, 14, 17), the Employment Medical Advisory Service set up a mortality study of vinyl chloride workers in the United Kingdom; it was reported by Fox & Collier (11). The purpose of the study was to establish the general picture of the mortality experience of workers engaged in the manufacture of polyvinyl chloride (PVC) in the United Kingdom and to relate this picture to various factors, including exposure to VCM. Two cases of angiosarcoma were identified, but the excess of mortality from liver cancer was not statistically significant when analyzed by categories defined in the International Classification of Diseases (ICD).

Since the association between VCM exposure and the development of angiosarcoma was established, various papers have suggested a carcinogenic effect for VCM in the induction of lung (6, 27) and brain (4, 7) cancers, melanoma (12), and malignancies of the hematopoietic system (28). However, despite the volume of literature now available on vinyl chloride exposure, it has yet to be established that this chemical causes an increase in malignancies at sites other than the liver.

Evidence of chronic liver disease, including hepatic fibrosis and portal hypertension, has been reported for VCM workers (13, 19, 20, 25). Noncirrhotic portal fibrosis, like angiosarcoma, is a prescribed disease for this occupation in the United Kingdom under the Industrial Injury Provision of the Social Security Act of 1975 (9). The role of chronic liver disease in the mortality pattern of these workers is not so clear (22).

Possible health effects of PVC dust have been the subject of a number of studies (2, 15, 16, 21, 26), although some doubt remains as to whether the recorded changes in lung function and radiographic appearance are indicative of any increase in respiratory disease.

This paper describes a mortality analysis of British VCM workers that has primarily been based on the population reported on by Fox & Collier (11). However, different criteria reducing the total cohort size, have been used for the entry of workers into the survey. The exposure categories have been based upon the more-detailed occupational information that is now available, and data on an extra 10 years of follow-up have been added.

Subjects and methods

Study population

A nominal roll was compiled from the personnel records of nine chemical plants manufacturing or polymerizing vinyl chloride. A prerequisite for entry into the cohort was employment for at least one year in a job or jobs that involved potential exposure to VCM for at least 25 % of the workweek. Only individuals first employed in the period 1940—1974 were included. Persons were entered into the study at the time of completion of one year’s employment in such an occupation. Identification details for each individual were sent to the Office of Population Censuses and Surveys, which flagged the records of the individual on the Na-
tional Health Service Central Register. Whenever an individual was found to have died, a copy of the death certificate duly coded to the appropriate ICD revision was sent to the investigators. The eighth revision of the ICD was used for deaths occurring to the end of 1978. Deaths occurring in 1979 to 1984 were coded to both the eighth and ninth revisions.

Expected deaths
Male mortality rates for England and Wales were calculated for selected ICD categories by five-year age groups for quinquennial periods of the study. The number of deaths expected for each ICD category was calculated by applying these rates to the person-years at risk in each five-year age group for the appropriate quinquennial period of the study. The person-years at risk were calculated from the date one year after first exposure to VCM up to the earliest of date of death, date of emigration, or 31 December 1984.

Table 1. Exposure data by occupational category. (VCM = vinyl chloride monomer, PVC = polyvinyl chloride)

| Occupational category | VCM exposure estimate (ppm) | PVC dust exposure (mg/m³) |
|-----------------------|-----------------------------|---------------------------|
|                       | 1940—1955                   | 1956—1974                 |
| Autoclave operators (group A) | 500—800 150—500 | 0.23—0.46 |
| Baggers and driers (group B) | <400 <40 | 0.38—2.88 |
| Craftsmen (group C) | 240—440 50—300 0.52—0.84 |
| Other workers (group D) | <100 <100 | ≤0.93 |

Mortality analysis
The use of ICD-categorized data is not ideal for studying rare tumors such as angiosarcoma, which would normally be expected to make only a tiny contribution to any particular ICD category. Even when all primary liver tumors are considered together, they account for less than 0.25 % of deaths. Because the primary nature of the tumor is often not specifically mentioned on the death certificate, many of these deaths are not coded as primary liver cancer. In order to include these deaths, we found it necessary to include liver cancer deaths that were “not specified whether primary or secondary.” By the aggregation of deaths coded to ICD categories 155.0 and 197.8 (eighth revision) and categories 155.0 and 155.2 (ninth revision), cases of liver cancer not specifically certified as metastatic were considered. Aggregated deaths from these causes have been referred to as “nonsecondary liver cancer.”

Noncirrhotic fibrosis of the liver is not specifically mentioned in any ICD revision. It would presumably be coded to liver disease (ICD 570—573, eighth and ninth revisions). Within ICD categories 570—573 there are differences of classification between the eighth and ninth revisions, but it is very likely that noncirrhotic portal fibrosis would have been coded to 573 in the eighth revision and 571.9 or 573 in the ninth revision. The five certificates coded to an underlying cause between 570 and 573 were extracted and scrutinized. The underlying cause of death in all of these had been coded to 571. An expected figure was therefore calculated for

Table 1 shows the VCM exposure estimates for the occupational groups. These figures are not dissimilar to those reported by Ott et al (23). Because there was some movement between jobs, with a general tendency for workers to move from groups A and B to group D (job movement among the craftsmen in group C was much more limited) and because this movement tended to be from areas of high exposure to areas of low exposure, mortality by occupational exposure was analyzed from the population categorized as ever group A, ever group B never group A, ever group C never group A or B, and always group D.

Since 1974 exposure to VCM in the industry has been much more rigidly controlled. The levels fell almost immediately to less than 50 ppm, and even greater control has been achieved since. The present control limit for VCM is 3 ppm annually with a maximum time-weighted average per workshift of 7 ppm. This level is many orders of magnitude less than the levels that existed for much of the study period, and therefore the present analysis was limited to persons who had worked in the industry prior to 1975. All workers in the study have thus had the opportunity for at least 10 years of follow-up.
ICD 571, which accounts, in the general population, for the vast majority of deaths from liver disease by either ICD revision.

The mortality analysis has been carried out with the OCMAP computer program (18). The standardized mortality ratios have been calculated in the normal manner, and the 95% confidence intervals for these ratios were calculated under the assumption that the observed number of deaths followed a Poisson distribution. The results are stated as significant when the standardized mortality ratio (SMR) 100 lies outside the 95% confidence interval (95% CI).

**Results**

**General mortality pattern**

The number of workers meeting the criteria for entry into the study was 5,560 men and 105 women. Because of the small number of female workers, detailed analysis was restricted to the male population. A total of 5,498 men was traced (98.9%), and 780 deaths were identified. Table 2 shows the observed (O) and expected (E) deaths from major causes and other causes where there was a significant excess or deficit.

There were significant deficits in mortality from circulatory (O 381, E 429, SMR 89, 95% CI 80—90) and respiratory (O 76, E 105, SMR 72, 95% CI 57—90) diseases. These deficits contributed substantially to the overall significant deficit in mortality observed (O 780, E 894, SMR 87, 95% CI 81—94). There was a clearly significant overall excess of nonsecondary liver cancer (O 11, E 1.94, SMR 567, 95% CI 283—1,015). Other causes of mortality for which there were significant deficits in mortality were diseases of the digestive system (O 14, E 23.9, SMR 59, 95% CI 32—98), peptic ulcer (O 2, E 7.5, SMR 27, 95% CI 3—96), and diseases of the genitourinary tract (O 5, E 11.9, SMR 42, 95% CI 14—98).

**Analysis of cancer by occupation**

Cancer mortality by occupation is shown in table 3 for malignancies which have been reported in excess in at least one population of VCM workers. There was an obvious excess of nonsecondary liver cancers among autoclave workers, but no statistically significant excesses of other cancers.

From table 1 it is clear that the greatest exposure to VCM was experienced by the autoclave workers,

### Table 2. Mortality of the men traced. (O = number of observed deaths, E = number of expected deaths, SMR = standardized mortality ratio, 95% CI = 95% confidence interval)

| Cause of death                      | O    | E    | SMR  | 95% CI  |
|-------------------------------------|------|------|------|---------|
| Major causes of death               |      |      |      |         |
| All causes                          | 780  | 894  | 87   | 81—94   |
| All malignant neoplasms             | 235  | 228.6| 103  | 90—117  |
| Stomach cancer                      | 26   | 23.9 | 108  | 71—159  |
| Lung cancer                         | 81   | 92.1 | 88   | 70—109  |
| Circulatory disease                 | 381  | 428.7| 89   | 80—98   |
| Ischemic heart disease              | 276  | 287.8| 96   | 85—108  |
| Respiratory disease                 | 76   | 105.3| 72   | 57—90   |
| Bronchitis                          | 36   | 43.6 | 82   | 57—113  |
| Accidents and suicides              | 40   | 49.7 | 80   | 57—109  |
| Nonsecondary liver cancer           | 11   | 1.94 | 567  | 283—1,015 |
| Disease of the digestive system     | 14   | 23.9 | 59   | 32—98   |
| Peptic ulcer                        | 2    | 7.5  | 27   | 3—96    |
| Disease of the genitourinary system | 5    | 11.9 | 42   | 14—98   |

| Other causes with a significant excess or deficit |
|--------------------------------------------------|
| Nonsecondary liver cancer                       | 11   | 1.94 | 567  | 283—1,015 |
| Disease of the digestive system                  | 14   | 23.9 | 59   | 32—98   |
| Peptic ulcer                                     | 2    | 7.5  | 27   | 3—96    |
| Disease of the genitourinary system              | 5    | 11.9 | 42   | 14—98   |

### Table 3. Mortality from malignant diseases where association with exposure to vinyl chloride monomer was previously suggested. (O = number of observed deaths, E = number of expected deaths)

| Cause of death                  | Autoclave operators | Baggers and driers | Craftsmen | Other workers |
|--------------------------------|---------------------|--------------------|-----------|---------------|
| All cancer                      | 41                  | 43.3               | 20        | 21.8          | 20           | 23.2         | 154         | 139.7         |
| Malignant neoplasm              |                     |                    |           |               |              |              |             |               |
| Liver                           | 1                   | 0.28               | —         | 0.14          | —            | 0.14         | 2           | 0.80          |
| Liver, not specified primary or secondary | 6                  | 0.10*              | 1         | 0.05          | —            | 0.06         | 1           | 0.36          |
| Larynx                          | 1                   | 0.42               | —         | 0.20          | —            | 0.22         | 3           | 1.37          |
| Lung                            | 16                  | 17.1               | 5         | 8.75          | 4            | 9.52         | 56          | 56.5          |
| Malignant melanoma              | —                   | 0.41               | —         | 0.20          | —            | 0.17         | 2           | 0.94          |
| Brain                           | 1                   | 1.42               | 1         | 0.74          | 1            | 0.62         | 1           | 3.35          |
| Lymphosarcoma and reticulo cell sarcoma | 2                  | 0.47               | —         | 0.23          | —            | 0.23         | 2           | 1.41          |
| Other lymphoid tissue           | —                   | 0.47               | —         | 0.24          | —            | 0.21         | 1           | 1.11          |
| Lymphatic leukemia              | —                   | 0.31               | 1         | 0.14          | —            | 0.15         | 3           | 1.01          |
| Thyroid                         | 1                   | 0.08               | 1         | 0.04          | —            | 0.04         | 0           | 0.26          |
| Colon                           | —                   | 2.63               | 1         | 1.29          | 1            | 1.39         | 7           | 8.60          |

*The workers were classified by the job held with the highest exposure to vinyl chloride monomer, ie, ever A, ever B, never A, etc, as described in the text.

*P < 0.05.
Table 4. Observed (O) and expected (E) mortality for nonsecondary liver cancers by latency and cumulative exposure among autoclave workers (ie, workers exposed only as autoclave operators).

| Time since first starting job (latency) | Length of exposure | O | E | O | E | O | E | Total |
|----------------------------------------|--------------------|---|---|---|---|---|---|-------|
| ≤9 years                               | ≤1 year            | 0.00 | 1 | 0.04 | 0.00 | 1 | 0.10 |       |
|                                       | 2–4 years          | 0.03 | 0.03 | 0.03 | 0.07 | 2 | 0.16 |       |
|                                       | 5–9 years          | 0.03 | 0.00 | 0.01 | 4 | 0.08 | 4 | 0.13 |       |
| ≥20 years                              | Total              | 0.07 | 1 | 0.08 | 2 | 0.06 | 4 | 0.15 | 7 | 0.35 |

* P<0.05.

Table 5. Mortality from respiratory disease for baggers and driers and for craftsmen.* (O = number of deaths observed, E = number of deaths expected)

| Cause of death                  | Baggers and driers | Craftsmen |
|--------------------------------|--------------------|-----------|
|                                | O    | E   | O   | E   |
| Lung cancer                    | 9    | 15.4| 4   | 9.5 |
| All nonmalignant respiratory disease | 4 *  | 12.7| 8   | 9.8 |
| Bronchitis                     | 1    | 5.0 | 4   | 4.1 |

* See the paragraph relating to polyvinyl chloride dust exposure and disease for a definition of the groups.
* P<0.05.

Vinyl chloride exposure and nonmalignant disease

Nonmalignant liver disease (ICD 570—573) was responsible for five deaths, all of which had been coded to ICD 571 by the Office of Population Censuses and Surveys. For this disease category there was no excess of mortality in the population as a whole (O 5, E 4.9) although the autoclave workers did contribute two cases (O 2, E 1.1), one of which had been certified as hepatic fibrosis and accepted by the coroner as a case of industrial disease. The remaining four deaths were due to cirrhosis of the liver. Death certificates for the 11 cases of nonsecondary liver cancer (which included the seven angiosarcomas found in the autoclave workers) gave no mention of hepatic fibrosis, although two (one hepatoma and one angiosarcoma) contained reference to cirrhosis.

Polyvinyl chloride dust exposure and disease

Baggers and driers (group B) were considered the high exposure group for PVC dust, craftsmen having less exposure and groups A and D the least. Table 5 shows the mortality from respiratory disease for the men who had ever been baggers or driers, regardless of previous or subsequent VCM or PVC exposure, and craftsmen who had never been autoclave workers or baggers or driers. The table shows that there was a non-significant deficit of malignant disease and a significant deficit of nonmalignant respiratory disease among the baggers and driers. The mortality for craftsmen showed no evidence of any significant excess of respiratory disease.

Discussion

This study reports the mortality experience of workers engaged in the manufacture and polymerization of vinyl chloride for the major chemical companies in the United Kingdom from 1940 on. In order to restrict the population to persons with definite occupational exposure and thereby prevent dilution of the cohort with substantial numbers of workers who had very small exposures, we have included only persons who have worked for more than one year in jobs judged to involve some exposure to VCM for at least 25% of the workshift. These selection criteria reduced the size of the cohort originally reported on by Fox & Collier (11) from 7 409 to 5 498. Restriction of recruitment to the period for which the previous report was written ensured a minimum possible follow-up period of 10 years. In addition to any considerations of latency,
work conditions would have been very different in the post-1974 period with much lower exposures to VCM.

Objective hygiene data, along with estimates based on individuals' personal memory and judgement, showed that, while levels of exposure had fallen during the time period studied, substantial reductions had been particularly associated with the mid to late 1950s and then again in the early 1970s. The hygiene data available indicated that autoclave workers had the highest exposure to VCM, baggers and driers the highest PVC dust exposure, and craftsmen intermediate exposure for both the monomer and the polymer.

In the absence of detailed information on individual exposure, the correlation of exposure and effect could have been attempted in a number of ways. After due consideration we decided that the analysis should be by occupation in accordance with the hygiene data. It is accepted that grouping the population in this way is a relatively crude method of assessing exposure and correlating this exposure with effect, and the accuracy of such a method depends upon the relevance of the groupings chosen and the precision of historical occupational data.

Another possible weakness of the study is that, while comparable mortality rates were available for the period in which over 80% of the deaths occurred, expected deaths for the period before the eighth ICD revision were calculated with the use of mortality data that were not directly comparable. This period would have accounted for over 25% of the expected mortality. The differences between the eighth and ninth revisions dictate the way in which the observed deaths have been categorized. Any bias introduced by attempts to define comparable data coded under different ICD revisions would operate differently for different diseases according to the changes made in the classification.

Overall mortality

The overall mortality of the subjects studied (table 2) shows a strong healthy worker effect, more obvious for respiratory than circulatory diseases. The fact that the effect is more evident for some occupational groups than for others may be a reflection of different physical demands of work activity in different jobs.

Liver cancer

There was an overall statistically significant excess of mortality from nonsecondary liver cancer (O 11, E 1.94, SMR 567, 95% CI 283—1 015), largely due to seven cases of angiosarcoma, six of which occurred at the same plant and all of which occurred in autoclave workers. No other nonsecondary liver tumors occurred among the autoclave workers, but these seven cases were sufficient to produce a huge excess for this disease category in this group (O 7, E 0.38, SMR 1842, 95% CI 741—3 795). The results vividly demonstrate the association between VCM exposure and an increased risk of primary liver tumor, even though this oncogenic effect is probably limited to the induction of angiosarcoma. This was not the case at the time of Fox & Collier's analysis when only two angiosarcoma deaths had occurred. Ten years of additional follow-up have produced sufficient deaths from angiosarcoma for nonsecondary liver tumors to be significantly in excess for the whole population; yet it must be realized that this excess is the result of seven angiosarcomas, all of which occurred in autoclave workers, and the remaining workers contribute little to the nonsecondary liver tumor deaths (O 4, E 1.58, SMR 253, 95% CI 69—648). This nonsignificant excess cannot be taken as evidence of an association between VCM and nonangiosarcoma primary liver tumors. If VCM does play a part in the genesis of other primary liver tumors, its effect is clearly far weaker than for angiosarcoma, and the power of this study is insufficient to permit further comment.

Mortality studies are dependent upon the accuracy of death certification. Subsequent classification of the information on the certificate is subject to coding as carried out by a nosologist within the constraints imposed by the ICD. Comparative mortality data are not therefore a completely accurate measure of disease incidence, even for fatal conditions. The smaller the true incidence of the disease, the more easily any measure of it will be affected by allocation of individual cases to a particular category. Because of co-existing recordings of angiosarcoma (3, 10), it was possible to check the results of this mortality analysis against the figure for cases of VCM-related angiosarcoma of the liver in the United Kingdom. Two cases of angiosarcoma were identified in our cohort, for which the underlying cause of death had not been classified to any code for liver cancer. One described as hemangioendothelioma of the liver was coded to ICD (eighth revision) 227 (benign hemangiomalamphangioma). In the case of the other man, histological evidence of angiosarcoma was found, but no mention was made of it on the death certificate, even though a verdict of industrial disease was given. Both men had been autoclave workers.

Lung cancer

There was a nonsignificant deficit of lung cancer in the cohort overall. If VCM does have a carcinogenic effect on the lung, then, given the usual latency for occupational lung cancer, any excesses should be seen in the longer follow-up groups. Table 6 shows the results for different periods of follow-up. No clear evidence of any increased lung cancer risk emerges with longer periods of follow-up. Autoclave workers followed for 20 years or more show a nonstatistically significant excess of lung cancer (O 10, E 6.5, SMR 154, 95% CI 74—283), but a nonstatistically significant excess in such small numbers must be viewed with caution. Thus the results of the study do not demonstrate
Table 6. Lung cancer by period of follow-up.

| Occupational group* | ≤ 9 years | 10—19 years | ≥ 20 years after first exposure |
|---------------------|-----------|-------------|-------------------------------|
|                     | E | O  | O  | E | O  | O  | E |
| Autoclave operators | — | 3.5 | 6  | 7.1 | 10 | 6.5 |
| Baggers and driers  | 1  | 2.3 | 1  | 3.7 | 3  | 2.8 |
| Craftsmen           | — | 2.1 | 2  | 3.8 | 2  | 3.7 |
| Other workers       | 7 | 10.3 | 21  | 18.8 | 28 | 27.5 |

* The workers were classified by the job held with the highest exposure to vinyl chloride monomer, i.e., ever A, ever B, never A, etc., as described in the text.

any association between VCM exposure and lung cancer deaths.

For any study of this kind its power (i.e., ability to demonstrate excess disease risks where they exist) will be far greater for common causes of death such as lung cancer than for uncommon tumors such as primary liver cancer. A negative result could therefore be taken as evidence that, if VCM had any etiologic role in the development of lung cancer, it must be small in comparison with that seen for angiosarcoma of the liver. It should be remembered, however, that lung cancer is a common tumor because of the high prevalence of smoking during the time of this study period. Without smoking, lung cancer would be a far more uncommon disease. If vinyl chloride exerted a carcinogenic effect on the respiratory system that was not synergistic with the carcinogenic effect of smoking, then such an effect would be masked by the commonality of smoking-induced tumors. Thus the power of the study to detect excess lung cancer is not the only consideration to be borne in mind when VCM is being assessed as a possible respiratory carcinogen.

**Brain cancer**

On the whole, the population showed no excess of brain cancer, and, because of the small numbers associated with the individual exposure categories, the results do not warrant further discussion. The exposure and latency details for the four cases included in the analysis are given in table 7 along with two cases that have occurred in the post-1974 starters. This study does not offer any anecdotal or statistical evidence for an association between brain cancer and VCM exposure.

**Lymphatic cancer**

Because of the close association between non-Hodgkin’s lymphoma and chronic lymphatic leukemia, it is pertinent to consider the diseases which span the three different ICD codings 200, 202, and 204 together. Two deaths coded to ICD 200 for autoclave operators were numerically in excess of the expected figure (O 2, E 0.47, SMR 426, 95% CI 52—1537), but this value did not reach statistical significance. There was also a nonstatistically significant excess of lymphatic leukemia among the workers with low exposure (group D) (O 3, E 1.1, SMR 273, 95% CI 56—797). The problems of interpreting such small numbers are considerable. However, the evidence of this study alone cannot be considered suggestive of a causative role for VCM in the production of lymphatic cancer.

**Other cancers**

Although an association for VCM exposure and cancer of the colon has previously been commented upon (12, 24), this study provides no evidence of an excess of large bowel cancer in persons exposed to vinyl chloride.

In the population described in this study, only two deaths from malignant melanoma occurred. Both involved men from the low-exposure group (O 2, E 0.94, SMR 213, 95% CI 26—769). There was therefore, nothing in these results to support an association between VCM and the development of melanoma of the skin.

Two deaths from cancer of the thyroid occurred. One autoclave operator who worked in this job for one year died of thyroid cancer 11 years after his first exposure to vinyl chloride. The other case involved a man who was a bagger for 14 years and died some 23 years after first exposure. Although not as rare as angiosarcoma, cancer of the thyroid is still a very uncommon tumor in men (approximately 120 deaths per year and about double that number of male cancer registrations.

Table 7. Occupational exposure data for the cases of brain cancer.

| Case number | Age first employed (years) | Occupational category | Period of exposure (years) | Year of death | Latency (years) | Wording on death certificate |
|-------------|---------------------------|-----------------------|---------------------------|---------------|----------------|---------------------------|
| 1           | 36                        | Autoclave worker      | 13                        | 1964          | 13             | Left parietal glioblastoma |
| 2           | 22                        | Bagger                | 27                        | 1982          | 28             | Multicystic glioma of left cerebral hemisphere |
| 3           | 46                        | Craftsman             | 1                         | 1977          | 3              | Cerebral glioma           |
| 4           | 30                        | Miscellaneous, low    | 4                         | 1974          | 4              | “Lymphoma of corpuscalosa” |
| 5           | 47                        | Fitter                | 1                         | 1984          | 6              | Malignant cerebellar cyst |
| 6           | 23                        | Autoclave worker      | 1                         | 1983          | 6              | Frontal astrocytoma of the brain |
in England and Wales). While it is not possible to interpret the occurrence of these two cases as being due to VCM, they are described in detail because of a similar nonsignificant excess having been described in another study (12).

The significant excess of urinogenital cancers (largely bladder and prostate) limited to three factories was an unexpected finding. The facts that autoclave operators did not show such an excess, that it was heavily contributed to by low-exposure workers, and that it was confined to three particular factories make an association with VCM unlikely. Occupational exposure to other chemicals on such multiprocess sites must be considered. However, in a study in which so many comparisons have been drawn, the possibility of this being a chance finding must remain. A case-referent study of these cases is to be carried out in order to investigate other possible occupational explanations.

**Nonmalignant disease**

In addition to the well-known association between vinyl chloride and angiosarcoma of the liver, noncirrhotic perportal fibrosis and portal hypertension is a prescribed occupational disease in the United Kingdom under the Industrial Injuries Provisions of the Social Security Act 1975 (6). An analysis by underlying cause of death showed no evidence of an excess of nonmalignant liver disease, although one certificate included mention of hepatic fibrosis which was adjudged by the coroner to be an industrial disease.

Noncirrhotic perportal fibrosis in VCM workers has, of course, been described (25), and some of these workers have subsequently developed angiosarcoma of the liver. The certificates for one case of hepatoma and one of angiosarcoma mentioned cirrhosis, but this disease was not considered to be the underlying cause of death. Cases of perportal fibrosis among VCM workers are probably underreported in mortality studies because other pathological conditions, including subsequent development of angiosarcoma of the liver, are likely to be quoted as the underlying cause of death.

PVC dust exposure has been shown to produce radiographic changes and a reduction of the ratio of forced expiratory volume in 1 s to forced vital capacity, but the clinical significance of these changes is unclear. The workers deemed to be the most exposed to PVC dust in this study (table 5) had a deficit of mortality from respiratory disease; thus there is no evidence in this study to suggest a relationship between PVC exposure and increased mortality from respiratory disease. Respiratory disease is, of course, considerably affected by smoking habits. Little inference can therefore be drawn from such small numbers with smoking data unavailable.

To conclude, the overall mortality pattern of VCM workers in the United Kingdom shows a typical healthy worker effect associated with such cohort populations. These workers have a significant excess of primary liver tumor illustrating a link between the VCM exposure of autoclave workers and the development of angiosarcoma. There is little evidence of any relationship between other causes of mortality and VCM exposure.

**Acknowledgments**

The population studied was first reported on by Fox & Collier, and the collection and management of the data have been continued by various members of the Health and Safety Executive staff since that time. We wish to acknowledge the considerable help and cooperation that we have had from the companies concerned and, in particular, from Dr Paddle and Mr Irvine. The study would not have been possible without the help and work of the staff of the Office of Population Censuses and Surveys at Southport. Finally, we would like to thank Dr Carter for his support and comments, Mr Hodgson for his invaluable help, and Ms J Law for her patience in typing various drafts and tables.

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Received for publication: 20 July 1987