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Acute and Chronic Liver Toxicity Resulting From Exposure to Chlorinated Naphthalenes at a Cable Manufacturing Plant During World War II

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Historical records were used to reconstruct an outbreak of chloracne and acute liver toxicity due to chlorinated naphthalene exposure at a New York State plant which manufactured "Navy cables" during World War II. A cohort mortality study was conducted of the population (n = 9,028) employed at the plant from 1940 to 1944. Vital status was followed through December 31, 1985. The study found an excess of deaths from cirrhosis of the liver [observed (OBS) = 150; standardized mortality ratio (SMR) = 1.84; 95% confidence interval (CI) = 1.56–2.16]; cirrhosis deaths were elevated to a similar degree in the 460 individuals who had chloracne (OBS = 8; SMR = 1.51; CI = 0.65–2.98). The SMR for "non-alcoholic cirrhosis" (OBS = 83; SMR = 1.67; CI = 1.33–2.07) was similar to the SMR for "alcoholic cirrhosis" (OBS = 59; SMR = 1.96; CI = 1.49–2.53). There was no evidence for increased alcoholism in the overall cohort based on mortality from alcohol-related causes of death other than cirrhosis (SMR for esophageal cancer = 1.01 and for deaths from alcoholism = 0.99). We conclude that the excess mortality from cirrhosis of the liver observed in this cohort is due to the chronic effect of chlorinated naphthalene exposure. © *1996 Wiley-Liss, Inc.**

KEY WORDS: chlorinated naphthalenes, chloracne, cirrhosis, cohort mortality study, epidemiology, occupational health

INTRODUCTION

The plant under study used chlorinated naphthalenes (sold under the trade name "Halowax") to insulate electrical cable from 1939 to 1944. Chlorinated naphthalenes consist of two fused aromatic rings with from one to eight of their hydrogens substituted with chlorine. Commercial products often contain a mixture of chlorinated naphthalenes with varying degrees and positions of chlorination [EPA, 1983]. Historically, chlorinated naphthalenes have been used in cable insulation, wood preservatives, capacitors, engine oils, and cutting and grinding fluids [EPA, 1983]. Domestic manufacture of chlorinated naphthalenes declined from over 7 million pounds in 1956 to 700,000 pounds in 1978, and ceased in 1980 [EPA, 1983]. According to the National Occupational Exposure Survey (NOES) conducted in the early 1980s, there are no U.S. workers occupationally exposed to chlorinated naphthalenes.

Chlorinated naphthalenes were the first agents to cause widespread outbreaks of chloracne in the United States and European countries [Von Wedel et al., 1943]; an outbreak of chloracne associated with chlorinated naphthalene exposure was reported as recently as 1972 [Kleinfeld et al., 1972]. During the 1930s and 1940s, there were also a number of reports in the medical literature concerning deaths from "acute yellow atrophy of the liver" among workers exposed to chlorinated naphthalenes [Von Wedel et al., 1943].

Early in the 1940s, numerous cases of chloracne and

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fatal cases of "acute yellow atrophy of the liver" were recognized at the plant under study and reported in the local press and the medical literature [Strauss, 1944]. Our interest in studying the mortality experience of this group of workers stemmed primarily from the toxicologic similarity of chlorinated naphthalenes with chlorinated hydrocarbons of current public health concern—chlorinated dibenzodioxins and polychlorinated biphenyls (PCBs). These compounds are all chlorinated hydrocarbons which have been associated in varying degrees with chloracne and liver injury. Based on animal and human data on the carcinogenicity of chlorinated dibenzodioxins [Kociba et al., 1979; Huff et al., 1991; Halperin et al., 1982; Fingerhut et al., 1984, 1991] and PCBs [Kimbrough et al., 1975; Brown and Jones, 1981; Ward, 1985; Norback and Weltman, 1985; Brown, 1987] as well as the acute hepatotoxicity of chlorinated naphthalenes themselves, we hypothesized a priori that chlorinated naphthalene exposure might be associated with an increased risk of soft tissue sarcoma, lymphoma, malignant neoplasm (MN) of the liver, and cirrhosis of the liver. The cancer mortality experience of the cohort has been reported previously [Ward et al., 1994]. This report documents the chloracne outbreak and deaths from acute yellow atrophy of the liver that occurred in this cohort of workers exposed to chlorinated naphthalenes during the 1940s and presents the mortality study results for causes other than MN.

BACKGROUND

The plant under study is located in Westchester County, NY. The production areas and equipment used in the impregnation of cables with chlorinated naphthalenes no longer existed in the 1980s when the cohort was identified by the National Institute for Occupational Safety and Health (NIOSH). Although information about the process was very limited, historical records document that chlorinated naphthalenes were melted in open vats through which wires coated with asbestos were drawn to saturate them. The best available description of the process is provided in a medical report contained in a compensation case record, which states:

> "The patient states that he worked as an operator on the asbestos machine which put asbestos on either bare wire or insulated cables. The asbestos covered cable would go through a tank of Halowax to impregnate it. The patient was working on the whole machine. He would take a pail of Halowax that had been melted in another tank and put it in the dipping tank that was kept heated and would let off fumes from the hot Halowax. The cable also went through a pair of revolving shoes for polishing. When the machine stopped, the Halowax would get cold and the patient would have to apply a torch to heat it again. The fumes from this came off in a greyish mist."

In the early 1940s, numerous cases of chloracne were recognized and documented in worker's compensation claims. In January 1943, a series of industrial hygiene studies was initiated in an attempt to contain the outbreak. Industrial hygiene reports contain measurements of air concentrations of chloride ion at approximately 20–30 sampling locations and suggest that chlorinated naphthalene exposure was widespread throughout the plant.

The industrial hygiene reports also mention the presence of Aroclor (a PCB) and carbon tetrachloride as possible explanations for high chloride ion concentrations in specific areas of the plant, but it is difficult to determine how extensive worker exposure to these compounds was. According to the industrial hygiene records, the use of chlorinated naphthalenes was phased out in the summer of 1944.

As of 1982, when the cohort was identified, the plant continued to manufacture cables at its original location. Since the majority of the work force employed during World War II did not continue employment after the war ended (only 3,254 persons remained employed after January 1, 1945), we did not evaluate processes and exposures at the plant after January 1, 1945.

MATERIALS AND METHODS

In 1982 and 1983, NIOSH investigators reviewed and microfilmed medical and personnel records necessary to document the outbreak of chloracne, to identify fatal and non-fatal cases of liver disease, and to obtain sufficient demographic and identifying information for vital status follow-up. Both personnel and payroll records were used to identify any individuals who worked at the plant from January 1, 1940, through December 31, 1944, and to code information necessary for vital status follow-up. These dates were selected because they corresponded to the years when plant records indicated that chlorinated naphthalenes had been used, and the years in which chloracne cases had occurred. The work history information was limited to plant and beginning and ending dates of employment because personnel records did not contain detailed work history information. Missing race, sex, and date of birth information was obtained through the Social Security Administration (SSA).

Individuals with chloracne and liver disease were identified by review of medical records which had been retained by the company. Medical records were located for only a third (3,700 of 9,028) of individuals employed during the time period of the study, raising the possibility that some records had been lost. However, attempts to identify an ancillary set of records to confirm the completeness of chloracne and liver disease ascertainment (such as New York

TABLE I. Creation of Rates for Cirrhosis of the Liver With and Without Mention of Alcohol or Alcoholism

Liver disease category	ICD 6 and 7 (1950–1967)	ICD 8 (1968–1978)	ICD 9 (1979–1989)
Liver disease with mention of alcohol or alcoholism	581.1—Cirrhosis with mention of alcoholism	571.0—Alcoholic cirrhosis	571.0—Alcoholic fatty liver 571.1—Acute alcoholic hepatitis 571.2—Alcoholic cirrhosis of liver 571.3—Alcoholic liver damage—unspecified
Liver disease without mention of alcohol or alcoholism	581.0—Cirrhosis without mention of alcoholism	571.8, 571.9—"Other specified" and unspecified cirrhosis of liver without mention of alcohol or alcoholism	571.5—Cirrhosis without mention of alcohol 571.6—Biliary cirrhosis 571.8—Other chronic, non-alcoholic liver disease 571.9—Unspecified chronic liver disease without mention of alcohol

State compensation or insurance records) were unsuccessful. Medical records with mention of occupational dermatitis or liver disease were microfilmed. These consisted for the most part of New York State Worker's Compensation Claims. In order to be considered to be a case of probable chloracne, the medical record either had to state that the person had chloracne or to include one of the following: 1) "fumes from Halowax caused skin to break out"; 2) "waxy compound caused skin to break out"; and 3) no notation of Halowax or chloracne but description of comedones, pustules, and cystic lesions. Chloracne cases were identified independently by two sets of coders who reviewed the 740 medical records of dermatitis cases. Discrepancies between the two sets of coders were resolved by one of us (A.S.).

The vital status of all workers in the study was determined as of December 31, 1985. Follow-up was extended to December 31, 1989, for the chloracne subcohort to increase the statistical power of the analysis for this small subgroup. Sources used to determine vital status were the SSA, the Internal Revenue Service, the post office serving the last known address, the Veteran's Administration, the Health Care Financing Administration, and the National Death Index. Death certificates were obtained from state vital statistics offices and were coded according to the International Classification of Diseases (ICD) revision in effect at the time of death. The mortality experience of the cohort was analyzed using a modified life-table system (LTAS) developed by NIOSH [Waxweiler et al., 1983; Steenland et al., 1990], using both U.S. and Westchester county rates. We present 95% confidence intervals (CIs) and two-sided p values throughout the paper. CIs and p values were calculated using Fisher's exact method (if either the observed or expected was less than 10) or an approximate method (if observed and expected frequencies were 10 or more) [Rothman and Boice, 1979]

The NIOSH life table [Waxweiler et al., 1983; Steenland et al., 1990] includes deaths from "cirrhosis with mention of alcohol" and "cirrhosis without mention of alcohol" in a single category of death. In order to explore the excess risk of death from cirrhosis in more detail, we created separate comparison rate files for deaths from alcoholic and non-alcoholic cirrhosis for the time period 1950 through 1990 (computerized death information for the detailed causes is not available prior to 1950). The ICD categories grouped into alcoholic and non-alcoholic cirrhosis are shown in Table I.

RESULTS

There was a total of 9,028 workers included in the study, among them 460 individuals who met our criteria of having been diagnosed with chloracne. Table II provides and contrasts the demographic characteristics and work history of the chloracne subcohort and the total cohort. The major discrepancy between the chloracne subcohort and the cohort as a whole was the relatively small proportion of females in the chloracne subcohort. The chloracne subcohort also appeared to have longer duration of employment than the cohort as a whole. Table III provides the vital status of the chloracne subcohort and the total cohort. The higher percentage of deceased individuals in the chloracne subcohort is related to their longer duration of follow-up.

Figure 1 shows the distribution of chloracne cases by date of initial diagnosis. The chloracne outbreak appears to have peaked during late 1942 to early 1943. Figure 2 shows the intervals from initial starting employment to date of diagnosis, which for most individuals was under 6 months. Some of the chloracne cases occurring in this cohort were severe, and a number of individuals were compensated for serious permanent facial disfigurement because of extensive scarring and pitting of their skin.

There were (eight) deaths from acute yellow atrophy of the liver identified from company records and/or death certificates. Table IV summarizes the characteristics of these

TABLE II. Demographic Characteristics and Work History of Individuals With Chloracne and Total Cohort at a Cable Manufacturing Plant

Characteristic	Chloracne subcohort	Total cohort
Age at starting employment (years)		
<25	176 (38.3%)	2852 (31.6%)
≥25–<35	170 (37.0%)	2806 (31.1%)
≥35	114 (24.8%)	3370 (37.3%)
Gender		
Female	29 (6.3%)	3042 (33.7%)
Male	431 (93.7%)	5986 (66.3%)
Race		
White	407 (88.5%)	7688 (85.1%)
Non-white	53 (11.5%)	1340 (14.8%)
Year of first employment		
<1940	33 (7.2%)	564 (6.3%)
1940	24 (5.2%)	287 (3.2%)
1941	113 (24.6%)	969 (10.7%)
1942	204 (44.3%)	2449 (27.1%)
1943	84 (18.3%)	3108 (34.4%)
1944	2 (0.4%)	1651 (18.3%)
Duration of employment during the time period chlorinated naphthalenes were used (1940–1944)		
<6 months	51 (11.1%)	3345 (37.1)
≥6 months–<2 years	162 (35.2%)	2668 (29.6)
≥2 years	247 (53.7%)	2978 (33.0)
Unknown		37 0.4

TABLE III. Results of Vital Status Ascertainment of Individuals With Chloracne and Total Cohort at a Cable Manufacturing Plant

Vital status	Chloracne subcohort (through December 31, 1989)	Total cohort (through December 31, 1985)
Alive	166 (36.1%)	3,669 (40.6%)
Unknown	20 (4.3%)	824 (9.1%)
Deceased	274 (59.6%)	4,535 (50.3%)

cases. Approximately ten other individuals were noted in company records to have had abnormal liver function tests and/or symptoms of liver dysfunction that were thought to be associated with chlorinated naphthalene exposure.

Table V shows the mortality experience of the chloracne subcohort and the total cohort for causes other than MN. Aside from the excess in mortality from MN of the esophagus and "benign and unspecified neoplasms," which were previously reported [Ward et al., 1994], there were no substantial differences in the mortality patterns of the chloracne subcohort and the total cohort. The only striking excess in mortality is for cirrhosis of the liver in the overall cohort [observed (OBS) = 150; standardized mortality ratio (SMR) = 1.84; CI = 1.56–2.16], which is not more pronounced among individuals who developed chloracne (OBS = 8; SMR = 1.51; CI = 0.65–2.98). The SMR for cirrhosis of the liver was significantly elevated in white males (OBS = 118; SMR = 2.06; CI = 1.70–2.46) and was also elevated in non-white males (OBS = 13; SMR = 1.79; CI = 0.95–3.06). Females did not demonstrate a substantial excess in this cause of death (white females: OBS = 15; SMR = 1.22; CI = 0.68–2.02; non-white females: OBS = 4; SMR = 0.89; CI = 0.24–2.26). The potential contribution of regional excesses for this cause of death was evaluated by comparing SMRs for cirrhosis of the liver based on Westchester County and U.S. rates for 1960–1985. The SMR based on Westchester County rates was 1.59 (CI = 1.31–1.90) and the SMR based on U.S. rates was 1.97 (CI = 1.63–2.35). Thus, the SMR based on county rates was lower than the SMR based on U.S. rates, but still substantial.

A major non-occupational risk factor for cirrhosis of the liver is alcohol consumption [Klatsky and Armstrong, 1992]. There was no evidence for increased alcoholism in this cohort based on mortality from other alcohol-related causes of death (SMR for esophageal cancer = 1.01 and for deaths from alcoholism = 0.99). To further explore the excess risk of cirrhosis in this cohort, we calculated SMRs separately for "cirrhosis of the liver, with mention of alcohol or alcoholism" and "cirrhosis of the liver without mention of alcohol or alcoholism." Both categories of cirrhosis were significantly elevated; the "SMR for cirrhosis of the liver without mention of alcohol" (OBS = 83; SMR = 1.67; CI = 1.33–2.07) was similar to the "SMR for alcoholic cirrhosis" (OBS = 59; SMR = 1.96; CI = 1.49–2.53). For alcoholic cirrhosis, there was a steady increase in the SMRs with increasing latency, and a bimodal relationship with duration of exposure (highest SMRs in the <6 months and ≥2 years exposure categories (Table VI), while deaths from non-alcoholic cirrhosis (Table VII) were increased in earlier latency intervals and had significantly elevated SMRs in the 6 months–1 year and ≥2 years duration of exposure categories.

Among the other non-malignant causes of death, deaths from ischemic heart disease were significantly elevated with an SMR of 1.07. This increased risk was not related to a regional increase in heart disease (SMR based on Westchester County rates for 1960–1985 = 1.18; CI = 1.10–1.25; SMR based on U.S. rates for 1960–1985 = 1.14; CI = 1.07–1.21).

DISCUSSION

The major finding of this study was an excess in deaths from cirrhosis of the liver, which is likely to be due to the chronic effects of exposure to chlorinated naphthalenes. The

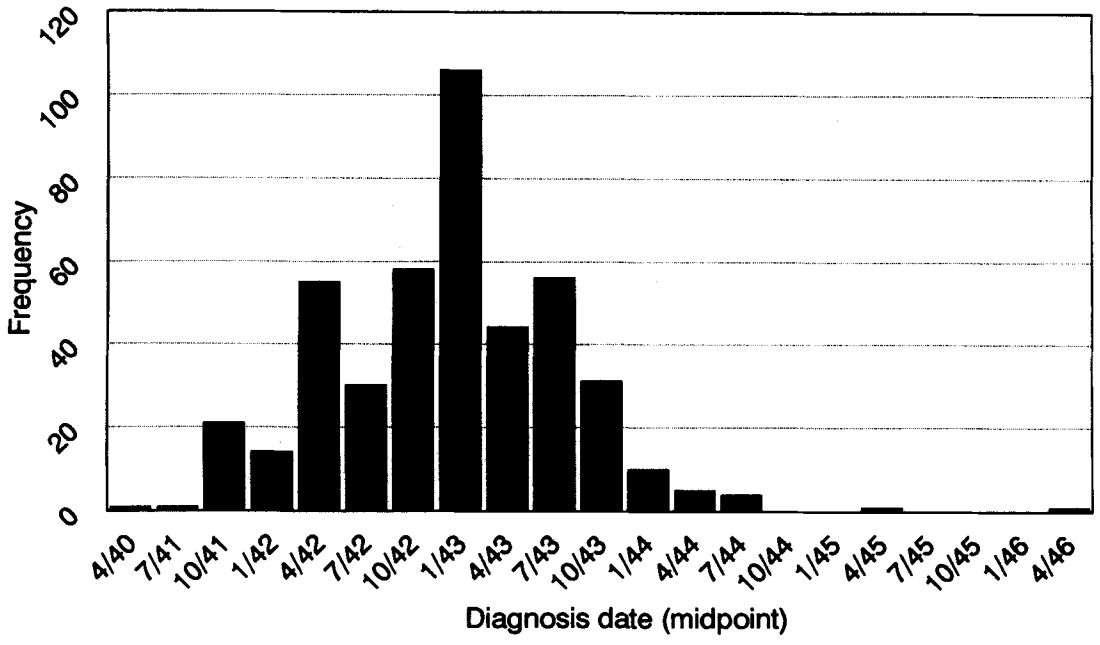

FIGURE 1. Study of workers in a cable manufacturing plant: distribution of chloracne diagnosis date among 460 workers with chloracne. Five cases had unknown date of diagnosis.

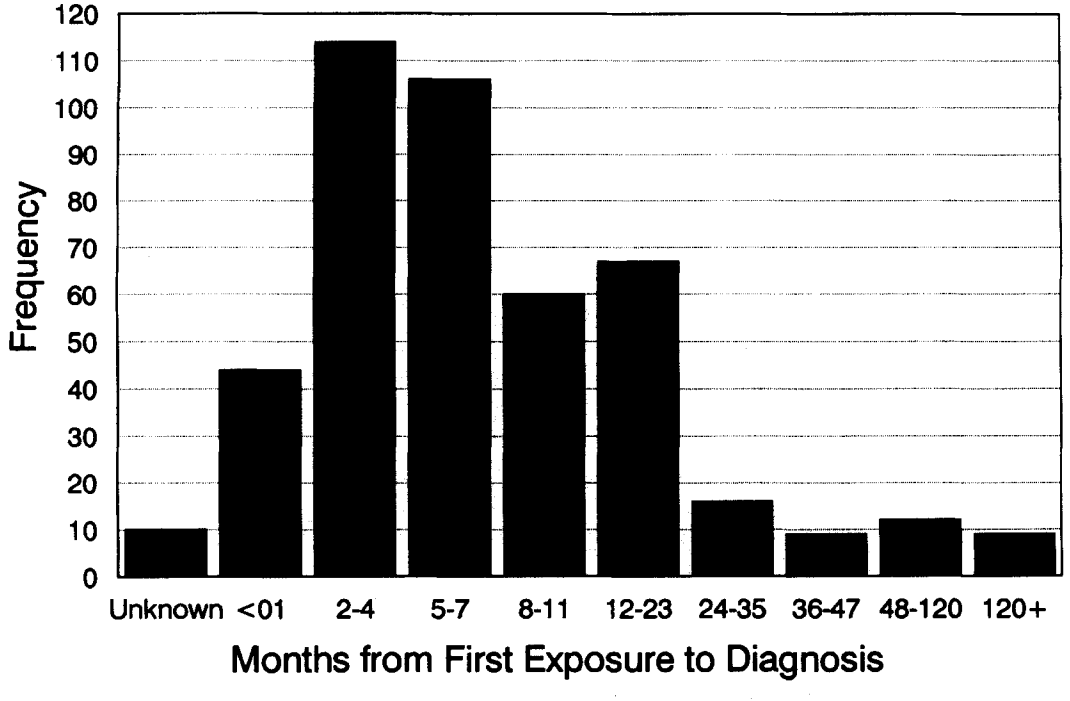

FIGURE 2. Study of workers in a cable manufacturing plant: time in months from date first exposed to diagnosis date.

fact that the increase occurs in both cirrhosis without and cirrhosis with mention of alcohol is consistent with the toxicologic literature which demonstrates that pretreatment with chlorinated naphthalenes exacerbates the effects of ethyl alcohol on the liver. Some workers at the study plant may have been exposed to carbon tetrachloride and PCBs. We believe, however, that the primary cause of chloracne, acute liver disease, and increased mortality from cirrhosis of the liver is chlorinated naphthalenes, both because exposure to Halowax was widespread in the plant and the toxicity

TABLE IV. Deaths From Acute Yellow Atrophy of the Liver Among Workers at a Cable Manufacturing Plant

Case No.	Date of death	Age at death (years)	Duration of employment (months)	Chloracne	Diagnosis on death certificate and ICD 5 code[a]
1	12/28/42	22	17	Unknown	Death certificate not obtained; company records state "acute yellow atrophy of the liver"
2	9/13/42	36	3	Unknown	Acute yellow atrophy of the liver, coded "125a"
3	6/9/43	54	3	Yes	Subacute yellow atrophy of the liver, coded "125a"
4	5/26/41	43	17	Unknown	Acute toxic hepatitis, coded "125b"
5	3/25/45	55	12	Yes	Chronic perihepatitis (toxic chemical), coded "200a"
6	1/11/43	40	8	Unknown	Acute yellow atrophy of the liver, coded "125a"
7	7/25/42	36	8	Unknown	Subacute hepatitis—acute yellow atrophy of the liver, coded "125a"
8	3/25/43	50	7	Yes	Cirrhosis of the liver—acute yellow atrophy, coded "124b"

[a]ICD 5 codes: 124b = cirrhosis of the liver without alcoholism; 125a = acute yellow atrophy of the liver (non-puerperal); 200a = ill-defined and unknown causes.

observed was consistent with the experimental and medical literature on chlorinated naphthalenes. It is possible that workers in areas of the plant where both chlorinated naphthalenes and other chlorinated hydrocarbons were present may have experienced synergistic effects, since pretreatment with chlorinated naphthalenes has been shown to potentiate the effects of carbon tetrachloride in producing liver toxicity. A limitation of this study is that while there are industrial hygiene data available, there are significant gaps and omissions in the data which make it difficult to interpret in a quantitative way.

Female workers had a lower rate of chloracne, no deaths from acute yellow atrophy of the liver, and only a slight increase in cirrhosis of the liver. The most likely explanation for this difference is that female workers were assigned to jobs with lower exposure to chlorinated naphthalenes; however, we do not have access to the detailed work history data required to investigate this further. The chloracne subcohort had a lower SMR for cirrhosis than the total cohort. In interpreting this finding, it is important to note that chloracne cannot be considered a simple marker of higher exposure. While both chloracne and death from acute yellow atrophy are recognized as acute effects of chlorinated naphthalene exposure, only three of the eight individuals who died of acute yellow atrophy are known to have had chloracne. Factors influencing the development of chloracne vs. liver toxicity may include individual susceptibility, concurrent or subsequent exposure to other hepatotoxins, and route of exposure.

There is no obvious exposure associated with the increase in ischemic heart disease, which is small in magnitude but statistically significant. One would not expect a cohort defined as having worked during a 5 year period over 40 years ago to continue to exhibit a "healthy worker" effect, because the effects of initial favorable cardiovascular risk factors involved in selection into the work force could have been attenuated over such a long period [Steenland and Stayner, 1991].

It has been hypothesized that workers hired into U.S. industries during World War II might be less healthy than the U.S. population in general because they were "unfit" for military service. Other authors who have examined the mortality of World War II industrial cohorts have not found excesses in deaths from cirrhosis of the liver [Bond et al., 1989; Steenland, 1993; Wen et al., 1986]. Two of these studies found that death rates from major causes did not differ between cohorts hired prior to World War II, during World War II, or after World War II [Bond et al., 1989; Steenland, 1993]. The third study found excess mortality due to deaths from external causes (homicide, accidents, and motor vehicle accidents) and alcoholism [Wen et al., 1986].

Relatively little is known about occupational causes of cirrhosis of the liver, which is the ninth leading cause of death in the United States [Anon., 1993]. One prior mortality study has found an excess of deaths from cirrhosis of the liver among workers exposed to tetrachloroethylene [Teta and Ott, 1988]. A number of common solvents, such as trichloroethylene, are potentially hepatotoxic [Hall et al., 1991]. A recent study has found that rats exposed to carbon tetrachloride vapor at a concentration that by itself caused only fatty change with minimal liver damage caused extensive hepatic fibrosis and cirrhosis when given in association with chronic alcohol feeding [Hall et al., 1991]. The authors conclude that their study raises the possibility that some chronic liver injury in humans may be due to alcohol potentiation of other hepatotoxins present in the environment at subtoxic levels. The finding of an increase in both alco-

TABLE V. *Mortality From Causes Other Than MN of Individuals With Chloracne and Total Cohort at a Cable Manufacturing Plant*

Cause	ICD code (9th revision)	Chloracne subcohort (through December 31, 1989)			Total cohort (through December 31, 1985)		
		OBS	SMR[a]	95% CI	OBS	SMR	95% CI
Tuberculosis	010–018	1	0.31	0.01–1.70	31	0.51	0.35–0.73
Diabetes mellitus	*250*	5	1.25	0.40–2.91	68	0.86	0.66–1.08
Blood and blood-forming diseases	281–289	0	0.00	0.00–0.00	11	0.87	0.43–1.55
Alcoholism and mental disorders	290–319	1	0.62	0.02–3.43	16	0.73	0.42–1.18
Alcoholism	303	1	1.14	0.03–6.31	12	0.99	0.51–1.72
Nervous system diseases	320–337, 340–389	1	0.37	0.01–2.06	19	0.47	0.28–0.74
Diseases of the heart	390–398, 402–404, 410–414, 420–429	114	1.07	0.88–1.29	1,858	1.02	0.98–1.07
Rheumatic heart disease	390–398	3	1.28	0.26–3.74	52	1.13	0.84–1.48
Ischemic heart disease	410–414	97	1.13	0.92–1.38	1,575	1.07	1.02–1.13
Chronic disease of endocardium	424	0	0.00	0.00–0.00	13	0.90	0.48–1.53
Other myocardial degeneration	429.0, 429.1	0	0.00	0.00–0.00	29	0.68	0.45–0.97
Hypertension with heart disease	402, 404	4	0.94	0.26–2.40	92	0.98	0.79–1.20
Other diseases	420–423, 425–428	10	0.85	0.41–1.56	97	0.63	0.51–0.77
Diseases of the circulatory system	401, 403, 405, 415–417, 430–438, 440–459	18	0.67	0.39–1.05	366	0.68	0.61–0.76
Hypertension without heart disease	401, 403, 405	1	0.88	0.02–4.89	20	0.91	0.56–1.41
Cerebrovascular disease	430–438	12	0.64	0.33–1.12	233	0.60	0.53–0.68
Diseases of arteries, veins, and pulmonary circulation	415–417, 440–459	5	0.70	0.22–1.62	113	0.89	0.73–1.07
Respiratory system diseases	460–466, 470–478, 480–487, 490–519	20	1.09	0.66–1.68	271	0.98	0.87–1.10
Influenza	487	0	0.00	0.00–0.00	5	0.60	0.20–1.41
Pneumonia	480–486	0	0.00	0.00–0.00	105	0.91	0.75–1.11
Other acute infections	460–486	0	0.00	0.00–0.00	2	1.01	0.12–3.63
Chronic and unspecified bronchitis	490–491	7	1.01	0.40–2.08	17	1.44	0.84–2.31
Emphysema	492	3	0.97	0.20–2.82	52	1.07	0.79–1.40
Asthma	493	0	0.00	0.00–0.00	9	0.81	0.37–1.54
Pneumoconiosis and other respiratory disease	470–478, 490–491, 494–519	9	1.36	0.62–2.59	81	1.02	0.81–1.27
Digestive system diseases	520–537, 540–543, 550–553, 555–558, 560, 562–579	18	1.52	0.90–2.41	276	1.40	1.23–1.57
Diseases of stomach and duodenum	531–537	4	2.15	0.59–5.51	38	1.16	0.82–1.59
Hernia and intestinal obstruction	550–553, 560	1	1.25	0.03–6.93	18	1.06	0.63–1.67
Cirrhosis of the liver	571	8	1.51	0.65–2.98	150	1.84	1.56–2.16
Other diseases of digestive system	520–579	5	1.29	0.42–3.02	70	1.05	0.82–1.33
Diseases of genitourinary system	580–608, 610, 611, 614–629	6	1.31	0.48–2.84	81	0.96	0.76–1.20
Acute glomerulonephritis, nephrotic syndrome, and acute renal failure	580, 581, 584	1	2.54	0.06–14.1	6	0.98	0.36–2.14
							0.66–1.33
Chronic and unspecified nephritis, renal failure, and other renal sclerosis	582, 583, 585–587	2	0.96	0.11–3.45	34	0.95	0.56–1.73
Infection of kidney	590	1	1.72	0.04–9.60	14	1.03	0.08–1.15
Hyperplasia of prostate	600	1	3.21	0.08–17.8	3	0.39	0.38–5.46
Other diseases of male genital organs	*601–608*	0	0.00	0.00–0.00	3	1.87	0.61–1.73
Other genitourinary system diseases	588, 589, 591, 593, 595–599	0	0.00	0.00–0.00	16	1.07	0.32–2.29
Diseases of skin and subcutaneous tissue	680–686, 690–709	1	3.44	0.09–19.1	5	0.98	0.32–2.29
Musculoskeletal diseases	710–739	1	2.12	0.05–11.8	5	0.54	0.17–1.27
Symptoms and ill-defined conditions	780–796, 798, 799	3	0.89	0.18–2.60	28	0.51	0.34–0.74
Accidents	E800–848 E850–888, E890–949	8	0.60	0.26–1.17	128	0.65	0.54–0.77
Suicide and homicide	E950–978	2	0.34	0.04–1.22	45	0.53	0.39–0.71
All other causes	Residual ICD categories	1	4.23	0.00–1.32	62	0.86	0.66–1.11
Certificates not obtained		4			203		
All cancers	140–208	66	1.17	0.90–1.49	1,052	1.14	1.07–1.21
All deaths		274	1.03	0.91–1.16	4,535	1.01	0.98–1.04

TABLE VI. SMRs for Mortality From Cirrhosis of the Liver, With Mention of Alcohol or Alcoholism by Duration of Employment and Time Since First Employment Among Workers at a Cable Manufacturing Plant

	Duration of employment									
	<6 months		6 months–1 year		>1–2 years		≥2 years		Total	
Time since first employment (years)	OBS	SMR	OBS	SMR	OBS	SMR	OBS	SMR	OBS	SMR
<10	1	1.19	0	0.00	1	1.93	0	0.00	2	1.03
10–<20	4	1.45	0	0.00	0	0.00	6	2.61	10	1.31
20–<30	11	2.98[b]	0	0.00	3	1.49	3	1.06	17	1.74[a]
30–<40	8	2.52[a]	3	2.53	4	2.26	7	2.57	22	2.48[b]
≥40	2	3.78	2	8.14	0	0.00	4	5.34[b]	8	4.25[b]
Total	26	2.37[b]	5	1.31	8	1.26	20	2.24[b]	59	1.96[b]

[a]$p < 0.05$.
[b]$p < 0.01$.

TABLE VII. SMRs for Mortality From Cirrhosis of the Liver, Without Mention of Alcohol or Alcoholism by Duration of Employment and Time Since First Employment Among Workers at a Cable Manufacturing Plant

	Duration of employment									
	<6 months		6 months–1 year		>1–2 years		≥2 years		Total	
Time since first employment (years)	OBS	SMR	OBS	SMR	OBS	SMR	OBS	SMR	OBS	SMR
<10	0	0.00	2	4.69	2	2.35	1	2.00	5	1.62
10–<20	5	1.10	4	2.65	2	0.68	7	1.83[a]	18	1.41[b]
20–<30	5	0.82	8	3.86[b]	3	0.84	10	2.01	26	1.55[a]
30–<40	12	2.49[b]	3	1.67	6	2.15	8	1.84	29	2.11[b]
≥40	1	1.10	0	0.00	0	0.00	4	3.14	5	1.56
Total	23	1.30	17	2.74[b]	13	1.21	30	2.01[b]	83	1.67[b]

[a]$p < 0.05$.
[b]$p < 0.01$.

holic and non-alcoholic cirrhosis in this cohort is consistent with this hypothesis.

In summary, a cohort of workers with documented cases of acute toxicity related to chlorinated naphthalene exposure was found to have elevated mortality due to cirrhosis of the liver. Although exposure to chlorinated naphthalenes ceased in 1945, the elevated mortality from cirrhosis persisted through the 1980s. The elevated cirrhosis mortality is likely to be due to subacute toxicity from chlorinated naphthalene exposure, possibly in association with other chlorinated hydrocarbon solvents.

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