Primary Liver Cancer Death and Occupation in Texas

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A death certificate case-control study of primary liver cancer and occupation was conducted to determine if the high risk of liver cancer in Mexican-Americans can be explained by farmworker exposures to pesticides. The association of liver cancer with the petroleum and chemical industry and with other potentially high-risk occupations was also examined. For the years 1969 to 1980, 1,742 deaths from primary liver cancer were identified for Texas males. Controls were randomly selected from other causes of deaths among males excluding all neoplasms, liver and gallbladder diseases, infectious hepatitis, and alcoholism, and were frequency matched to cases by age, race, ethnicity, and year of death. Risk for farmworkers based on age, race, and ethnicity-adjusted odds ratios (ORs) was not excessive (OR = 1.4, 95% confidence limits [C.L.] 0.8–2.2) but was larger than the risk for farmers (OR = 1.0, 95% C.L. 0.8–1.2). Excess risk in the petroleum and chemical manufacturing industries was confined to oil refinery workers (OR = 2.0, 95% C.L. 1.1–3.5). Other occupations with twofold risk or greater were plumbers and pipefitters (OR = 2.0, 95% C.L. 1.0–3.8), butchers and meat cutters (OR = 2.6, 95% C.L. 1.1–6.6), textile workers (OR = 3.1, 95% C.L. 1.2–7.8), cooks (OR = 2.2, 95% C.L. 1.1–4.5), and longshoremen (OR = 2.2, 95% C.L. 0.6–7.4).

Key words: farmworkers, oil refinery workers, meat cutters, textile workers, cooks, longshoremen

INTRODUCTION

Recently, we reported an increased risk for primary liver cancer in Texas Mexican-Americans [Suarez and Martin, 1987]. The prevalence of known risk factors for primary liver cancer, such as chronic hepatitis B infection, alcoholic cirrhosis, and aflatoxin and pesticide exposures among Mexican-Americans is unknown. However, death certificates can provide a basis for study of occupation as an etiologic factor in the observed excess risk in this ethnic group. Geographic analysis of primary liver cancer mortality shows the highest excesses in Texas counties along the Mexican border, primarily an agricultural region. Since the majority of farmworkers in Texas are Mexican-American, these observations suggest that the risk in Mexican-Americans may be partly explained by occupational exposures to pesticides. This hypothesis is strengthened by a case-control study of primary liver cancer in New Jersey, in which an excess risk was observed for farm laborers but not for farm

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owners [Stemhagen et al., 1983]. Farm laborers would more likely be exposed to agricultural pesticides than farm owners.

In 1975, Hoover and Fraumeni reported excess male liver cancer rates in 139 'chemical industry' counties, including four petrochemical industry counties along the Texas gulf coast. Yet, with the notable exception of hepatic angiosarcomas in vinyl chloride workers [Tabershaw and Gaffey, 1974], many cohort studies of petrochemical and oil refinery workers have not reported a significantly increased risk of liver cancer for these workers [Wen et al., 1983; Hanis et al., 1979,1982; Thomas et al., 1980,1982; Bond et al., 1985; Austin and Schnatter, 1983; Thériault and Goulet, 1979]. These studies are of limited use in assessing the relationship of occupations in the petrochemical industry to liver cancer because of the small number of cases and the inclusion of nonliver cancer cases. Liver cancers were usually defined as including both liver and biliary cancers or were not considered separately from digestive cancers.

We conducted a case-control study of primary liver cancer and occupation based on 12 years of Texas death certificates. We specifically wanted to examine if the risk of liver cancer in Mexican-Americans could be explained in part by farmworker exposures to pesticides. Additionally, because of the large series of liver cancer deaths available for study, we could examine the risk of liver cancer among occupations in the petroleum and chemical industry and other potentially high-risk occupations.

METHODS

Computerized death certificate records with underlying cause coded to primary cancer of the liver (International Classification of Disaster [ICD] code 155.0, 8th and 9th revisions) for Texas male residents of all races and ethnicity aged 20 years or older were obtained from the Texas Bureau of Vital Statistics for the years 1969–1980. A total of 1,771 primary liver cancer deaths were identified; 17 were excluded because the death occurred out of state; 2 more were excluded because, upon review, one was female and the other was not actually coded to liver cancer. Ten liver cancer deaths coded to "other race" (not white, non-Spanish surname, nor black, nor white Spanish surname) were also excluded, leaving 1,742 cases of primary liver cancer for study. An equal number of control male death certificate records were selected from all other causes of deaths, a population-based pool of 537,000 male deaths. All neoplasms (ICD 140–239), diseases of the liver and gallbladder (ICD 570–576), infectious hepatitis (ICD 070), and alcoholism (ICD 303) were excluded from the controls because of the possible misclassification of cases into other cancers or diseases and the known association of liver cancer with hepatitis and alcoholism. Controls were randomly selected and were frequency matched to the distribution of cases by 5-year age groups, race, ethnicity, and year of death.

The usual occupation and kind of business or industry as recorded on the death certificate were coded according to the United States Bureau of the Census 1980 Classified Index of Industries and Occupations [1980]. Each study subject could then be grouped either by the occupation held or by the industry he worked in or both. The grouping of cases and controls into exposure categories in general followed industrial categories outlined in the United States Census Classified Index. Industry groupings were loosely based on a previously reported classification scheme by Hoar et al. [1980], who classified industries by product or exposure. The large number of cases in this study and the larger presence of some industries in Texas made it possible to have more specific industrial groupings than Hoar (e.g. agriculture classified into farming, ranching). The petrochemical industry was defined to include both the manufacturing of industrial and miscellaneous chemicals and petroleum refining, since many oil companies in Texas do both. Twenty-two other industrial or product exposure categories, each with at least ten persons, were determined and included: cotton ginning; landscaping; oil extraction; construction; meat products; beverage; miscellaneous food; textiles; baking products; paper and wood; newspaper; printing; leather; stone, clay, glass; metal manufacturing; machinery manufacturing; auto manufacturing; aircraft manufacturing; shipbuilding/shipping; gasoline service stations; eating and drinking places; and dry cleaning services. Specific occupations or groups of occupations within these product exposure categories and with at least ten persons were evaluated and included: farmers, farmworkers, ranchers, ranch workers, oil drillers and workers, electricians, painters, carpenters, plumbers/pipefitters, construction laborers, butchers or meat cutters, printing machine operators, oil refinery workers, shoemakers or repairers, seamen, longshoremen, service station attendants, cooks, cafe owners, and dry cleaning operators.

To determine the risk associated with each occupational or industrial category, Mantel-Haenszel summary odds ratios (ORs) were computed for each race and ethnic group and for all groups combined, adjusting for age. Since liver cancer risk is higher for Mexican-Americans and blacks, ORs were additionally adjusted for race and ethnicity to lessen the effects of any correlated factors (i.e. hepatitis B infection) from the association of occupation and liver cancer. In calculating the summary OR, the comparison or "nonexposed" group was the same for each "exposed" category and was defined mainly by excluding agriculture and manufacturing industries. With certain exceptions (water transportation, wholesale apparel/fabrics, retail lumber, retail bakeries, gasoline service stations, retail apparel, eating and drinking places, dry cleaning, shoe repair), the comparison group included all individuals in transportation, communications and public utilities, wholesale trade, retail trade, finance, insurance and real estate, business and repair services, personal services, entertainment and recreation services, professional and related services, public administration, retired, unemployed, and individuals with unknown industry. There was a total 1,604 individuals in the nonexposed group; 781 were liver cancer deaths and 823 were control deaths. Test-based 95% confidence intervals for adjusted ORs were formed by Miettinen's method described in Kleinbaum et al. [1982]. Deaths coded to white Spanish surnames are assumed to be Mexican-American, and deaths coded to white non-Spanish surnames are referred to as "other whites".

RESULTS

Table I gives the age at death, race, and ethnic distribution of the study cases; 62.9% of the cases were other whites, 18.4% were Mexican-American, and 18.7% were black. The mean age of the cases was nearly identical to the mean age of the controls (65.8 vs 65.9). The most frequent causes of death among the controls were ischemic heart disease (40.4%), cerebrovascular diseases (12.1%), and external injuries (11.7%).

Occupations and their industries with elevated ORs of at least twofold are listed

TABLE I. Age at Death, Race, and Ethnic Distribution of Primary Liver Cancer Cases in Texas During 1969–1980

Age (years)	Other whites	Mexican-American	Black
20–24	6	1	1
25–29	5	0	5
30–34	7	3	4
35–39	3	4	6
40–44	16	5	11
45–49	39	11	22
50–54	57	12	43
55–59	123	34	50
60–64	171	47	48
65–69	214	52	52
70–74	182	55	42
75–79	151	48	22
80–84	74	29	13
85+	48	20	6
Total	1,096	321	325

in Table II. To simplify presentation, only ORs for all race and ethnic groups combined are shown. Texas males who worked in meat products had an adjusted OR for primary liver cancer of 2.4; restricting the category to butchers and meat cutters slightly increased the OR to 2.6. Persons working in textiles had a threefold risk for liver cancer. The excess risk in the petroleum and chemical manufacturing industries was confined to oil refinery workers who had an OR of 2.0. 'Oil refinery workers' includes technical and operator personnel and excludes workers who were thought to have relatively little exposure to hazardous chemicals or fuels (e.g. administrative managers, accountants, executives). Of the oil refinery workers, 80% were other whites, 20% were black, and none were Mexican-American. The excess primary liver cancer risk in oil refinery workers was due to a high risk in other white males, who had an OR of 2.6 (95% confidence limits [C.L.] 1.4–5.0). Black oil refinery workers had no excess (OR = 0.7, C.L. 0.2–2.5), though the numbers were small.

Plumbers and pipefitters, and cooks were also shown to have elevated risks. The OR for plumbers and pipefitters was similar for other whites and blacks (OR = 1.8); however, Mexican-American males had an OR of 4.5 (95% C.L. 0.7–27.9). The risk for cooks was especially high for other whites (OR = 4.4, 95% C.L. 1.1–18.5). Not shown are ORs for electricians, which were not increased for black or Mexican-American males but were significantly increased for other white males (OR = 2.5, 95% C.L. 1.1–5.7). The OR for longshoremen (2.2) had an interval estimate that included one (95% C.L. 0.6–7.4).

For occupations that have been linked to liver cancer in previous studies [Neugut et al., 1987], ORs for our data are presented in Table III. None of the occupations listed had ORs much greater than one. The OR for farmworkers adjusted for race and ethnicity (1.4) was larger than the OR for farmers (1.0). Mexican-American farmworkers who constituted the majority (71%) of farmworkers also had an OR of 1.4.

DISCUSSION

We were not able to confirm a strong relationship between farmworking with possible exposure to agricultural chemicals and liver cancer in this study. Accordingly, the risk observed in our study for farm workers (OR = 1.3, C.L. 0.8–2.2) is not sufficiently high to explain the excess risk of primary liver cancer in Mexican-Americans. However, the risk estimated for farmworkers in Texas was compatible with relative risks (RR) reported by Stemhagen et al. [1983] (RR = 1.9) and Austin

TABLE II. Occupations and Industries With at Least a Twofold Risk for Primary Liver Cancer (In Texas, 1969–1980)

	Cases	Controls	Adjusted odds ratio	95% Confidence limits
Construction	236	208	1.21	0.97–1.49
Plumbers, pipefitters	26	14	1.97[a]	1.03–3.76
Meat products[b]	27	12	2.42[a]	1.27–4.62
Butchers, meat cutters	15	6	2.63[a]	1.05–6.59
Textiles[c]	14	5	3.08[a]	1.22–7.76
Petrochemical[d]	49	43	1.21	0.79–1.84
Oil refinery workers[e]	33	18	1.95[a]	1.11–3.45
Eating and drinking places	47	33	1.54	0.98–2.42
Cooks	23	12	2.22[a]	1.10–4.47
Shipbuilding, shipping[f]	23	18	1.35	0.71–2.56
Longshoremen	8	4	2.17	0.64–7.38

[a]$p = .05$, two-tailed test.
[b]Includes all occupations in manufacturing of meat products (industry code 100) and butchers or meat cutters (occupations code 686) in any industry.
[c]Includes all occupations in manufacturing of textile mill products (industry codes 132–150); manufacturing of apparel and other finished textile products (industry codes 151–152); wholesale trade of apparel, fabrics, and notions (industry code 542); retail trade of apparel and accessory stores, except shoe (industry 630).
[d]Includes all occupations in manufacturing of industrial and miscellaneous chemicals (industry code 192) and petroleum refining (industry code 200).
[e]Includes chemical technicians (occupation code 224); janitors (453); supervisors, mechanic and repairer (503); plumbers, pipefitters, and steamfitters (585); miscellaneous plant operators (699); furnace, kiln, and oven operators (766); laborers (889); supervisors, production occupations (633); boilermakers (643); production inspectors, checkers, and examiners (796), in the manufacturing of industrial and miscellaneous chemicals and petroleum refining.
[f]Includes all occupations in ship and boat building and repairing (industry code 360) and in water transportation (industry code 420).

TABLE III. Occupations and Industries Associated with Primary Liver Cancer in Other Studies (Results for Texas, 1969–1980)

	Cases	Controls	Adjusted odds ratio	95% Confidence limits
Farming	193	202	1.02	0.82–1.28
Farmers	155	172	0.96	0.75–1.23
Farmworkers	38	30	1.35	0.82–2.23
Ranching	45	41	1.21	0.79–1.88
Ranchers	32	30	1.16	0.70–1.92
Ranchworkers	13	11	1.32	0.57–3.02
Gasoline service stations	20	21	1.04	0.55–1.98
Service station attendants	10	9	1.19	0.47–3.03
Dry cleaning services	11	12	0.98	0.44–2.20
Dry cleaning operators	4	8	0.55	0.17–1.75

et al. [1987] (RR = 1.4). All other related studies are of farmers, and only one out of five studies, a proportional mortality study in Washington State, has shown a positive association with liver cancer [Milham, 1976; Burmeister, 1981; Dubrow and Wegman, 1984; MacCubbin et al., 1986; Wiklund and Holm, 1986]. None of the previous studies of agricultural workers appeared to have accounted for ethnicity.

A twofold excess of primary liver cancer was demonstrated in petrochemical workers who have a likelihood of exposure to chemicals. To date, neither cohort nor case-control studies of petroleum and chemical workers have reported an increased risk of liver cancer [Wen et al., 1983; Hanis et al., 1979,1982; Thomas et al., 1980,1982; Bond et al., 1985; Austin and Schnatter, 1983; Thériault and Goulet, 1979; Austin et al., 1987; Buffler, 1980], even though geographic analyses of cancer mortality have consistently shown counties along the Texas gulf coast to have excessively high rates of liver cancer compared to other areas [Hoover and Fraumeni, 1975; Mason et al., 1975]. A review of the studies of petroleum refineries and petrochemical plants that specifically examined liver and gallbladder cancers showed that four investigators found standard mortality ratios below one [Wen et al., 1983; Hanis et al., 1982; Thomas et al., 1982; Bond et al., 1985], and two reported nonsignificant ratios of twofold [Austin and Schnatter, 1983; Thomas et al., 1980]. Two Canadian oil refineries reported elevated risks for digestive organ cancers [Hanis et al., 1979; Thériault and Goulet, 1979]. These studies have been flawed, however, for one or more of the following reasons: 1) inclusion of workers with no possibility of exposure; 2) insufficient number of cases to detect a positive association; 3) lack of a required minimum latency period between exposure and development of disease; and 4) inclusion of gallbladder or other digestive cancers with liver cancer. In a case-control study of 137 primary liver cancer deaths in three Texas gulf coast counties during the years 1964–1976, more controls than cases had a history of employment in chemical industries [Buffler, 1980]. The hospital-based case-control study by Austin et al. [1987] showed a nonsignificant RR of 1.7 for employment in chemical or petrochemical industries. Both studies lacked sufficient power in that the former study could only confirm one-third of the death certificate cases as primary liver cancer and the latter study was based on only six exposed cases.

In our study, an increased risk was not apparent for the broader industry category of petrochemicals; the risk was only observed in operator and technical personnel. Petrochemical workers may have potential exposure to various hepatotoxic chemicals common to their work environment. These chemicals may include arsenic, arsine, carbon tetrachloride, metal carbonyls, chlorinated diphenyls and napthalenes, dimethyl formacide, nickel, nitrobenzene, trichloroethylene, and vinyl chloride. Arsenic and vinyl chloride have been associated with cancer of the liver in humans, and nickel has been reported as being carcinogenic to the lungs [Tabershaw et al., 1978]. Based on animal studies, metal carbonyls, polychorinated biphenyls, carbon tetrachloride, and trichloroethylene have been reported as probable liver carcinogens in humans [Tabershaw et al., 1978; Tomatis et al., 1982].

Increased risks were also found for plumbers and pipefitters, textile workers, occupations in eating and drinking places, electricians, longshoremen, and butchers. A study of plumbers and pipefitters by Kaminski et al. [1980] showed an excess of liver cancer mortality based on a very small number of cases. Potential exposures common to plumbers include asbestos, carbon tetrachloride and vinyl chloride, metal fumes, and other solvents. The one other specific mortality study of plumbers showed

a deficit of liver cancer deaths [Cantor et al., 1986]. An elevated RR for Genoa dockyard workers compared to the general male population has been reported. Genoa dockyard workers were thought to have been exposed to asbestos, polycyclic aromatic hydrocarbons, and halogenated hydrocarbons [Puntoni et al., 1979]. We did not find an association of liver cancer with occupations in dry cleaners as reported previously [Stemhagen et al., 1983; Blair et al., 1979]; however, an increased risk was observed for workers in the textile industry who may have similar exposures to dry cleaning agents such as carbon tetrachloride, solvents, and trichloroethylene. Excess risks for primary liver cancers in textile industry workers, electricians, and butchers have not been reported in the literature. Electricians have potential exposures to chlorinated diphenyls and naphthalenes, epoxy and phenolic resins, rubber, solder fumes, solvents, synthetic waxes, and varnishes.

Since our study was based on death certificate information, we were unable to consider the role of possible confounders such as alcohol consumption or hepatitis B infection, risk factors in the development of primary liver cancer. Because alcohol-related causes of death were deleted from the control group, some excess risks seen in occupations in eating and drinking places may be due to higher consumption of alcohol among the cases. Stemhagen et al. [1983], however, noted an excess risk for workers in eating and drinking places even after adjustment for alcohol consumption. Alternatively, the excess risk in cooks as well as in butchers and meat cutters may be due to a higher risk of contracting hepatitis. It is difficult to imagine that alcohol consumption and hepatitis B would account for the excess risks in all the occupations reported here. Although cigarette smoking may be associated with certain occupations, it has not been shown to be a risk factor for primary liver cancer [Austin et al., 1986].

The obvious lack of exposure information and the nonspecific nature of occupation and industry data are weaknesses of a study based on death certificate information. The reliability of occupation and industry listed on death certificates has a reported accuracy of about 60 to 75% [Gute and Fulton, 1985; Schumacher, 1986]. The effects of random misclassification and the nonspecificity of the occupation information are to dilute a true association and bias the OR towards the null; thus the associations reported here may be stronger. Misclassification of occupation and industry does not appear to be associated with any particular industry [Schumacher, 1986]. Death certificate statements of primary liver cancer are less reliable than for other cancers; only 77% are confirmed by hospital records [Percy et al., 1981]. The inclusion of nonliver cancer among the cases would again have the effect of dampening any occupational association.

CONCLUSION

The increased risk of primary liver cancer in Mexican-Americans is probably not due to farmworker exposures to pesticides but to other etiologic factors such as hepatitis B infection. We recommend that studies of the association between occupation and primary liver cancer adjust for race and ethnicity. We also recommend that past studies of the petrochemical industry be reevaluated for possible risks of primary liver cancer. Other occupations that may require further study are plumbers, textile workers, and shipyard workers.

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