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Mortality experience of workers exposed to vinyl chloride monomer in the manufacture of polyvinyl chloride in Great Britain

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ABSTRACT Identification particulars were obtained for over 7000 men who were at some time between 1940 and 1974 exposed to vinyl chloride monomer in the manufacture of polyvinyl chloride. Approximately 99% of these men have been traced and their mortality experience studied. The overall standardised mortality ratio, 75.4, shows a significant reduction compared with the national rates. Four cases of liver cancer were found. Two of these have been confirmed by a panel of liver pathologists as angiosarcoma and two as not angiosarcoma. There is no evidence to support the hypothesis that cancers other than those of the liver are associated with exposure to vinyl chloride monomer. The two cases of angiosarcoma were found in men who had been exposed to high concentrations of the monomer although the second man died only eight years after first exposure. The industry in Great Britain has expanded considerably since the second world war with over 50% of men having entered within the last decade. Conclusions drawn about the effect of vinyl chloride monomer on the mortality experience of men in this industry must consequently be tempered by the reservation that the full impact may not yet be in evidence.

In 1974 three cases of angiosarcoma of the liver in workers at a plant manufacturing polyvinyl chloride (PVC) in the United States of America were reported (Creech and Johnson, 1974). Further investigation by the firm led to the identification of two further cases who had died some years previously (Block, 1974). A programme of medical surveillance at the plant (Makk *et al.*, 1974) resulted in the identification of two cases of angiosarcoma of the liver among current workers (Falk *et al.*, 1974).

The rarity of this tumour may be judged from the incidence of reported cases: for the USA 20 to 25 cases a year (*British Medical Journal*, 1974) and for England and Wales some three to four cases a year (Baxter and Fox, 1975). Previously the only agents reported as associated with the development of angiosarcoma of the liver were arsenic (Regelson *et al.*, 1968) and thorotrast (MacMahon *et al.*, 1947).

The first case of angiosarcoma of the liver in a man known to have been exposed to vinyl chloride monomer (VCM) in the manufacture of PVC in

Great Britain was reported by Lee and Harry (1974). The man had been a process worker for 20 years and he died in 1972 aged 71 years. At this time 19 cases of angiosarcoma in workers who had been exposed to VCM in the manufacture of PVC had been reported throughout the world. All these men had been exposed to extremely high concentrations of VCM usually as autoclave 'pot' cleaners. By 1975 some 32 cases had been reported all of which were in men who had been associated with the manufacture of PVC (Lloyd, 1975). These included a second British patient who had been exposed for four years and died aged 37 years only eight years after first exposure.

Early reports of epidemiological studies in the USA have been given by Monson *et al.* (1974), Tabershaw and Gaffrey (1974), Falk *et al.* (1974), Makk *et al.* (1974), and Nicholson *et al.* (1975). The Employment Medical Advisory Service (EMAS), with the assistance of company medical representatives and the support of the unions, co-ordinated a prospective mortality study covering the manufacturing industry in Great Britain. The objectives of this study were to present a general picture of the mortality experience of workers engaged in the in-

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dust in Great Britain and to relate this to factors such as sex, age, year of entry into the industry, length of time exposed, and exposure levels.

Methods

The study covers all workers who may have been exposed to VCM through having been employed in this industry in Great Britain. All new entrants are being added to the population annually. Only four companies manufacture PVC and they have kept most of their personnel records at least since these processes were introduced. The companies were asked to supply EMAS with the names, sex, address (date at which pertinent), date of birth, year of entry into the industry, year of departure, job resulting in highest exposure, and maximum level of exposure for each person who had entered their employment.

As full job histories were not readily available for the population as a whole, it was decided to record the activity in which the maximum exposure was likely to have occurred and to follow-up individual cases, such as those dying with the mention of liver disease on their death certificate, to obtain a more complete job history. No measurement of the levels of exposure experienced by people employed before the mid-1960s was available. Estimates were made by the companies using the definitions:

High	— greater than 200 parts per million	Time weighted average
Medium	— between 25 and 200 parts per million	
Low	— below 25 parts per million	
Constant	— most of the time	
Intermittent	— occasionally.	

All data provided by the companies were subsequently re-checked by them once they had been computerised. Throughout this analysis and discussion it is assumed that the information given to EMAS is accurate. It is also necessary to assume that persons not included in this analysis, either because they were not identified or because adequate data were not available, do not constitute a biased sample.

The number of deaths observed is compared with that expected using sex and age standardised death rates for England and Wales. Five-year age groups have been used for ages between 15 and 74 years. The Office of Population Censuses and Surveys (OPCS) provided death rates in accordance with the *International Classification of Diseases* (8th Revision) for the certified causes of interest and re-coded

all death certificates for people in the study population who died before 1968 (the year the 8th Revision was introduced). Death rates calculated for 1951, 1961, and annually after 1966 were applied to the person-years-at-risk for 1940-55, 1956-65, and annually after 1966. As 1974 death rates were not available, 1973 death rates were applied to 1974 person-years-at-risk. A comparison between observed and expected values is made by assuming a Poisson distribution with mean equal to the expected value. Pearson and Hartley (1962) give the probabilities of individual terms of the Poisson distribution. For a mean greater than 15.0 the normal (gaussian) approximation to the Poisson distribution has been assumed.

Results

THE POPULATION

These results cover the period between 1940 and 1974. Information relating to the deaths in people who entered in 1973 is not included nor is the fact that some people left during 1975. This information was made available during 1975 and will therefore be added to future analyses. Complete information on 7717 workers was obtained from the companies participating in the study. This was forwarded to the OPCS who notified EMAS of those whom they had traced together with the findings. Table 1 shows that 85 workers, only 1.1% of the initial population, had not been traced at the time of analysis. This figure includes 59 workers at one factory for whom identifying information was scanty. Another 72 workers (0.9%) who were traced were excluded because of inadequate information on their work history in the industry. A total of 409 deaths were recorded, 393 men and 16 women, and 148 workers emigrated before 1975. Two who emigrated returned during 1975 to live in Great Britain and will be included in future analyses. Little deaths have been studied in detail, but because so few women are involved in this industry their deaths are summarised in Appendix 1. Appendix 2 gives the deaths in 1940-74 notified since the analysis.

Figure 1 shows the number of men employed in the industry each year from 1910 onwards and the number who had been previously employed. The work force in 1974 represents some 53% of men ever employed in the industry, reflecting the rapid growth since its inception. Table 2 shows that approximately 12% of men were exposed to high levels, almost all to constant high levels. The newness of the industry is reflected by the fact that only 8% of the workers have been employed in the industry for more than 20 years. Of these, only 34 men had been exposed to constant high levels.

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Table 1 Summary of the number of persons identified, traced, and flagged by the Office of Population Censuses and Surveys according to factory

Factory (date of initial production) ¹	Number identified		Not traced	Missing information	Deaths ^a 1940-74	Emigrations 1940-74
	Men	Women				
1 (1944)	397	67	—	3	88	13
2 (1948)	1100	—	—	3	13	34
4 (1940)	1940	34	3	27	142	26
5 (—)	41	—	—	—	4	—
10 (1953)	640	3	39	36	2	—
11 (1948)	2149	22	13†	3	133	84
12 (1969)	326	7	—	—	3	1
13 (1970)	1968	21	10	—	3	10
Total population	7561	136	83 (1.1%)	72 (0.9%)	409	148

^aDeaths in men and women.

†Includes one person who died abroad who has been excluded from the study.

‡First year in which more than 50 people were in current employment.

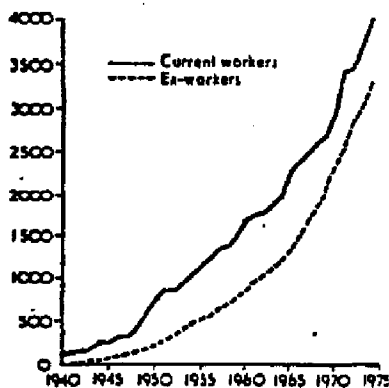


Fig. 1 Number of men in the industry and the total number who had left the industry for each year since 1940.

OVERALL MORTALITY PATTERN

Table 3 shows that only 393 deaths have been recorded as compared with 521.22 expected and the standardised mortality ratio (SMR) is 75.4. The SMR for cancers as a group is higher than this whereas the SMR for circulatory disease is approximately the same and that for respiratory disease, digestive disease, accidents, and suicides is below the overall SMR.

It is difficult to identify angiosarcoma of the liver from death certificates (Baxter and Fox, 1975). Some cases will be classified as primary liver cancers (ICD no. 155), some as secondary or unspecified liver cancer (ICD no. 197.7 or 197.8), and others may be in other categories (for example ICD no. 227). Only one death was certified as being caused by primary liver cancer compared with 0.71 expected. There were however three deaths, nearly 2½ times the expected number, in these other categories. Histories for these four people are summarised in Table 4. Slides for microscopical analysis obtained from these cases were referred with no

Table 2 Levels of exposure and lengths of exposure for men included in the survey

Length of exposure (years)	Levels of exposure						Total no. (%)
	Constant			Intermittent			
	High	Medium	Low	High	Medium	Low	
0-9	883	1202	890	66	1237	1094	5708 (77.6%)
10-19	142	117	343	35	210	351	1118 (15.1%)
20 +	34	92	214	13	130	202	583 (7.9%)
Total (%)	761 (10.5%)	1412 (19.0%)	1246 (17.1%)	106 (1.4%)	2197 (29.7%)	1647 (22.2%)	7409 (100%)

Constant = 1½ out of the time.

Intermittent = Occasionally.

High = > 200 parts per million.

Medium = 200 parts per million to < 25 parts per million.

Low = < 25 parts per million.

} Time weighted average.

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technology

UK study reveals extent of VCM-related cancer risk

THE first comprehensive re-evaluation of data on the UK incidence of angiosarcoma of the liver, believed to have been responsible, worldwide, for over 55 deaths of workers in the PVC industry, has concluded that the association between the disease and the PVC industry could be less than was originally thought.

Although only preliminary, the report from the UK's Health and Safety Executive, suggests that between 1963 and 1973 only one death could be confidently associated with workplace exposure to VCM. It also failed to show any geographical link between the incidence of the disease and the location of PVC plants, nor any firm evidence that there was any risk of contracting the disease through exposure in PVC fabrication plants.

The report refers to the one worker whose death was attributable to VCM exposure as having been exposed "to levels of VCM exceeding 200 parts per million for over 20 years".

Organized by the HSE's Dr. Peter Baxter and three other medical experts, the study involved the examination of histological data, where it was available, relating to 47 deaths which had been previously attributed to angiosarcoma. In only 37 of these cases was such evidence available, but of

those the cause of death could only be confirmed as being due to angiosarcoma in 14 cases. Occupational histories of 12 of these revealed, besides the one PVC worker already referred to, only one other death which could be associated with PVC—a glass fibre worker who died at the age of 56, but who had previously worked in a rubber factory which also produced PVC coated fabrics. There was no evidence to suggest that he had worked in that section of the plant, however.

The authors describe the findings as "generally reassuring" in that angiosarcoma incidence is so low, and that there are grounds to hope that the chemical will turn out to be less of a cancer risk than was originally supposed when the US epidemiological findings were first announced in 1974.

But they say that there remains a possibility that angiosarcoma may be associated with VCM at low exposure "so a close watch on the occurrence of this tumour should be maintained".

The work was carried out in parallel with other studies, as yet incomplete, in other industrialized countries since 1974. So far 21 angiosarcoma deaths have been attributed to exposure to VCM in the USA, the next highest national incidence being West Germany, with 11 deaths.

Osha pushes controversial control plan

THE US Occupational Safety and Health Administration is to go ahead with its controversial plan to classify all potential industrial carcinogens into four broad categories and to regulate them accordingly.

Although criticized by the Society of Plastics Industry, the plan is said by Osha to be necessary to cope with the high incidence of cancer which is said to be attributable to environmental factors. The SPI calls the move a rush to enforce judgement "on the basis of limited scientific knowledge of carcinogens".

The new plan is expected to put about 100 substances into the first category of confirmed carcinogens which OSHA says it will control by issuing "emergency temporary standards" similar to those already issued for VCM and acrylonitrile.

The agency says that it will put into 'category one' all those substances which have been shown to be carcinogenic in man or in two animal tests carried out with mammals. It would include asbestos, VCM, coke oven

emissions, arsenic, benzene, kepone and beryllium.

The second category would include "suspected carcinogens", substances for which there is evidence from other animal species or tests, and this is expected to include about 200-300 substances.

The third category, which would contain substances for which there is insufficient data to confirm a link with cancer, Osha expects to contain about 1 500 substances.

All these compounds and those contained in 'category four' (which could belong to the other three if they were found to be present in the workplace) would be expected to total about 2 000 substances, according to Osha.

● A US National Cancer Institute study published earlier this month reported a higher incidence of deaths due to cancers of the lung, nasal cavity and sinuses of the skin, among the population in states with petroleum refining industries, than among the population in other states.

In brief

□ The Coca-Cola company, having lost the opportunity of further exploiting acrylonitrile-based bottles, has been holding discussions with three chemical companies over possible contracts for the supply of bottles based on polyethylene terephthalate. One company, Sewell Plastics, has already signed a contract with Coca-Cola on the bottles, while those with Amoco Chemical and Continental Diversified Industries are still under discussion.

□ The New Zealand government has initiated a study into the feasibility of using methanol as blending agent for gasoline (as a motor fuel) up to concentrations as high as 20 per cent. It has its eye on the future exploitation of natural gas which will soon be available from fields offshore near the country's North Island.

Oxirane to manufacture TBA gasoline additive

OXIRANE has applied to the local authorities in Botlek, near Rotterdam, for permission to construct a 260 000 ton/year plant for the production of tertiary butyl alcohol, following a previous application to expand its propylene oxide manufacturing capacity at the site.

Oxirane intends to market the tertiary butyl alcohol production as a fuel additive to increase the octane of low-grade gasoline. The company completed tests with the compound in its employees' cars last year and is optimistic about the market potential.

Since the original application, made in 1974, Oxirane has lowered the size of the proposed propylene oxide expansion from the original 180 000 to 100 000 ton/year. The authorities had demanded that pressurized storage facilities should be replaced by cryogenic facilities.

Both plants would start production around 1980.

Mitsubishi licence for KTI

KTI has been granted a non-exclusive licence to use the ground flare stack technology developed jointly by Mitsubishi Petrochemical Engineering and Hitachi Shipbuilding and Engineering. The licensing agreement, which covers Europe and runs for a period of 10 years, represents the first export of this technology.

Developed in 1972, the ground flare stack is said to be non-polluting. Unlike conventional flare stacks used to burn off gas and often criticized because of the visible flame, noise and smoke, the Japanese ground flare stack eliminates smoke and greatly reduces noise.

Table 3 Observed and expected deaths, for 1940 to 1974, for all men covered by the survey, according to certified cause of death

Cause of death (ICD* no.)	1940-1974		
	Observed	Expected	SMR
All cancers (140-239)	115	126.77	90.7
Cancer of stomach (151)	34	35.35	91.3
Primary cancer of liver (155)	1	0.71	140.3
Cancer of lung (162-163)	46	51.23	89.8
Cancer of brain (191)	2	2.66	84.6
Other liver cancers (197.7, 197.8, etc)	3	0.91	333.6
Lymphatic and haematopoietic tissues (200-207)	9	9.01	99.3
Endocrine, nutritional, and metabolic diseases (240-279)	4	4.22	94.8
Diseases of circulatory systems (390-433)	180	234.13	76.9
Ischaemic heart disease (410-414)	123	152.14	80.8
Disease of respiratory system (460-519)	42	67.09	62.6
Bronchitis (490-491)	23	32.57	70.6
Disease of digestive system (520-577)	8	15.56	57.4
Liver disease (570-573)	1	2.68	37.3
Accidents (E800-E849)	20	22.93	86.1
Self-harm (E950-E959)	7	10.63	65.7
All deaths (1-999)	393	521.22	75.4

*All deaths have been coded according to the International Classification of Diseases, 8th Revision.

Table 4 Deaths due to liver cancer

Factory no.	Date of birth	Date of death	Certified cause of death	Year joined	Year left	Exposure levels	Job description
1	27/10/1913	10/12/1970	Ascites; carcinoma of liver† and omentum	1941	1947	Low/intermittent	Filter
3	20/4/1901	23/12/1972	Haemangioendothelioma of liver*; verruca, natural causes	1945	1945	High/constant	Autoclave operator (1942-45)
3	15/6/1913	4/3/1973	Undifferentiated carcinoma of liver, primary	1951	1969	Medium/intermittent	Process operator
11	2/6/1927	24/12/1974	Carcinomatosis; angiosarcoma of liver*; hepatic cirrhosis	1946	1974	High/constant	Polycleaner

*Confirmed by panel of histopathologists as due to angiosarcoma of liver.

†Confirmed by panel of histopathologists as *not* due to angiosarcoma of liver.

Table 5 Observed and expected deaths and standardised mortality ratio for all deaths between 1940 and 1974 according to factory

Factory no.	Observed deaths	Expected deaths	SMR
2	77	86.57	88.8
3	15	35.43	23.4
4	127	163.17	84.0
9	4	5.19	77.1
10	2	16.29	12.3
11	153	176.90	86.4
12	2	4.35	45.0
13	5	17.02	28.4
Total population	393	521.22	75.4

details of their work history to a panel of liver pathologists (Baxter, 1976). A diagnosis of primary angiosarcoma of the liver was confirmed in two of them and the remaining two were confirmed as *not* being due to angiosarcoma.

INDIVIDUAL FACTORY EXPERIENCE

Table 5 shows that significantly fewer deaths were observed for men employed in factories 3, 10, and 13 than would be expected from the numbers employed and their ages. In factory 10, 59 workers could not be traced and a further 36 were excluded from the analysis because of inadequate exposure information. Of these 36, three have died. The proportion of persons from this factory not traced is so much higher than for the other factories that it may include a disproportionately high number of deaths. Some early records for factory 3 were not accessible and these may also include a high proportion of deaths. The factories with the highest number of expected deaths (factories 2, 4, and 11) had similar SMRs (88.8, 84.0, and 86.5 respectively). The low number of expected deaths for factory 13 relative to the number employed is a reflection of its expansion during recent years.

Three of the liver cancer deaths occurred in

factory 2 after 1966 (Table 4). This is significantly in excess of the expected 0.13 ($p < 0.01$). The number of deaths attributed to cancer, 21 observed, is marginally in excess of the expected 20.71, whereas the number from circulatory disease is below that expected (37 observed, 40.27 expected). Factory 4 shows a similar pattern with 41 observed cancers compared with 39.26 expected and 60 deaths attributed to circulatory disease compared with 73.58 expected, as does factory 11 with 44 observed cancers, 43.14 expected, and 71 circulatory disease deaths compared with 80.08 expected. While these differences are not statistically significant they indicate that in the three factories with the highest expected number of deaths, the SMR for cancer deaths was in excess of the SMR for all deaths and that for deaths associated with circulatory disease.

Little further information was gained by analysing deaths by certified cause separately for each factory. Therefore in the following analysis all data have been combined.

MORTALITY BY YEAR ENTERING THE INDUSTRY

Table 6, by comparing cohorts who entered the industry in different quinquennia, shows that the ratio of observed to expected deaths is lower for those men who entered the industry recently. Figure 2 shows this to be the case for cancer and circulatory disease. The opposite trend is shown for accidents. Although the downward slope with succeeding year of entry is seen in Fig. 3 and Table 7 to be due to more recent cohorts having lower SMRs than earlier cohorts, the SMR for each cohort is seen to rise the longer the cohort is followed-up (Table 8). The SMRs increase from 40.5 for the first five years of follow-up, to 83.1 for between 15 and 20 years of follow-up, to 106.5 for 30 to 35 years of follow-up.

MORTALITY BY EXPOSURE LEVEL

The overall SMR in Table 9 is seen to be lowest in the group with the highest exposure, 67.8, and highest in the group with the lowest exposure, 78.0. The SMR for liver cancer was however highest in the group exposed to the highest concentration of

VCM. The two liver cancers in this group were both angiosarcomas whereas the liver cancers in the low and medium exposure groups were not (Table 4). The only other high SMR in Table 9 is for brain cancer in the high exposure group. This results from one case being observed whereas 0.36 were expected. There is no indication of a dose-response relationship for cancer as a group, lung cancer, or diseases of the circulatory system and only a slight indication for diseases of the respiratory system where the SMR is increased from 39.7 to 64.4 to 69.1 with successive rises in exposure group; and only a slight and probably meaningless increase for diseases of the respiratory system.

The SMR (Table 10) for those men who experienced constant exposures to VCM, 55.3, is significantly below that for men who experienced only intermittent exposures, 84.1. The SMR for liver cancer is however higher in the former group. The two angiosarcoma deaths were men who had experienced constant exposure (Table 4). This table indicates an excess of lung cancers in men constantly exposed (17 observed, 15.72 expected, $p > 0.05$) which arises from men exposed constantly to medium concentrations (13 observed, 7.75 expected, $p > 0.05$). This group also had a slightly raised bronchitis rate (6 observed, 4.56 expected, $p > 0.05$).

In Table 11 cohorts based on men not in the industry but who were alive 15 years after entry are subdivided according to the length of time spent in the industry. Fifteen-year survivors are considered in order to eliminate the biases that occur in a simple comparison with length of exposure. These arise because a man exposed for 15 years cannot have died before he completed this exposure, whereas a man who was exposed for less than five years may have died within five years of entering the industry. The mortality experience of the four cohorts considered in Table 11, men who entered between 1940 and 1944, between 1945 and 1949, between 1950 and 1954, and between 1955 and 1959 have been studied for 16 years, 11 years, six years, and one year respectively. Although there is a slight drop in the SMR in relation to the length of exposure for the 1940-44 cohort, there is an overall tendency for the

Table 6 Analysis of observed and expected deaths by year of entry

All deaths	Year of entry						
	1940-44	1945-49	1950-54	1955-59	1960-64	1965-69	1970-74
Observed	89	103	87	83	24	19	9
Expected	101.85	123.87	123.41	76.64	40.09	30.84	16.96
SMR	87.4	83.1	69.7	87.2	63.9	61.6	53.1

Six deaths in men who entered before 1940 are not included in this table.

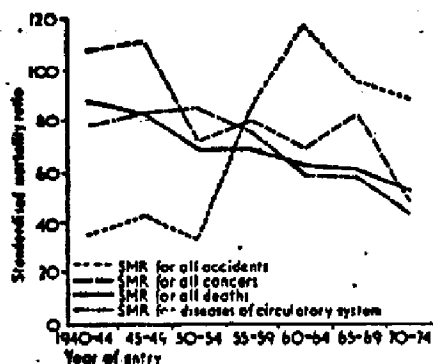


Fig. 2 Standardised mortality ratios for all deaths, all cancers, diseases of circulatory system, and accidents related to the year of entry into industry.

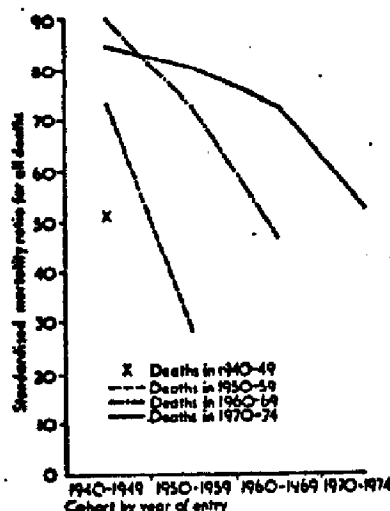


Fig. 3 Standardised mortality ratios for deaths from all causes according to year of death for cohorts based on year of entry into industry.

SMR to increase with increased exposure. The total SMR increases from 100.6 for those exposed for four years or less, to 104.7 for those exposed for five to nine years, to 113.3 for those exposed for 10 to 14 years.

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Table 7 Observed and expected deaths from all causes and SMRs according to year of death for cohorts based on year of entry to the industry

Year of entry	Year of death	1940-49	1950-59	1960-69	1970-74
1940-49	6	11.71	51.2	37	73.5
1950-59	8	28.12	27.3	86	90.0
1960-69	13	27.73	46.9	67	74.26
1970-74	9	16.96	53.1	80.5	73.1

Six deaths in men who entered before 1940 are not included in this table.

Table 8 Observed and expected deaths in relation to length of time each cohort has been followed-up

Length of time cohort followed-up (years)	Observed deaths	Expected deaths	SMR
0-4	26	89.32	40.5
5-9	30	84.44	37.8
10-14	63	83.37	69.3
15-19	87	102.22	85.1
20-24	80	92.60	86.3
25-29	34	70.41	70.7
30-34	30	28.18	106.5

Six deaths in men who entered before 1940 are not included in this table.

Discussion

This industry has grown approximately tenfold since the second world war (Fig. 1). It is nearly twice as large as it was only 10 years ago. The environmental conditions in the manufacturing processes are also known to have altered since men were first employed in the industry in the early 1940s. The main factors affecting the exposure levels were firstly, in the mid-sixties the discovery that exposure to high concentrations of VCM can cause acro-osteolysis and Raynaud-like phenomena which have since been classified under the heading vinyl chloride disease; and secondly, in 1974 the discovery that men exposed to high concentrations of VCM had an increased risk of dying from angiosarcoma of the liver.

These changes in the size of industry and exposure mean that more than half of the people who have ever been exposed to VCM in the manufacture of PVC in Great Britain are currently employed in the industry; approximately 75% of men who have been employed in the industry have been employed for less than 10 years; only 8% have been employed for 20 years or longer; approximately half the persons who have been exposed to VCM have been intermit-

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Table 9 *Observed and expected deaths according to whether exposure was thought to be high, medium, or low*

	High			Medium			Low		
	Observed	Expected	SMR	Observed	Expected	SMR	Observed	Expected	SMR
All causes	9	9.99	93.8	31	39.66	83.8	53	57.32	92.1
Liver cancer	3	0.13	1533.5	1	0.77	129.3	1	0.78	133.3
Lung cancer	2	3.67	54.5	23	34.42	64.2	21	23.15	90.7
Brain cancer	1	0.36	277.8	—	1.60	—	1	1.09	99.2
Diseases of circulatory system	12	16.79	71.5	83	110.99	76.9	83	104.81	77.7
Diseases of respiratory system	3	4.34	69.1	21	33.62	64.4	18	30.13	59.7
All deaths	27	39.85	67.8	180	244.18	73.7	185	237.16	78.0

Excludes one death in a man for whom an invalid measure of exposure was recorded.

Table 10 *Observed and expected deaths according to whether exposure was constant or intermittent*

Cause of death	Constant			Intermittent		
	Observed	Expected	SMR	Observed	Expected	SMR
All causes	28	39.70	70.5	87	87.07	99.3
Liver cancer	2	0.34	370.6	2	1.11	180.2
Lung cancer	17	13.72	108.1	29	35.42	81.9
Brain cancer	1	1.42	70.4	1	2.23	—
Diseases of circulatory system	36	69.82	51.6	144	164.37	87.6
Diseases of respiratory system	11	17.82	61.7	31	49.27	62.9
All deaths	89	160.94	55.3	303	360.25	84.1

Excludes one death in a man for whom an invalid measure of exposure was recorded.

Table 11 *Observed and expected deaths in relation to the length of exposure and year of entry for men who were alive 15 years after they entered*

Year of entry	Length of exposure					
	0-4 years			5-9 years		
	Observed	SMR	Expected	Observed	SMR	Expected
1940-44 (Deaths occurring in 1959-74)	33	—	32.06	10	—	10.30
	103			97		
1945-49 (Deaths occurring in 1960-74)	26	—	24.47	7	—	6.43
	111			100		
1950-54 (Deaths occurring in 1969-74)	18	—	19.83	4	—	3.85
	91			164		
1955-59 (Deaths occurring in 1974)	—	—	2.13	2	—	1.97
	—			146		
Total	79	—	78.51	33	—	31.97
	100.6			164.7		
				119.3		

tently exposed; and only 10% of those who have been constantly exposed, have been exposed to high concentrations. Thus relatively few persons have been exposed for a long time to high levels of vinyl chloride monomer and even in cases in which men have completed 20 years of service, because their service has only recently been completed, the follow-up period is too short to evaluate the carcinogenic effect of VCM.

SELECTION AND SURVIVAL IN THE INDUSTRY
This population comprises men who at one time since 1940 were fit enough to obtain a job in the plastics industry. Because in general people entering employment are healthy their expected mortality rate should be lower than that observed for the population as a whole with whom comparison is made. Table 6, in which the population was subdivided into cohorts according to year of entry into the industry,

shows that the cohorts of men who entered more recently had lower overall mortality ratios than those men who entered long ago. Figure 2 shows that similar associations are observed for cancers and for circulatory disease. Figure 3 confirms that this association between SMR and year of entry into the industry is not a function of the cohort but is related to the length of time that it has been pursued and therefore to the length of time since the individual entered the industry. Table 8 shows that it may take 20 to 30 years for this effect to disappear.

As this population comprises all men who have been identified as having worked with VCM since the industry began in Great Britain in the early 1940s, it includes men who have spent short periods in the industry as well as those who have had longer exposures. In any evaluation of the role duration of exposure plays in a model of cause and effect it is necessary to account for differences in characteristics between those subjects who stay a long time in the industry and those who leave. Most of the latter leave for reasons unrelated to health, but there are some who will leave because they are not fit enough to continue working or because they consider the job to be affecting their health. It is difficult to separate this effect, the survivor effect, from the healthy population selection effect described above. They were both clearly described by Oyle (1883) but have not been measured. The 15-year survival effect for this population has been estimated by separating those persons alive 15 years after entering the industry into those working and those not working in the industry after the 15 years. The mortality patterns after these 15 years were then compared. The SMR for men not in the industry, 108.4, was approximately 30% higher than for those still in the industry, 74.0. In a separate report we have considered at greater length the implications of these effects and the effect of the period of follow-up on the interpretation of occupational mortality studies (Fox and Collier, 1976); they are of major importance in the interpretation of these data.

Other studies

Some hypotheses concerning the effects on man of exposure to VCM have been proposed as a result of the animal experiments conducted by Maltoni and Lefemini (1975) and the epidemiological studies conducted by, for example, Tabershaw and Gaffrey (1974) and Nicholson *et al.* (1975). Maltoni and Lefemini (1975) have suggested that vinyl chloride monomer produced tumours in the three animal species studied: rats, mice, and hamsters. Liver angiosarcomas were observed in all three species. In addition other tumours that occurred included

cerebral neuroblastomas and pulmonary adenomas. Tabershaw and Gaffrey (1974) confirmed the clinical suggestions by Creech and Johnson (1974) that there was strong epidemiological evidence that exposure to VCM caused angiosarcoma of the liver in humans. Their study also indicated an excess of cancer of the respiratory system and brain although this was not statistically significant. Nicholson *et al.* (1975) also confirmed that exposures to vinyl chloride monomer can cause liver cancer in humans. Although they observed three angiosarcomas of the liver and one brain cancer no deaths were due to lung cancer.

Comparisons between the findings in Great Britain and those in the USA are limited because of the differing experiences in the two countries. If we apply the same population definition as employed by Tabershaw and Gaffrey (1974), we find 331 deaths observed and 462.29 expected. This gives an SMR of 72 compared with one of 75 found by Tabershaw and Gaffrey (1974). Men in the high exposure group have an SMR of 59.4 compared with one of 71.7 in the medium exposure group and 73.5 in the low exposure group. An unexplained trend similar to this was noted by Tabershaw and Gaffrey (1974). We believe the trend is due to selection and survival in the industry and to the length of follow-up. Using the same population definition as Tabershaw and Gaffrey we would have found two liver cancer deaths, one of which would have been due to angiosarcoma.

Nicholson and co-workers in their study of all men in one plant with greater than five years' exposure followed-up 10 years from first employment, observed 24 deaths compared with 19.0 expected, and nine cancers compared with 3.9 expected. Included in these nine cancers were three angiosarcomas. The last two columns in Table 11 show what might be termed a high risk group in that these are people who have experienced between five and 14 years' exposure and have left the industry. They are studied here 15 years after first employment. In this group 48 deaths were observed compared with 44.03 expected. For cancer 13 were observed compared with 11.48 expected and for lung cancer six observed compared with 4.66 expected. It should be emphasised that none of the cases of liver cancer occurred in this high risk group. From Table 4 it can be deduced that a study in Great Britain similar to that conducted by Nicholson *et al.* (1975) would have identified one angiosarcoma and one other primary liver cancer.

General assumptions and limitations

Certain environmental factors are known to affect man's longevity. Some of these have been associated

with particular causes of death such as cigarette smoking with lung cancer, heart disease, and bronchitis. Other associations such as those between social class and area of residence with cancers and bronchitis have not been fully explained. Epidemiology does not provide the immediate answer because the cause and effect models are complex and individual susceptibility confuses the issue. In this particular study no account has been taken of these other factors. We have assumed that the social class, smoking, and geographical distributions are similar to those for the national population with which comparison is made.

The mortality study provides a relatively crude epidemiological technique for evaluating the risk to health in the group under study. It cannot account for all the factors that may be relevant to the hypotheses that have been tested and its power is limited with respect to the detection of hazards which produce small excesses of mortality. Such studies can confirm relationships between exposures to specific chemicals and the subsequent development of uncommon tumours such as mesotheliomas, bladder cancers, and liver tumours. Unless the chemical considered is a powerful carcinogen these studies are less sensitive when studying common causes of death.

Conclusions

It is not yet possible to evaluate the overall impact of exposures to VCM on this population of workers but bearing in mind reservations discussed above two conclusions can be drawn at this stage.

The first relates to whether or not there is evidence that exposure of men to VCM in Great Britain in the manufacture of PVC caused cancer. We have observed four liver cancers, two of which were subsequently confirmed as angiosarcomas, significantly more than would have been expected. All these cancers occurred between 1970 and 1974 and similar experiences have been reported in the USA and in animal experiments. We therefore conclude that VCM is probably a carcinogen causing liver cancer in workers exposed to it. Although in this study there is little relationship with length of exposure, the angiosarcomas were associated with exposures to very high concentrations of VCM.

The second conclusion relates to whether VCM causes cancers other than those of the liver. We find no evidence to support this suggestion. Only two brain cancers were observed and there is little indication of an excess of lung cancers. The SMR for cancer as a group is consistently higher than for all deaths but because of population selection factors this is difficult to evaluate.

The effect of VCM on the mortality experience of

workers exposed will only become clear after continuing this study for a further 10 years at least. Although the recently adopted hygiene standards may in future be shown to have a residual risk associated with them, men who entered the industry in recent years should be at lower risk than those who were exposed at a time when conditions were less controlled.

No study such as this could have been conducted without the assistance and co-operation of the industry and unions involved. Dr S. Gauvain was involved with the planning of this project and an early draft of this report was discussed with Dr M. Greenberg, Dr A. M. Adelsheim, and Dr P. J. Baxter to all of whom we are grateful.

The EMAS Survey Control Section administered the survey, individual companies identified people who had worked in this industry, and the Office of Population Censuses and Surveys obtained and coded all death certificates.

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Appendix 1 Deaths in women

Factory no.	Date of birth	Date of death	Certified* cause of death ICD code	Year joined	Year left	Exposure levels	Job description
2	8.12.1903	22.3.1963	5900, 2901	1944	1945	Medium/intermittent	Process worker
2	21.2.1899	4.7.1963	4129	1942	1943	Medium/intermittent	Process worker
2	2.3.1893	28.2.1972	4129, 4271	1944	1945	Medium/intermittent	Process worker
2	10.2.1894	12.10.1948	9300	1943	1946		Process worker
2	17.10.1879	22.5.1950	4319	1940	1946		Process worker
2	12.7.1897	8.3.1971	4403, 7824	1943	1945		Process worker
2	13.11.1902	3.7.1974	4109, 2930	1944	1945		Process worker
2	23.3.1921	3.8.1968	3949, 4500, 4930	1944	1945		Process worker
2	12.7.1894	11.10.1962	4409, 4270	1942	1945		Process worker
2	1.7.1894	5.8.1952	1579	1942	1945		Process worker
2	19.3.1909	18.12.1967	1519	1942	1945	Medium/intermittent	Process worker
4	8.10.1890	7.2.1971	4540, 9389	1943	1945	Low/intermittent	Man room attendant
4	22.8.1914	28.8.1949	4290, 4109, 5140	1941	1941		Worker with solvents
4	3.10.1894	14.11.1972	5010, 5932	1941	1946		Analytical laboratory attendant
4	22.1.1893	7.12.1948	5110, 7834, 4380	1940	1940		Analytical sampler
4	7.1.1894	26.3.1946	5900, 4271, 4110	1941	1944		Worker with solvents

*Primary cause in italics.

Appendix 2 Deaths in 1940-74 notified since analysis

Factory no.	Date of birth	Date of death	Certified* cause of death ICD code	Year joined	Year left	Exposure levels	Job description
4	15.11.1904	25.8.1963	2500, 4230, 4529	1953	1954	Low/intermittent	Maintenance labourer
4	21.12.1892	20.8.1953	9310	1954	1955	Medium/intermittent	Maintenance labourer
4	13.7.1901	31.3.1962	4000, 7920	1940	1959	Medium/constant	Electrician
10	7.7.1904	15.12.1973	4109, 4272	Not known	1971	Low/intermittent	Security/keeper
10	18.8.1923	7.7.1972	4309	Not known	1972	Medium/constant	Recovery/keeper
11	1.1.1907	13.4.1972	5131, 4270, 4380, 5130	1933	1956	Medium/intermittent	Filter
11	12.10.1900	20.10.1960	7027, 4500, 4930, 4109	1931	1933	Low/intermittent	Grinder
11	25.2.1892	10.9.1968	1500, 4500	1931	1940	Medium/intermittent	Filter
11	9.7.1902	8.8.1969	4360	1937	1967	Low/intermittent	Pneum operator

*Primary cause in italics.

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