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A Case-Control Study of Chemical Exposures and Brain Tumors in Petrochemical Workers

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The relationship between chemical exposures and deaths attributable to primary brain tumors among employees of a Texas petrochemical plant was investigated. Cases consisted of 21 deaths in which the underlying cause was confirmed as a primary brain tumor. Two control groups of 80 employees each were randomly selected from 450 decedents known to the company in June, 1979. Potential exposures while employed were compared between cases and controls for five known or suspect carcinogens. Exposure potentials were also compared for an additional 37 chemicals to which at least four cases were potentially exposed. Overall and 15-year latency analyses were performed. The proportion of cases exposed to the five potentially carcinogenic chemicals (including vinyl chloride) were lower than or consistent with the proportion of exposed controls. No statistically significant differences between the proportions of cases and controls exposed to the 37 other chemicals were found.

In mid-1978 a cluster of brain tumor cases (deaths) was identified among former employees of the Union Carbide Corporation (UCC) chemical plant in Texas City, Tex.[1,2] As a result of a formal employee request to the Occupational Safety and Health Administration (OSHA), the National Institute for Occupational Safety and Health (NIOSH) and UCC initiated a two-pronged investigation to determine the likelihood of an occupational association with this cluster. The first prong of the investigation was a retrospective cohort mortality study of all employees who ever worked at the Texas City Plant and a comparison of their overall mortality experience (through December, 1977) with the mortality experience of a comparable segment of the U.S. population. The second prong of the NIOSH investigation was a case-control study to identify any exposure or work areas that were shared in common by the brain tumor cases.

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In addition to assisting NIOSH in data collection requirements for its studies, UCC also initiated studies independently of NIOSH. The purpose of this report is to describe results of an independent UCC case control study.

Purpose

The principal purpose of this study was to identify any occupational factors that could serve to distinguish the brain tumor cases from a randomly selected sample of all former UCC employees. Specifically, the study was intended to assess the likelihood that exposures to known or suspect carcinogens at the UCC Texas City plant could have been related to the occurrence of the brain tumors among the population of employees who ever worked at the plant.

A second purpose of the study was to attempt to replicate the results of the NIOSH case-control study using an independently selected comparison population. This was considered an appropriate objective, since the validity of these studies often depends on the adequacy with which the comparison populations selected for study represent the underlying population from which the cases were drawn. Since both the UCC and NIOSH studies selected samples of the UCC Texas City employee population to serve as "controls," both studies are subject to some degree of sampling error that could lead to spurious results. Although these studies are not totally independent, the chances that both studies will obtain the same spurious results are rather small; therefore, the results of the two analyses, taken together, should provide some assurance that a positive association between some chemical and the brain tumor cases will not be missed.

Methods

The methods used in this study involved comparisons between the proportion of brain tumor cases exposed to a particular chemical during employment at Texas City with the proportion of non-brain tumor controls exposed to the same chemical during employment at Texas City.

Carcinogens – The five known or suspected carcinogens that were studied in this investigation include benzene, ethylene dichloride, ethylene oxide, diethyl sulfate and

vinyl chloride. Although ethylene dichloride was a suspect carcinogen at the time this study was initiated, an additional long term animal study has been completed that has resulted in uncertainty concerning the potential carcinogenicity of this chemical.[3] For this study, however, results for ethylene dichloride will be presented together with the other four suspect human carcinogens.

Other Chemicals – For the purpose of replicating the results of the NIOSH case-control study, the same 37 chemicals under investigation in that study were also included for study in this investigation (Table 1). These chemicals were selected using NIOSH's criteria that at least four brain tumor cases were found to have had the potential for exposure to the chemicals at some time during their employment at UCC Texas City.

Description of Cases – For the purpose of this study, a case was defined as any former UCC Texas City employee known to have had a primary brain tumor on the basis of autopsy information, histopathology reports, clinical evidence in medical records or death certificates. Cases were identified primarily through death certificate searches although tumor registries throughout the state of Texas were also investigated and searched. Therefore, it is possible that incident cases were not ascertained if they survived or died from another underlying cause.

Case validation was performed by NIOSH and resulted in the identification of 21 cases shown in Table 2. This table indicates the most accurate diagnosis available in this investigation as determined by NIOSH. The "source of confirmation" for which the most valid basis was found for determining the specific diagnosis of the primary tumor is classified as follows: 1, tissue specimen interpreted by Armed Forces Institute of Pathology; 2, autopsy report; 3, histopathology report; 4, clinical diagnosis from hospital record; and 5, death certificate diagnosis. For the purpose of this analysis, codes 1, 2 and 3 were considered by UCC as confirmed and codes 4 and 5 were considered unconfirmed.

Table 1 – Listing of 37 Chemicals to Which Four Brain Tumor Cases Were Exposed at UCC Texas City

Acetaldehyde	Methanol
Acetic acid	Methyl ethyl ketone
Acetone	Methyl isobutyl ketone
Butadiene	Monoethanolamine
Carbon dioxide	Nonane
Chlorine	Phosphoric acid
Diethylene glycol	Potassium hydroxide
Diethanolamine	Propylene
Ethanol	Sodium carbonate
Ethylene	Sodium hydroxide
Ethylene glycol	Sodium sulfite
Hydrochloric acid	Styrene
Hydroxypropyl acrylate	Sulfuric acid
Isopropanol	Tergitols
Isopropyl acetate	Tetraethylene glycol
Isopropyl peroxydicarbonate	Toluene
Lubricating oils	Trichloroethane
Methane	Triethylene glycol
	Vinyl acetate

In all, this case series comprised 21 cases: 17 classifiable as gliomas and four classifiable as meningiomas. (Of the four meningiomas, three were benign tumors and one was malignant.) Of the 17 gliomas, 13 were confirmed by available autopsy or pathology reports.

Selection of Controls – For purposes of comparison with cases, two series of control groups were selected from all former UCC Texas City employees whose deaths were known to the company. Decedents were used as controls because their causes of death were known and could be verified as non-brain tumors. The two control groups differed in that control group 1 excluded employees whose cause of death was attributable to any malignant neoplasm. A strictly noncancer control group was selected to allow for the possibility that a general chemical carcinogen may have been associated with malignancies of sites other than the brain. Such an association could theoretically be missed if other cancers were included in the control group. Both control groups consisted of 80 male employees randomly selected from 450 decedents known to the company in June, 1979. (Company-identified deaths were known through the corporate employee benefits department and through locally published obituary notices routinely screened by the plant medical department.)

Exposure Determination – Exposure determinations were made on the basis of official employment records available at the Texas City plant. These records contained detailed job title and department assignment codes for each employee from date of hire to date of termination at UCC Texas City. This information was coded and entered on magnetic tapes by UCC and NIOSH staff. For each unique department code symbol, principal chemicals used or produced at any time in the history of the plant were identified and correlated with that department by UCC industrial hygienists. It was not feasible to specify these associations by year because this would have involved a great deal of time of former long-term employees (e.g., retirees) whose memories were the sole source of information regarding detailed process changes throughout the history of the plant.

An employee was considered "exposed" to a given chemical if he ever worked in a department associated with that chemical. An employee was considered "unexposed" if he never worked in a department associated with that chemical. The "unknown" exposure designation was reserved for employees who were never known to have been exposed to a given chemical but who had ever worked in a department (e.g., maintenance) for which no specific chemicals could be listed.

Analyses

The proportion of cases exposed to a particular chemical was compared with the proportion of controls exposed to the same chemical. Analyses were performed where (1) unknowns were considered exposed, (2) unknowns were considered unexposed, and (3) unknowns were excluded from the analyses.

To determine whether specificity with respect to glial tumor production and exposure to particular chemical

Table 2 – Listing of 21 Brain Tumor Cases: UCC Texas City

Case No.	Dates Employed	Age at Hire	Years Employed	Latency*	Date of Death	Sex/ Race	Source of† Confirmation	Diagnosis
1	3/41-9/44	28	03	23	5/64	W/M	4	Glioblastoma: brain
2	5/41-1/66	31	25	25	2/66	W/M	1	Meningiosarcoma
3	7/41-5/74	31	33	35	5/76	W/M	1	Glioblastoma: brain
4	11/41-3/62	31	20	24	12/65	W/M	3	Menigioma
5	7/44-6/58	45	14	19	12/63	B/M	5	Postoperative meningioma
6	7/44-4/79	24	35	35	10/79	W/M	1	Glioblastoma: brain
7	9/44-10/44	26	00	30	5/74	W/M	1	Glioblastoma: CNS
8	10/45-2/48	45	02	25	10/70	W/M	3	Glioblastoma: brain
9	9/46-1/73	36	26	26	3/73	W/M	3	Glioblastoma: brain
10	9/46-12/78	22	32	32	3/79	B/M	4	Astrocytoma grade IV
11	3/47-3/57	34	10	27	6/74	B/M	2	Meningioma
12	9/48-7/51	23	03	27	7/75	W/M	1	Astrocytoma grade II
13	3/49-6/71	38	22	22	6/71	W/M	4	Malignant brain tumor
14	1/50-8/66	48	16	18	1/68	W/M	1	Astrocytoma grade III
15	10/50-11/67	36	17	23	4/74	W/M	1	Astrocytoma grade III
16	10/50-4/79	28	28	29	2/80	W/M	1	Astrocytoma grade III
17	9/51-12/73	29	22	22	1/74	W/M	1	Glioblastoma: brain
18	4/53-5/53	28	00	03	10/56	W/M	5	Glioblastoma: brain
19	8/53-3/62	21	09	09	4/62	W/M	2	Glioblastoma
20	8/53-12/70	26	17	18	5/71	W/M	3	Astrocytoma grade IV
21	10/53-6/78	24	25	25	12/78	W/M	1	Anaplastic astrocytoma

* Latency means date of death minus date of hire

† Source of confirmation: 1 indicates Armed Forces Institute of Pathology; 2, autopsy report; 3, surgical pathology report; 4, clinical diagnosis – hospital record; 5, death certificate diagnosis

agents exists, the proportion of glioma cases exposed to specific chemicals was also calculated for comparison.

In addition to overall analyses in which the comparison was between proportions of cases and controls ever exposed to specific chemicals at any time during their employment with UCC Texas City, a separate analysis was performed in which the latent period of chemical carcinogenesis was taken into consideration. In these analyses, comparisons between cases and controls were restricted to employees whose first exposure to a particular chemical occurred a minimum of 15 years prior to death. (Date of death was used as a proxy for date of disease onset in all latency analyses.)

Because the nature of this study was primarily descriptive, no tests of statistical significance were performed routinely. When tests were used, the uncorrected Mantel-Haenszel chi-squared statistic[4,5] was calculated to determine whether the observed difference between two proportions could have been due to "chance."

Results

Demographic and Occupational Characteristics – A comparison of selected characteristics of cases and controls reveals that a slightly higher proportion of brain tumor cases than controls were employed less than 10 years at the Texas City Plant (Table 3). This is attributable in part to the manner in which controls were selected, i.e., employees whose deaths were known to the company were more likely to have had somewhat longer periods of employment than employees whose deaths were not known. However, the mean number of employment years for cases and controls were very similar: for cases, 17.5 years; for control group 1, 18.9 years; and control group 2, 17.8 years.

A comparison of other selected characteristics of cases and controls indicates that cases resembled controls closely on year of hire, payroll status and race. A higher proportion of cases than controls terminated for reasons other than death, disability or retirement (voluntary quit, layoff, etc.). Cases were also found to be generally younger at hire than the controls. It is possible that these factors are interrelated, i.e., employees with brief periods of employment who terminate for reasons other than death, disability or retirement may be younger at hire than employees with longer periods of employment.

Fewer cases than controls survived to their 70th birthday, reflecting the fact that the peak incidence of brain tumors is in the fifth and sixth decades of life. Fewer cases died before 1960 than controls and a greater proportion survived a minimum of 15 years following hire at the Texas City Plant. Although these observations are not inconsistent with an occupational etiology, these discrepancies are more likely due to the fact that deaths from cardiovascular disease and accidents typically occur at earlier ages than deaths from brain tumors.

With the possible exception of the differences related to age at hire, all discrepancies between cases and controls

Table 3 – Comparison of Cases and Controls for Selected Characteristics

Characteristic	Cases, No. (%)	Control 1, No. (%)	Control 2, No. (%)
Termination reason			
Death	10 (47.6)	38 (47.5)	36 (45.0)
Disability	2 (9.5)	16 (20.0)	21 (26.3)
Retirement	3 (14.3)	19 (23.8)	14 (17.5)
Other	6 (28.6)	7 (8.8)	9 (11.3)
Years of service			
< 10	7 (33.3)	13 (16.2)	12 (15.0)
11-20	5 (23.8)	38 (47.5)	35 (43.8)
> 21	9 (42.8)	29 (36.2)	33 (41.2)
Mean	17.5	18.9	17.8
Year of hire			
1940-1945	8 (38.1)	30 (37.5)	34 (42.5)
1946-1950	8 (38.1)	31 (38.8)	29 (36.2)
1951-1955	5 (23.8)	13 (16.2)	13 (16.2)
1956+	0 (0.0)	6 (7.5)	4 (5.0)
Age at hire, yr			
< 25	5 (23.8)	14 (17.5)	11 (13.8)
25-34	10 (47.6)	27 (33.8)	30 (37.5)
> 35	6 (28.6)	39 (48.8)	39 (48.8)
Mean	30.4	33.9	34.2
Payroll type status			
Ever hourly	21 (100.0)	72 (90.0)	73 (91.3)
Never hourly	0 (0.0)	8 (10.0)	7 (8.8)
Race			
White	18 (85.7)	63 (78.8)	66 (82.5)
Other	3 (14.3)	17 (21.3)	14 (17.5)
Age at death, yr			
< 50	4 (19.0)	24 (30.0)	18 (22.5)
50-69	16 (76.2)	46 (57.5)	52 (65.0)
> 70	1 (4.8)	10 (12.5)	10 (12.5)
Year of death			
1950-1959	1 (4.8)	7 (8.8)	12 (15.0)
1960-1969	6 (28.6)	28 (35.0)	17 (21.2)
1970+	14 (66.7)	45 (56.2)	51 (63.8)
Latency, yr			
< 15	2 (9.5)	20 (25.0)	18 (22.5)
> 15	19 (90.5)	60 (75.0)	62 (77.5)
Cause of death			
Neoplasms	21 (100.0)	18 (22.5)	0 (0.0)
Circulatory diseases	0 (0.0)	36 (45.0)	52 (65.0)
Accidents	0 (0.0)	10 (12.5)	13 (16.3)
Other	0 (0.0)	16 (20.0)	15 (18.7)
Total	21 (100.0)	80 (100.0)	80 (100.0)

appear to be attributable to differences in cause of death between cases and controls or to the higher proportion of cases terminating for reasons other than death, disability or retirement. It is unlikely that these differences have any epidemiologic significance, nor do they appear to be large enough to affect the comparability of exposure histories of cases and controls.

Exposure Characteristics – *Carcinogens* – Table 4 indicates overall exposure determinations for cases and controls for each of the five known or suspect human carcinogens, benzene, diethyl sulfate, ethylene dichloride, ethylene oxide and vinyl chloride. It can be seen from this table that exposure determinations could not be made for 48%-57% of the cases and for 56%-67% of the controls in each group. This is due to the high proportion of UCC Texas City employees who are assigned to maintenance departments where plantwide travel makes exposure to all chemicals theoretically possible, but technically unknown. Analyses were conducted in which employees whose exposure status was unknown were (*a*) treated as exposed to all chemicals, (*b*) treated as unexposed to all chemicals and (*c*) treated as unknown and excluded from the analysis. Only the results of the third analysis, in which unknowns were excluded from the analysis, are presented in the remaining tables because this analysis was considered the most objective. In general, however, the analyses in which these employees were considered exposed to all chemicals resulted in increasing exposure estimates more among controls than cases.

Table 5 compares exposures between cases and controls for each of the five suspect carcinogens. It can be seen that the proportion of cases exposed differs only slightly between all cases and all glioma cases. In addition the proportion of cases exposed is generally lower than or consistent with that for either control group for each of these chemicals.

Because salaried employees have a lower risk of exposure to chemicals than hourly employees, analyses are shown in Table 5 using only hourly controls. Again, there is little difference between the proportions of cases and the proportions of controls exposed to these chemicals.

A more meaningful analysis is one that allows for some minimum latent period between initial exposure to a given chemical substance and the onset of disease or death. Table 6 shows the comparison of exposure frequencies among cases and controls for only those persons who were employed at UCC Texas City a minimum of 15 years prior to death. For all five chemicals, the proportion of cases exposed were comparable with the proportion of controls exposed. This result was obtained even when salaried employees were removed from the control groups (Table 6).

Other Chemicals – Although no associations were detected between suspect carcinogenic chemical exposures and brain tumor cases, the possibility of an association between other chemicals used or produced at the plant and the brain tumors was also investigated. In these analyses, proportions of exposed cases and controls were compared for each of the 37 chemicals to which at least four of the brain tumor cases were exposed.

Table 7 compares exposures of cases with all controls and with hourly controls for each of the 37 chemicals. For 15 of the 37 chemicals listed, both "all cases" and "all glioma cases" were exposed less frequently than either control group 1 or control group 2. The actual number of chemicals for which this was true increased by two when salaried employees were removed from the control groups (Table 7).

For seven chemicals (carbon dioxide, chlorine, ethylene, isopropanol, sodium sulfite, trichloroethane, and vinyl

Table 4 – Exposure Status of Cases and Controls for Five Chemicals Used or Produced at the Texas City Plant (1941-1977)

Chemical	Cases			Control 1			Control 2		
	Exposed No. (%)	Unexposed No. (%)	Unknown No. (%)	Exposed No. (%)	Unexposed No. (%)	Unknown No. (%)	Exposed No. (%)	Unexposed No. (%)	Unknown No. (%)
Benzene	1 (4.8)	8 (38.1)	12 (57.1)	11 (13.8)	18 (22.5)	51 (63.8)	5 (6.2)	21 (26.3)	54 (67.5)
Diethyl sulfate	5 (23.8)	6 (28.6)	10 (47.6)	17 (21.3)	18 (22.5)	45 (56.3)	13 (16.3)	19 (23.8)	48 (60.0)
Ethylene dichloride	5 (23.8)	6 (28.6)	10 (47.6)	14 (17.5)	19 (23.8)	47 (58.8)	14 (17.5)	17 (21.3)	49 (61.3)
Ethylene oxide	3 (14.3)	7 (33.3)	11 (52.4)	9 (11.2)	22 (27.5)	49 (61.3)	11 (13.8)	20 (25.0)	49 (61.3)
Vinyl chloride	4 (19.0)	7 (33.3)	10 (47.6)	12 (15.0)	20 (25.0)	48 (60.0)	13 (16.2)	19 (23.8)	48 (60.0)

Table 5. Proportions of Cases, Controls and Hourly Controls Exposed to Five Chemicals at UCC Texas City

Chemical	All Cases		Gliomas		Control 1		Control 2		Hourly Control 1		Hourly Control 2	
	Total	% Exposed	Total	% Exposed	Total	% Exposed	Total	% Exposed	Total	% Exposed	Total	% Exposed
						Cases and Controls						
Benzene	9	11.1	8	12.5	29	37.9	26	19.2	26	38.5	24	16.7
Diethyl sulfate	11	45.5	10	40.0	35	48.6	32	40.6	31	48.4	30	40.0
Ethylene dichloride	11	45.5	10	50.0	33	42.4	31	45.2	30	43.3	29	44.8
Ethylene oxide	10	30.0	9	33.3	31	29.0	31	35.5	28	32.1	29	34.5
Vinyl chloride	11	36.4	10	40.0	32	37.5	32	40.6	29	37.9	29	37.9

Table 6. Proportions of Cases, Controls and Hourly Controls Exposed to Five Chemicals at UCC Texas City at Least 15 Years Prior to Death

Chemical	All Cases		Gliomas		Control 1		Control 2		Hourly Control 1		Hourly Control 2	
	Total	% Exposed	Total	% Exposed	Total	% Exposed	Total	% Exposed	Total	% Exposed	Total	% Exposed
Benzene	9	11.1	8	12.5	30	26.7	23	4.3	26	26.9	22	4.5
Diethyl sulfate	10	40.0	9	33.3	33	42.4	27	29.6	29	44.8	26	30.8
Ethylene dichloride	10	40.0	9	44.4	31	32.3	26	34.6	27	33.3	25	36.0
Ethylene oxide	9	22.2	8	25.0	30	20.0	26	23.1	26	23.1	25	24.0
Vinyl chloride	10	30.0	9	33.3	33	30.3	27	33.3	29	31.0	25	32.0

acetate) cases were exposed more frequently than controls. When salaried employees were removed from the control groups, only trichloroethane was removed from this list.

Table 8 shows the comparison of exposure frequencies among cases and controls for those persons who were employed at UCC Texas City a minimum of 15 years prior to death. For 13 of the 37 chemicals, both "all cases" and "gliomas" were exposed less frequently than either of the control groups. When cases were compared with only hourly controls, there were 18 chemicals with lower exposure frequencies among cases.

For 13 other chemicals (chlorine, diethylene glycol, ethylene, isopropyl peroxydicarbonate, methane, methyl ethyl ketone, potassium hydroxide, sodium sulfite, sulfuric acid, tetraethylene glycol, trichloroethane, triethylene glycol and vinyl acetate) cases were exposed more frequent-

Table 7. – Proportions of Cases, Controls and Hourly Controls "Ever Exposed" by Chemical

Chemicals*	All cases No.† (%)‡	Gliomas No. (%)	Control 1 No. (%)	Control 2 No. (%)	Hourly Control 1 No. (%)	Hourly Control 2 No. (%)
Acetaldehyde	10 (50.0)	9 (44.4)	31 (48.4)	31 (51.6)	28 (53.6)	29 (51.7)
Acetic acid	11 (36.4)	10 (40.0)	37 (59.5)	36 (61.1)	33 (60.6)	33 (60.6)
Acetone	11 (72.7)	10 (80.0)	41 (85.4)	37 (83.8)	37 (89.2)	34 (85.3)
Butadiene	8 (44.4)	7 (42.9)	30 (66.7)	26 (65.4)	27 (70.4)	25 (68.0)
Carbon dioxide	10 (70.0)	9 (77.8)	34 (58.8)	31 (64.5)	31 (64.5)	29 (65.5)
Chlorine	8 (44.4)	7 (42.9)	28 (39.3)	24 (37.5)	25 (40.0)	23 (39.1)
Diethanolamine	11 (45.5)	10 (50.0)	36 (61.1)	32 (62.5)	33 (63.6)	30 (63.3)
Diethylene glycol	11 (36.4)	10 (40.0)	33 (36.4)	31 (38.7)	30 (36.7)	29 (37.9)
Ethanol	11 (45.5)	10 (40.0)	33 (48.5)	32 (40.6)	30 (50.0)	30 (40.0)
Ethylene	8 (88.9)	8 (87.5)	34 (76.5)	28 (67.9)	31 (80.6)	26 (69.2)
Ethylene glycol	11 (54.5)	10 (50.0)	35 (54.3)	36 (58.3)	32 (56.3)	33 (57.6)
Hydrochloric acid	11 (54.5)	10 (60.0)	35 (62.9)	32 (68.8)	32 (65.6)	29 (69.0)
Hydroxypropyl acrylate	11 (36.4)	10 (40.0)	30 (26.7)	31 (38.7)	27 (29.6)	29 (37.9)
Isopropanol	11 (54.5)	10 (60.0)	36 (52.8)	33 (51.5)	32 (53.1)	30 (50.0)
Isopropyl acetate	11 (36.4)	10 (40.0)	37 (54.1)	36 (55.6)	33 (54.5)	33 (54.5)
Isopropyl peroxydicarbonate	11 (36.4)	10 (40.0)	30 (26.7)	31 (38.7)	27 (29.6)	29 (37.9)
Lubricating oils	10 (60.0)	9 (55.6)	34 (64.7)	32 (68.8)	31 (71.0)	30 (70.0)
Methane	8 (62.5)	7 (57.1)	32 (71.9)	27 (55.6)	29 (79.3)	26 (57.7)
Methanol	11 (45.5)	10 (50.0)	37 (73.0)	33 (66.7)	34 (76.5)	31 (67.7)
Methyl ethyl ketone	11 (36.4)	10 (40.0)	32 (34.4)	32 (40.6)	29 (34.5)	29 (37.9)
Methyl isobutyl ketone	11 (36.4)	10 (40.0)	32 (34.4)	32 (40.6)	29 (34.5)	29 (37.9)
Monoethanolamine	11 (45.5)	10 (50.0)	36 (66.7)	32 (62.5)	33 (69.7)	30 (63.3)
Nonane	11 (36.4)	10 (40.0)	30 (26.7)	31 (38.7)	27 (29.6)	29 (37.9)
Phosphoric acid	11 (36.4)	10 (30.0)	33 (39.4)	32 (37.5)	30 (40.0)	30 (36.7)
Potassium hydroxide	11 (36.4)	10 (40.0)	33 (36.4)	31 (38.7)	30 (36.7)	29 (37.9)
Propylene	8 (44.4)	8 (37.5)	35 (77.1)	28 (57.1)	31 (80.6)	26 (57.7)
Sodium carbonate	10 (50.0)	9 (55.6)	33 (54.5)	31 (64.5)	30 (60.0)	29 (65.5)
Sodium hydroxide	12 (83.3)	10 (80.0)	40 (90.0)	37 (91.9)	36 (91.7)	34 (94.1)
Sodium sulfite	8 (44.4)	7 (42.9)	28 (39.3)	24 (37.5)	25 (40.0)	23 (39.1)
Styrene	11 (36.4)	10 (40.0)	33 (51.5)	31 (45.2)	30 (53.3)	28 (42.9)
Sulfuric acid	10 (80.0)	8 (75.0)	34 (85.3)	27 (74.1)	30 (86.7)	25 (76.0)
Tergitols	11 (45.5)	10 (50.0)	36 (61.1)	32 (62.5)	33 (63.6)	30 (63.3)
Tetraethylene glycol	11 (36.4)	10 (40.0)	33 (36.4)	31 (38.7)	30 (36.7)	29 (37.9)
Toluene	11 (36.4)	10 (40.0)	33 (51.5)	32 (46.9)	30 (53.3)	29 (44.8)
Trichloroethane	8 (44.4)	7 (42.9)	28 (39.3)	24 (41.7)	25 (40.0)	23 (43.5)
Triethylene glycol	11 (36.4)	10 (40.0)	33 (36.4)	31 (38.7)	30 (36.7)	29 (37.9)
Vinyl acetate	11 (54.5)	10 (60.0)	36 (47.2)	35 (51.4)	33 (48.5)	32 (50.0)

* Chemicals listed are those to which at least 4 cases could have been "exposed"
† No. refers to designated number of employees whose exposure status could be determined
‡ Refers to percent exposed

ly than either control group 1 or control group 2. When the comparison was restricted to hourly controls, only methane was dropped from this list. Due to the small differences between these proportions and the small numbers on which these proportions are based, none of the differences described are statistically significant.

Discussion

The results of this study have failed to identify any specific associations between brain tumors and exposure to five known or suspect carcinogens used at the UCC Texas City plant. This conclusion is based on the finding that employees who did not have malignant brain tumors were exposed to these carcinogens as frequently as employees who had primary brain tumors. This same result was found when a minimum 15-year latent period was required between the date of first exposure and the date of death.

The examination of an additional 37 chemicals to which a minimum of four cases had been exposed resulted in identification of 12 for which exposure frequencies among cases were higher than among hourly controls when a 15-year latent period was considered. Alternatively, cases were

Table 8. – Proportions of Cases, Controls and Hourly Controls "Ever Exposed" 15 Years or More Prior to Death by Chemical

Chemicals*	All cases No.† (%)‡	Gliomas No. (%)	Control 1 No. (%)	Control 2 No. (%)	Hourly Control 1 No. (%)	Hourly Control 2 No. (%)
Acetaldehyde	9 (22.2)	8 (25.0)	32 (31.3)	28 (46.4)	28 (35.7)	26 (46.2)
Acetic acid	10 (20.0)	9 (22.2)	35 (48.6)	30 (46.7)	31 (51.6)	28 (46.4)
Acetone	10 (70.0)	9 (77.8)	37 (70.3)	31 (74.2)	33 (75.8)	29 (75.9)
Butadiene	9 (44.4)	7 (42.9)	31 (58.1)	24 (58.3)	27 (63.0)	23 (60.9)
Carbon dioxide	9 (55.6)	8 (62.5)	34 (44.1)	28 (57.1)	30 (50.0)	26 (57.7)
Chlorine	9 (44.4)	7 (42.9)	30 (26.7)	23 (26.1)	26 (26.9)	22 (27.3)
Diethanolamine	10 (40.0)	9 (44.4)	33 (42.4)	27 (48.1)	29 (44.8)	26 (50.0)
Diethylene glycol	10 (30.0)	9 (33.3)	31 (25.8)	26 (23.1)	27 (25.9)	25 (24.0)
Ethanol	10 (40.0)	9 (33.3)	32 (40.6)	27 (25.9)	28 (42.9)	26 (26.9)
Ethylene	9 (88.9)	8 (87.5)	34 (55.9)	25 (52.0)	30 (60.0)	24 (54.2)
Ethylene glycol	10 (30.0)	9 (33.3)	33 (39.4)	30 (50.0)	29 (41.4)	28 (50.0)
Hydrochloric acid	10 (50.0)	9 (55.6)	35 (48.6)	28 (57.1)	31 (51.6)	26 (57.7)
Hydroxypropyl acrylate	10 (20.0)	9 (22.2)	32 (21.9)	27 (29.6)	28 (25.0)	25 (28.0)
Isopropanol	10 (40.0)	9 (44.4)	35 (37.1)	28 (42.9)	31 (38.7)	26 (42.3)
Isopropyl acetate	10 (20.0)	9 (22.2)	35 (42.9)	30 (46.7)	31 (45.2)	28 (46.4)
Isopropyl peroxydicarbonate	10 (30.0)	9 (33.3)	32 (21.9)	27 (29.6)	28 (25.0)	25 (28.0)
Lubricating oils	9 (33.3)	8 (37.5)	34 (44.1)	29 (62.1)	30 (50.0)	27 (63.0)
Methane	8 (62.5)	7 (57.1)	32 (53.1)	25 (52.0)	28 (60.7)	24 (54.2)
Methanol	10 (40.0)	9 (44.4)	33 (63.6)	27 (59.3)	29 (69.0)	26 (61.5)
Methyl ethyl ketone	10 (30.0)	9 (33.3)	33 (27.3)	27 (29.6)	29 (27.6)	25 (28.0)
Methyl isobutyl ketone	10 (20.0)	9 (22.2)	33 (27.3)	27 (29.6)	29 (27.6)	25 (28.0)
Monoethanolamine	10 (40.0)	9 (44.4)	33 (48.5)	27 (48.1)	29 (51.7)	26 (50.0)
Nonane	10 (20.0)	9 (22.2)	32 (21.9)	27 (29.6)	28 (25.0)	25 (28.0)
Phosphoric acid	10 (20.0)	9 (22.2)	31 (22.6)	27 (22.2)	27 (22.2)	26 (23.1)
Potassium hydroxide	10 (30.0)	9 (33.3)	31 (25.8)	26 (23.1)	27 (25.9)	25 (24.0)
Propylene	9 (33.3)	8 (37.5)	34 (61.8)	25 (48.0)	30 (66.7)	24 (50.0)
Sodium carbonate	9 (33.3)	8 (37.5)	34 (41.2)	28 (57.1)	30 (46.7)	26 (57.7)
Sodium hydroxide	11 (81.8)	9 (77.8)	37 (81.1)	31 (80.6)	33 (84.8)	29 (82.8)
Sodium sulfite	9 (44.4)	7 (42.9)	30 (26.7)	23 (26.1)	26 (26.9)	22 (27.3)
Styrene	10 (20.0)	9 (22.2)	33 (39.4)	27 (29.6)	29 (41.4)	25 (28.0)
Sulfuric acid	10 (80.0)	8 (75.0)	34 (70.6)	25 (64.0)	30 (73.3)	24 (66.7)
Tergitols	10 (40.0)	9 (44.4)	33 (42.4)	27 (48.1)	29 (44.8)	26 (50.0)
Tetraethylene glycol	10 (30.0)	9 (33.3)	31 (25.8)	26 (23.1)	27 (25.9)	25 (24.0)
Toluene	10 (20.0)	9 (22.2)	33 (39.4)	27 (33.3)	29 (41.4)	25 (32.0)
Trichloroethane	9 (44.4)	7 (42.9)	30 (30.0)	23 (30.4)	26 (30.8)	22 (31.8)
Triethylene glycol	10 (30.0)	9 (33.3)	31 (25.8)	26 (23.1)	27 (25.9)	25 (24.0)
Vinyl acetate	10 (50.0)	9 (55.6)	33 (36.4)	29 (37.9)	29 (37.9)	27 (37.0)

* Chemicals listed are those to which at least 4 cases could have been "exposed"

† No. refers to designated number of employees whose exposure status could be determined

‡ Refers to percent exposed

exposed less frequently than controls for 18 chemicals. None of these differences were statistically significant.

For the 12 chemicals identified with higher exposure frequencies among cases, carcinogenic potential was assessed using several computerized data bases. (Files searched included *Medline* [1976-present], *Toxline* [1974-present], *Registry of Toxic Effects of Chemical Substances* [RTECS] and *Toxicology Data Base.)* For four – isopropyl peroxydicarbonate, methyl ethyl ketone, sodium sulfite and tetraethylene glycol – the lack of available information suggested that few studies have been done to assess carcinogenicity. (Tetraethylene glycol is reported as "mutagenic.") For the remaining eight chemicals some information on carcinogenicity is available. Ethylene, sulfuric acid, and vinyl acetate have not been found to be carcinogenic in any of the studies reported to date. For five chemicals – chlorine, diethylene glycol, potassium hydroxide, trichloroethane and triethylene glycol – some evidence of carcinogenic potential has been reported. For chlorine, several epidemiologic studies have reported a link between chlorinated drinking water and cancer of the rectum, colon, and bladder.[6] Diethylene glycol is reported to have in-

creased bladder tumors in laboratory animals – likely a secondary effect of the ability of this substance to form bladder stones. There is no other evidence to implicate this substance as a primary carcinogen or mutagen. Potassium hydroxide produced skin tumors at the site of application in one mouse skin painting study; however, skin irritants are known to be capable of inducing an increase of skin tumors in laboratory animals. For trichloroethane, one of the two isomers (1,1,2) has shown positive results, but only in mice (not in rats).[7] The other isomer (1,1,1) has shown no evidence of carcinogenicity in mice or rats[8-10] and this is the isomer that has been handled almost exclusively at the Texas City plant. Intraperitoneal injections of triethylene glycol at extremely high levels has produced an increased incidence of lung tumors in mice. Most other reported studies for this substance have been negative, including a two-year rat feeding study.

On the basis of this information it is not likely that any of these 12 chemicals are causally associated with the brain tumor cases at the Texas City plant. Rather, it is more likely that these results were attributable to chance. Considering the way in which the 37 chemicals were selected, i.e., the requirement that at least 13% (4/21) of the cases were exposed, it is not surprising that for a few, exposures among cases were higher than among controls.

One of the principal methodological constraints of this study is that the control groups were selected from former employees whose deaths were known to the company. As a result, former UCC Texas City employees who voluntarily terminated employment before retirement or were laid off were underrepresented among controls. It can be argued that this restriction may have biased the study results since employees not represented among the controls had shorter lengths of employment and consequently less opportunity for exposure. However, the actual difference in average number of employment years among case and control series was less than 1.5 years – too small to have had a meaningful effect. In addition, the observation that a higher percentage of cases had less than 10 years of company service than controls draws attention to the fact that employment and potential exposures outside of UCC Texas City have not been considered in this or in NIOSH investigations.

A second limitation of this study regards the problem of accurately determining exposures among cases and controls. Because the Texas City plant (and all chemical plants in general) requires a high percentage of the work force to be employed in maintenance activities, worker mobility is extremely high and tracing employees from day to day is very difficult. As a result of this constraint, exposures to specific chemicals could not be determined with accuracy for approximately half of the employees. For this reason and because of the extremely small numbers involved, the results of this study must be interpreted cautiously. However, to the extent that employee exposures were known, no evidence of a significant association between exposures to specific chemicals and employment at the Texas City plant were found.

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