 British Journal of Industrial Medicine 1990;47:392–399

Morbidity prevalence study of workers with potential exposure to epichlorohydrin

S P Tsai, Sally R Cowles, D Lynne Tackett, M T Barclay, C E Ross

Abstract

This study examined the morbidity experience from 1981 to 1988 of two cohorts (Shell cohort and Enterline cohort) of workers who had potential exposure to epichlorohydrin (ECH). The morbidity prevalence data for this study were extracted from the morbidity section of the Shell health surveillance system which included all illness and absence records in excess of five days. For both cohorts, the standardised morbidity ratios (SMRs) for all causes and all neoplasms were similar to an internal comparison group. There were no increases in heart disease morbidity for the Shell cohort (SMR = 97) or the Enterline cohort (SMR = 90). The SMRs for heart disease in the lower exposure group of the Shell cohort were 101 and 93 for the corresponding Enterline cohort. They were 92 and 87, respectively, in the higher exposure group. The increased risk of heart disease mortality reported by Enterline *et al* in workers more heavily exposed to ECH was not confirmed in this morbidity study. Morbidity from skin and subcutaneous tissue disorders, however, was found to be increased significantly in the Shell cohort. The SMR was 98 for the lower exposure group and 195 for the higher exposure group. A review of the original morbidity reports for each case suggested that factors unrelated to exposure to ECH such as the physical demands of a particular job, amount of time outside—for example, exposure to poison ivy—and other underlying medical conditions may be of greater importance than exposure to ECH.

In a recent article Enterline *et al* reported results of a retrospective cohort mortality study of workers at two Shell manufacturing locations (one in Texas, one in Louisiana) who had potential exposure to epichlorohydrin (ECH).[1] This study showed overall low mortality for all causes and cancer. There were no statistically significant excesses of death from any cause except leukaemia. The leukaemia (three cases of different cell types) occurred in the follow up period starting 20 years after first exposure. Overall, there was no excess of heart disease in this cohort. The death rate due to heart disease in the nil to light exposure group, however, was statistically significantly lower than in the local comparison populations (standardised mortality ratio (SMR) = 39·2). When compared with the mortality of heart disease in the moderate to heavy exposure group (SMR = 105·4), the difference between the two groups was statistically significant due to the unusually low heart disease mortality in the lower exposure group. Enterline *et al* hypothesised that a relation may exist between exposure to ECH and heart disease mortality.

The Enterline *et al* mortality study did not contain information on heart disease risk factors such as smoking, obesity, cholesterol, and blood pressure. These potential confounders may have been responsible for the heart disease mortality differences seen between the two exposure groups. These results may also have been due to chance (especially since neither exposure group had a significant excess of death from heart disease). If a true association exists between exposure to ECH and heart disease the pattern of heart disease morbidity should be similar to that for heart disease mortality seen in the Enterline study since most deaths from heart disease are preceded by one or more heart disease morbidity events.[2]

The present study includes two populations. The first population consists of 713 workers with industrial hygiene confirmed potential exposure to ECH at the same two Shell manufacturing locations studied by Enterline *et al* (hereafter referred to as the Shell cohort). These employees for the most part were hired after those originally studied by Enterline. The morbidity experience of this group from 1981 to 1988 was examined. Since Enterline also raised the question of an association between heart disease and those exposed to allyl chloride and ECH, heart disease morbidity for workers who had potential exposure to both ECH and allyl chloride was also examined.

Shell Oil Company, Corporate Medical Department, PO Box 2463, Houston, Texas 77252-2463, USA
S P Tsai, S R Cowles, C E Ross
Safety and Industrial Hygiene Department
D L Tackett, M T Barclay

The second population consists of a subset (n = 280) of the original Enterline cohort members for whom morbidity data are available from 1981 to 1988 (hereafter referred to as the Enterline cohort). The entire Enterline population could not be studied due to insufficient morbidity and industrial hygiene monitoring information before 1981. All causes of morbidity in both cohorts were studied to examine not only heart disease but also any other potential exposure association. Distribution of heart disease risk factors by exposure group was also examined.

Material and methods

STUDY POPULATION

Shell cohort

The study population (n = 713) consisted of both hourly and salaried male employees who worked at two Shell chemical plants during the period 1 January 1981 to 31 December 1988. One of the chemical plants is in Deer Park, Texas, where production of ECH started in 1948. The other is in Norco, Louisiana, where production started in 1955. The cohort members were identified based on their assigned job exposure profiles (JEP) during the study period. A JEP includes a description of work activities and details the potential for exposure to chemical and physical agents present for a job in the workplace.[3] A set of the JEPs with potential exposure to ECH was used to identify the individuals who had potential exposure to ECH. After the cohort was established, each worker was further classified in terms of his level of exposure to ECH. The classification included moderate, light, and nil exposures and was based on industrial hygiene sampling data. The industrial hygiene data are from breathing zone air samples.

Enterline cohort

The population examined in the Enterline mortality study consisted of all men who worked at either of the two plants from start up (1948 for Deer Park, 1955 for Norco) until 1965. A total of 863 men with probable exposure to ECH at the two plants were followed up for death until 1983. A detailed description of the study population and methodology has been documented elsewhere.[1] After his cohorts were identified, Enterline classified each worker into one of five groups in terms of level of potential exposure to ECH (heavy, moderate, light, nil, or unknown). This classification, in the absence of air monitoring data, was based on the opinion of industrial hygiene personnel and recollection of plant employees. Each worker was placed into the exposure category for his highest exposure job.

Enterline provided a computer tape containing the ECH cohort data. Cause of death information was not included on the tape. This cohort was then matched with data (1981–8) from Shell's health surveillance system (HSS). Ninety nine workers with unknown exposure to ECH were excluded from further analyses. Of the original Enterline cohort, 280 were still working from 1981 to 1988 and were included in the present morbidity study. The remaining 484 had either left, retired, or died before 1981 and their morbidity experience could not, therefore, be evaluated.

HEART DISEASE RISK FACTORS

The data for heart disease risk factors such as smoking habit, cholesterol, blood pressure, and obesity were derived from the HSS which contains all employee preplacement and annual periodic examinations done since 1 January 1978.[4] The most current examination data were used; about 85% of these were done in 1985–8.

The smoking history was used to place each employee into one of three mutually exclusive categories: current cigarette smoker, former cigarette smoker, and non-smoker. A smoker who had stopped for less than five years was classified as an ex-smoker. A non-smoker was defined as a person who had never smoked or had stopped smoking for five years or longer.

Raised cholesterol was defined as values equal to or greater than 200 mg/dl. Raised blood pressures were those diastolic blood pressure readings equal to or greater than 90 mm Hg or systolic blood pressure readings equal to or greater than 140 mm Hg. Obesity was defined as body mass index, BMI = weight (kg)/height^2 (m), greater than or equal to 27·2. This value represents 20% more than ideal body weight based on the recommendations of the National Institutes of Health Consensus Development Panel.[5]

MORBIDITY DATA

Morbidity data for this study were extracted from the morbidity section of the HSS which includes all illness absence events for more than five days. Since records of absences are originally from personnel and payroll systems, the absence reporting is 100% complete. More than 90% of the morbidity reports had statements from physicians identifying the reason for the absence. The causes of morbidity were coded according to the International Classification of Diseases ninth revision clinical modification (ICD 9-CM).[6] Only the primary cause was used in the analysis. Morbidity prevalence was analysed by diagnostic categories.

A morbidity prevalence event in this study for both study cohorts and comparison groups was defined as occurring when a worker had a specific diagnostic condition resulting in an absence of more than five days during the eight year period from 1981 to 1988. Only one prevalence event per worker was counted in any given diagnostic category. For example, the category for heart disease would consist of all those with one or more absences in excess of five days due to heart disease during this period. A prevalence of one (1) is used regardless of the number of times that a single specific diagnostic condition occurs in the same individual. Both absences during the study period due to previously identified conditions as well as newly diagnosed conditions are included, providing a period prevalence. If a worker had absences from two different diagnostic categories during this period, two prevalance events (one for each diagnostic category) would be recorded. Thus prevalence measures the number of individuals with the condition during the study period rather than the total number of occurrences of that condition in the cohort.

INDUSTRIAL HYGIENE MONITORING DATA

The sampling strategy used by industrial hygienists for evaluating personal exposure has usually been based on representative sampling of various JEPs or worst case sampling during spills or turnaround. JEPs selected for sampling are usually those in which the highest potential for exposure exists during routine operation. ECH samples were taken, without regard to respirator use, in the breathing zones of individuals working at these JEPs to characterise the exposures.

Sampling data on exposure to ECH for the years 1981–8 were used to classify the level of exposure for each JEP. Data for the years before 1981 were not readily available for assessing the workers' exposure. The personal sampling exposure data for the eight year period were used to classify JEPs for ECH into two mutually exclusive groups, nil and light to moderate exposure to ECH. JEPs for the nil exposure group were those for which the 95% upper confidence limit of the geometric mean of samples was less than or equal to the detection limit, 0·1 ppm. JEPs for the light exposure group were those for which the 95% upper confidence limit of the geometric mean of the samples was less than or equal to 0·5 ppm but greater than 0·1 ppm.

JEPs for the moderate exposure group were those for which the 95% upper confidence limit of the geometric mean of the samples was less than or equal to 1 ppm but greater than 0·5 ppm. In addition, the moderate exposure group included those JEPs with one or more sample values greater than 1 ppm when the total number of samples was 10 or fewer, or with two or more values greater than 1 ppm when the total number of samples was more than 10. Those JEPs for which no sampling data were available were classified into exposure groups based on the judgment of the plant industrial hygienists. Most of these JEPs were classified into the nil exposure group, with a few in the light exposure group. These data characterised the exposures occurring during the study period and may not represent exposures of previous years. Exposures may possibly have been higher in the past before newer production techniques and work practices were initiated.

JEPs for most study subjects in the light to moderate group are: dockmen; pipefitters; welder; resins finishing; and various ECH production unit operators. JEPs for the nil exposure group include: dispatching operations foreman; quality assurance laboratory technicians for resins and intermediates/solvents; resins tank farm/utility operator; resins recovery/utility operators; and electrician.

ANALYTIC METHODS

Person-years at risk were accumulated for each worker beginning 1 January 1981 or the date of first exposure to ECH (whichever was later) and ending at the closing date of the study (31 December 1988), the date of retirement, the date of death, or the date of leaving (whichever was earlier). The number of years contributed by each worker was classified by age (< 40, 40–49, 50–59, and ≥ 60), pay status (hourly and salaried), and plant location (Deer Park and Norco). The morbidity experience of the two ECH groups was compared with that of an internal comparison group. The internal comparison group was defined as all men at the two locations who worked in jobs with no potential exposure to ECH during the study period. The expected numbers of morbidity events were calculated from the age, pay status, location, and cause specific morbidity rates of the internal comparison group. SMRs were computed as the ratio of the observed to the expected number of morbid events for each cause of interest. Significance tests were based on the assumption that the observed number of morbidity events follows a Poisson distribution.[7] A two sided test of significance was used. Since most of both the comparison group and the Shell cohort were white (88% and 83%, respectively), SMRs in this study were not adjusted for race.

Results

SHELL COHORT

Included in the analysis were 713 men, representing the total number of male employees who ever worked

Table 1 Cohort statistics of workers with probable exposure to epichlorohydrin, 1981–8: Shell cohort

	Level of exposure	
	Nil	*Light to moderate*
No studied	412	301
No person-years observed	2947	2110
Average age at entry	36·3	37·3
Average years of follow up (1981–8)	7·2	7·0
Average total duration of employment (y)	14·2	14·2
Hired pre-1970	72 (17·5%)	66 (21·9%)
Hired post-1970	340 (82·5%)	235 (78·1%)

Table 2 Observed and expected morbidity and SMRs for workers with probable exposure to epichlorohydrin 1981–8: Shell cohort

Cause of morbidity (ICD-CM 9th rev codes)	*Obs*	*Exp*	*SMR*
All causes (000–999)	1046	1084·87	96
Infective and parasitic diseases (000–139)	40	46·96	85
All neoplasms (140–239)	23	22·73	101
Endocrine, nutritional, and metabolic diseases (240–279)	16	15·67	102
Mental disorders (290–319)	33	36·53	90
Nervous system (320–389)	65	51·28	127
Heart disease (390–414, 420–429)	40	41·25	97
Cerebrovascular disease (430–438)	3	1·14	263
Diseases of arteries (440–448)	3	2·05	146
Diseases of veins and other circulatory systems (451–459)	25	19·64	127
Respiratory system (460–519)	156	181·65	86
Digestive system (520–579)	93	110·42	84
Genitourinary system (580–629)	42	38·03	110
Skin and subcutaneous tissue (680–709)	45	31·77	142*
Musculoskeletal system (710–739)	133	134·98	99
Symptoms and ill defined conditions (780–799)	113	110·93	102
Injury and poisoning (800–999)	213	235·09	91
All other causes	4	4·74	84

*$p < 0·05$.

at the Deer Park (n = 513) and Norco (n = 200) ECH units from 1 January 1981 to 31 December 1988. The total number of person-years of observation was 2947 for the nil and 2110 for the light to moderate groups. Average age at entry into the cohort, average years of follow up, and total duration of employment were essentially the same between the two groups (table 1). The average number of years of follow up were seven for both exposure groups or about a half of the total duration of employment. Slightly more than 82% of the workers in the nil exposure group were hired after 1970 compared with 78% of those in the light to moderate group. Based on a review of complete work histories of a 10% sample of the cohort, it is estimated that 92% of the workers in both groups had more than 11 years of potential exposure to ECH.

Table 2 shows observed and expected morbidity prevalence and SMRs for the entire ECH study group. For all causes, 1046 morbidity prevalence events were observed whereas 1084·87 were expected, resulting in an SMR of 96 or a morbidity experience about the same as that for the rest of the workers at these two locations. For all neoplasms, the observed (n = 23) and expected (n = 22·73) events were virtually the same (SMR = 101). There was no increase in heart disease with 40 observed and 41·25 expected (SMR = 97). Of the 18 causes of morbidity examined, only skin and subcutaneous tissue showed a statistically significant increase with 45 incidents observed and 31·8 expected (SMR = 142).

Among the total ECH group the SMRs for several morbidity categories showed a non-significant increase. Notable were diseases of the nervous system and diseases of veins and other circulatory systems (mainly due to haemorrhoids). The SMR for cerebrovascular disease was also raised (SMR = 263); however, this was based on only three cases. Non-significant decreased morbidity was observed for diseases of the respiratory (SMR = 86) and digestive systems (SMR = 84) and infective and parasitic diseases (SMR = 85). There were no morbidity events for cancer of the respiratory system or leukaemia.

When examined by level of exposure (table 3), there was no direct relation between SMRs and level of exposure for any morbidity categories except skin and subcutaneous tissue. The SMR for heart disease in the nil exposure group was 101 and 92 in the light to moderate exposure group. The raised SMR for skin and subcutaneous tissue (SMR = 195) in the

Table 3 Observed and expected morbidity and SMRs for workers by exposed levels 1981–8: Shell cohort

	Level of exposure					
	Nil			*Light to moderate*		
Cause of morbidity (ICD9-CM codes)	*Obs*	*Exp*	*SMR*	*Obs*	*Exp*	*SMR*
All causes (000–999)	587	613·97	96	457	470·90	97
Infective and parasitic diseases (000–139)	21	26·43	80	19	20·53	93
All neoplasms (140–239)	11	12·07	91	12	10·66	113
Endocrine, nutritional, and metabolic diseases (240–279)	8	8·14	98	8	7·53	106
Mental disorders (290–319)	19	21·24	90	14	15·29	92
Nervous system (320–389)	39	28·67	136	26	22·61	115
Heart disease (390–414, 420–429)	22	21·73	101	18	19·52	92
Cerebrovascular disease (430–438)	2	0·51	392	1	0·63	159
Diseases of arteries (440–448)	2	1·39	144	1	0·66	152
Diseases of veins and other circulatory systems (451–459)	17	11·12	153	8	8·52	94
Respiratory system (460–519)	88	103·26	85	68	78·39	87
Digestive system (520–579)	57	63·14	90	36	47·28	76
Genitourinary system (580–629)	24	21·46	112	18	16·57	109
Skin and subcutaneous tissue (680–709)	17	17·40	98	28	14·37	195*
Musculoskeletal system (710–739)	64	75·38	85	69	59·60	116
Symptoms and ill defined conditions (780–799)	72	66·54	108	41	44·39	92
Injury and poisoning (800–999)	124	133·01	93	89	102·08	87
All other causes	2	2·44	82	2	2·30	87

*$p < 0·05$.

Table 4 Observed and expected morbidity and SMRs for workers potentially exposed to epichlorohydrin and allyl chloride, 1981–8: Shell cohort

	Level of exposure					
	Nil			Light to moderate		
Cause of morbidity (ICD9-CM codes)	Obs	Exp	SMR	Obs	Exp	SMR
All causes (000–999)	357	324·83	110	346	338·07	102
Heart disease (390–414, 420–429)	13	11·96	109	14	15·15	92

light to moderate exposure group was statistically significant; the SMR of 98 for the nil exposure group was not statistically significant. None of the SMRs for other causes of morbidity was statistically significant. The SMR for diseases of veins and other circulatory systems was 153 (17 observed, 11·12 expected) for the nil exposure group but only 94 for the light to moderate exposure group (8 observed, 8·52 expected).

All the 200 workers at the Norco plant in the Shell cohort were potentially exposed to both ECH and allyl chloride whereas 235 of the 513 workers at the Deer Park plant had potential exposure to both chemicals. The heart disease SMR for workers who had nil exposure to ECH and probable potential exposure to allyl chloride was 109. The SMR for workers with light to moderate exposure to ECH and probable potential exposure to allyl chloride was 92 (table 4).

Table 5 shows the age and pay status adjusted prevalence rates for selected heart disease risk factors. Smoking information was available for 96% of the two ECH groups and 89% of the comparison group. Data for the other risk factors were available for 87% and 85% of the study subjects, respectively.

The light to moderate exposure group had higher prevalence rates for smoking (31·3%) and hypercholesterolaemia (66·6%) than the nil exposure group (25·5% and 57·9%, respectively) and the comparison group (27·0% and 55·4%, respectively). The two exposure groups had similar rates for high blood pressure (20·7% for light to moderate and 20·2% for nil) that were lower than those for the comparison group (23·4%). The nil exposure group had a higher obesity rate (54·9%) than the light to moderate exposure group (47·7%) and the comparison group (42·0%).

Table 5 Age and pay status adjusted prevalence rates for selected cardiovascular disease risk factors: Shell cohort*

	Level of exposure		
Risk factors	Internal comparison	Nil	Light to moderate
Smoking	27·0	25·5	31·3
High blood pressure	23·4	20·2	20·7
Hypercholesterolaemia	55·4	57·9	66·6
Obesity	42·9	54·9	47·7

*Per 100 workers. Adjusted to the internal comparison population using the direct standardisation method.

ENTERLINE COHORT

Table 6 presents the exposure and employment characteristics of the original Enterline cohort. Of the 280 men from the original Enterline cohort who were still working at 1 January 1981 and were included in the morbidity study, about 50% were in the nil to light exposure group whereas the remainder were in the moderate to heavy exposure group. The pattern is virtually the same for the 484 who had left the workplace before 1 January 1981 and so were excluded from the morbidity study. The employment characteristics in terms of the year of first exposure and years since first exposure were similar between the two groups. The distribution of the cohort by the year of first exposure shows that 89% of those included in the morbidity study and 84% of those excluded from the morbidity study began work in the ECH exposure job before 1960. Those workers included in the morbidity study showed a longer duration since first exposure, with 87% being longer than 25 years (compared with 67% for those excluded from the morbidity study). In addition, the

Table 6 Distribution of the original Enterline cohort by estimated level of exposure, year of first exposure, and years since first exposure: Enterline cohort

	Original Enterline cohort			
	Included in morbidity study		Excluded from morbidity study	
	No	%	No	%
Level of exposure:				
Nil to light	137	48·9	232	47·9
Moderate to heavy	143	51·1	252	52·1
Total	280	100·0	484	100·0
Year of first exposure:				
1945–9	27	9·6	57	11·8
1950–4	74	26·5	96	19·8
1955–9	149	53·2	254	52·5
⩾1960	30	10·7	77	15·9
Total	280	100·0	484	100·0
Years since first exposure:				
<20	7	2·5	33	6·8
20–4	29	10·4	126	26·1
25–9	145	51·7	204	42·1
⩾30	99	35·4	121	25·0
Total	280	100·0	484	100·0

Table 7 Observed and expected morbidity and SMRs for workers with probable exposure to epichlorohydrin 1981–8: Enterline cohort

Cause of morbidity (ICD9-CM codes)	*Obs*	*Exp*	*SMR*
All causes (000–999)	310	291·06	107
Infective and parasitic diseases (000–139)	8	7·37	109
All neoplasms (140–239)	14	15·09	93
Endocrine, nutritional, and metabolic diseases (240–279)	6	5·61	107
Mental disorders (290–319)	4	4·55	88
Nervous system (320–389)	21	15·95	132
Heart disease (390–414, 420–429)	30	33·25	90
Cerebrovascular disease (430–438)	1	1·12	89
Diseases of arteries (440–448)	4	2·10	190
Diseases of veins and other circulatory systems (451–459)	5	5·63	89
Respiratory system (460–519)	44	38·18	115
Digestive system (520–579)	37	30·74	120
Genitourinary system (580–629)	19	15·81	120
Skin and subcutaneous tissue (680–709)	9	8·18	110
Musculoskeletal system (710–739)	42	35·44	119
Symptoms and ill defined conditions (780–799)	16	31·97	50*
Injury and poisoning (800–999)	45	38·33	117
All other causes	1	1·78	56

*p < 0·05.

ages at first exposure were 27 and 29 for the two groups, respectively.

Table 7 presents the observed and expected morbidity prevalence events and SMRs for the Enterline cohort. For all causes, the number of observed morbidity events (310) was slightly higher than the expected resulting in an SMR of 107. The SMRs for several morbidity categories were non-significantly raised. Among these were diseases of the nervous system (SMR = 132) and the musculoskeletal system (SMR = 119). Non-significant decreases in morbidity were observed for heart disease (SMR = 90) and neoplasms (SMR = 93). The observed morbidity for ill defined conditions was significantly lower than expected (SMR = 50). In addition, there were no morbidity events for cancer of the respiratory system or leukaemia.

Table 8 presents SMRs by level of exposure. Of all 18 morbidity categories, only the SMR for symptoms and ill defined conditions in the moderate to heavy exposure group was significant (SMR = 42). The corresponding SMR for the nil to light exposure group was also lowered but not significantly (SMR = 59). The moderate to heavy exposure group's SMR for diseases of the genitourinary system was much lower than those of the nil to light exposure group. Similar findings were noted for diseases of the arteries and diseases of veins and other circulatory systems, but the SMRs were based on a small number of cases. The SMRs for the moderate to heavy exposure group were notably higher than those for the nil to light exposure group for the respiratory system (147 *v* 90) and skin and subcutaneous tissue (192 *v* 44).

Table 9 shows the age and pay status adjusted prevalence rates of the heart disease risk factors for the Enterline cohort. Smoking information was available for 90% of the two ECH groups and 81% of the comparison group. Blood pressure and body mass index data were available for 88% of the ECH groups and 82% of the comparison group. Cholesterol information was available for all of the ECH groups and 82% of the comparison group.

The moderate to heavy exposure group had a higher prevalence rate for smoking (25·6%) than the nil to light exposure group (17·6%) and the comparison group (21·9%). All exposure groups had similar rates for high blood pressure (35·6% for comparison, 37·0% for nil to light, and 31·8% for moderate to heavy) and obesity (49·3%, 50·4%, and 49·5%,

Table 8 Observed and expected morbidity and SMRs for workers by exposed levels 1981–8: Enterline cohort

	Level of exposure					
	Nil to light			*Moderate to heavy*		
Cause of morbidity (ICD9-CM codes)	*Obs*	*Exp*	*SMR*	*Obs*	*Exp*	*SMR*
All causes (000–999)	159	158·84	100	151	132·22	114
Infective and parasitic diseases (000–139)	5	4·25	118	3	3·12	96
All neoplasms (140–239)	6	8·61	70	8	6·48	123
Endocrine, nutritional, and metabolic diseases (240–279)	2	3·19	63	4	2·42	165
Mental disorders (290–319)	2	2·53	79	2	2·02	99
Nervous system (320–389)	13	8·61	151	8	7·34	109
Heart disease (390–414, 420–429)	17	18·26	93	13	14·99	87
Cerebrovascular disease (430–438)	1	0·65	154	0	0·47	—
Diseases of arteries (440–448)	3	1·01	297	1	1·09	92
Diseases of veins and other circulatory systems (451–459)	4	2·95	136	1	2·68	37
Respiratory system (460–519)	19	21·16	90	25	17·02	147
Digestive system (520–579)	18	16·69	108	19	14·05	135
Genitourinary system (580–629)	13	8·42	154	6	7·39	81
Skin and subcutaneous tissue (680–709)	2	4·54	44	7	3·64	192
Musculoskeletal system (710–739)	21	19·87	106	21	15·57	135
Symptoms and ill defined conditions (780–799)	9	15·23	59	7	16·76	42*
Injury and poisoning (800–999)	24	21·77	110	21	16·56	127
All other causes	0	1·12	—	1	0·66	152

*p < 0·05.

Table 9 Age and pay status adjusted prevalence rates for selected cardiovascular disease risk factors: Enterline cohort*

Risk factors	Level of exposure: Internal comparison	Nil to light	Moderate to heavy
Smoking	21·9	17·6	25·6
High blood pressure	35·6	37·0	31·8
Hypercholesterolaemia	66·9	66·8	49·9
Obesity	49·3	50·4	49·5

*Per 100 workers. Adjusted to the internal comparison population using the direct standardisation method.

respectively). The comparison group and the nil to light exposure group had nearly identical rates (66·9% and 66·8%) for hypercholesterolaemia which were higher than that for the moderate to heavy exposure group (49·9%).

Discussion

Unlike the mortality study results reported by Enterline, the morbidity experience of these cohorts working at the same plants does not suggest any exposure related effect on heart disease. Heart disease risk factors and morbidity in the groups studied showed no association to exposure level or to work in an ECH area. Subcohorts of those who were potentially exposed to both ECH and allyl chloride in the Shell cohort were also examined. The SMR for workers who had probable potential exposure to allyl chloride and higher exposure to ECH (SMR = 92) was exactly the same as their counterparts not exposed to allyl chloride. The one statistically significant association found in the Shell cohort was between exposure to ECH and morbidity due to skin and subcutaneous tissue conditions.

Causes of morbidity due to conditions affecting the skin were reviewed by examining the original morbidity reports for each case in the two ECH exposure groups for both the Shell and Enterline cohorts. Based on this review, it is difficult to attribute any major portion of the excess of skin conditions seen in the light to moderate group to exposures to ECH. Because ECH is severely irritating, and has been reported to be a skin sensitiser,[8] the expectation was that a preponderance of cases of irritative or allergic dermatitis would be found in the more exposed group. A slight increase was seen but not enough to account for the differences in overall skin conditions. In the Shell cohort only two cases of contact dermatitis and two of poison ivy occurred in the light to moderate exposure group compared with one case of each in the nil exposure group. Instead, ingrown toenails and pilonidal or sebaceous cysts contributed most to the higher frequencies of skin conditions seen in the more exposed group. The most common skin condition reported for both groups was superficial infection of an extremity (usually finger or toe) due to physical trauma. There were seven such cases in the light to moderate group and six in the nil group. Such a distribution of skin conditions suggests that factors unrelated to exposure to ECH such as the physical demands of a particular job, amount of time outside—for example, exposure to poison ivy—and underlying medical conditions may be of greater importance than exposure to ECH. In the Enterline cohort fewer skin conditions were reported. The nil to light exposure group experienced only two cases—a sebaceous cyst and a case of actinic keratoses. The moderate to heavy exposure group had three infections of hands and feet, one contact dermatitis (due to soap allergy), one case of shingles (herpes zoster), and two cysts (one abdominal, one on finger). Again, no particular pattern emerges that appears to be related to exposure.

The higher morbidity due to respiratory disease seen in the more highly exposed Enterline group is consistent with the higher rate of smoking seen in this group compared with the lower exposure group. Although a similar pattern of smoking is also seen in the Shell cohort, the lack of an increased respiratory morbidity rate in the higher exposed group may be due to the much younger age of the Shell cohort.

The absence of any consistent or statistically significant (except skin conditions) findings between the morbidity results of the two cohorts studied either with the Shell Deer Park and Norco populations as a whole or by exposure to ECH level provides rather strong evidence against exposure related effects on morbidity. Similarly, no consistent differences were found in cardiovascular disease risk factors studied. Of interest, too, is the absence of morbidity cases of leukaemia or lung cancer in the two cohorts studied. The original Enterline *et al* report found evidence for a possible excess of exposure related lung cancer as well as an excess of leukaemia (Shell to Environmental Protection Agency, 1981). The excess of lung cancer has declined with subsequent follow up but the excess of leukaemia (based on three cases of different cell types) has persisted. Shell plans to continue to follow up this cohort.

There does not appear to be sufficient evidence yet for any adverse health effect as reflected in morbidity events related to exposures to ECH at levels experienced by Shell employees currently or in the past. The two cohorts studied had little overlap, primarily due to a pronounced age difference between the two groups. The Enterline cohort represents a group hired before 1965 whereas the Shell cohort was for the most part hired after 1970. There may be exposure classification differences between the two cohorts, since the Shell cohort classification was based on more recent actual industrial hygiene sampling results whereas the Enterline exposures were assigned based on employee interviews regarding work practices and the judgment of plant industrial hygienists. For the 62 workers included in both Shell and Enterline cohorts, however, the difference in exposure classification was not statistically significant ($p = 0{\cdot}86$). The Enterline cohort is a "survivor" cohort of individuals who were still working at Shell during at least part of the period 1981–8. Although no age or exposure category differences were seen in those studied in the Enterline cohort compared with those not studied, it is possible that morbidity, and in particular heart disease morbidity, may have differed between the two groups. The fact that there was no selective loss from the higher exposure group would argue against exposure related differences, however.

Although heart disease morbidity does not always precede a death from heart disease, one would expect to see heart disease morbidity patterns similar to heart disease mortality patterns in the same population.[2] Just as the original Enterline cohort had no excess of heart disease mortality, the portion of the cohort for whom morbidity was available had no excess of heart disease morbidity. Unlike the mortality pattern, the heart disease morbidity experience for both exposure groups was essentially the same. Similarly, for a younger cohort (the Shell cohort) exposed to ECH for a shorter time, no association between exposure and heart disease morbidity was seen. This is important, since Enterline has hypothesised a short latency for an exposure related heart disease effect.[1]

Both morbidity cohorts studied did not include all older retired employees, although individuals who retired during the study period were included. This does not explain the differences seen between the Enterline *et al* mortality study and this morbidity study. The average age for the deaths from heart disease in that study was estimated to be about 57 and more than 80% died before the retirement age of 65. Of the five deaths in the Shell cohort none was due to heart disease.

We thank N D Siegel for typing the manuscript and C M Dowd for help in data analysis and preparing the manuscript.

1 Enterline EP, Henderson V, Marsh G. Mortality of workers potentially exposed to epichlorohydrin. *Br J Ind Med* 1990;**47**:69–76.

2 Gittelsohn A, Senning J. Studies on the reliability of vital and health records. I. Comparison of cause of death and hospital record diagnoses. *Am J Public Health* 1979;**69**:680–9.

3 Austin WB, Phillips CF. Development and implementation of a health surveillance system. *Am Ind Hyg Assoc J* 1983;**44**: 638–42.

4 Joyner RE, Pack PH. The Shell Oil Company's computerized health surveillance system. *J Occup Med* 1982;**24**:812–4.

5 National Institutes of Health consensus development panel on the health implications of obesity. Health implications of obesity: National Institutes of Health consensus development statement. *Ann Intern Med* 1985;**103**:1073–7.

6 *International classifications of diseases*. 9th rev. *Clinical modification*. Ann Arbor, Michigan: Commission on Professional and Hospital Activities, 1978.

7 Bailar JC, Ederer F. Significance factors for the ratio of a Poisson variable to its expectation. *Biometrics* 1964;**20**:639–43.

8 Beck MH, King CM. Allergic contact dermatitis to epichlorohydrin in a solvent cement. *Contact Dermatitis* 1983;**9**:315.

Accepted 6 November 1989