

Mortality Among Ethylene Oxide Workers

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Because of reports linking an increased risk of leukemia with exposure to ethylene oxide, a mortality study of workers with potential exposure to ethylene oxide at the Texaco Chemical Company Plant in Port Neches, Tex., was undertaken. A total of 767 males with potential exposure to ethylene oxide were identified. Forty-six deaths occurred in this cohort with 80 expected (standardized mortality ratio; SMR = 58). No deaths from leukemia were seen, nor were there any statistically significant excesses from any specific causes of death.

Ethylene oxide is a common industrial chemical with annual U.S. production probably exceeding 5,000 million pounds. It is used for the manufacture of numerous other chemicals, especially ethylene glycol, and used directly alone as a fumigant and sterilizing gas, especially in the hospital industry.

The human health effects usually attributed to ethylene oxide are those of acute toxicity and include effects due to irritation of skin and eyes, headache, vomiting, dyspnea, diarrhea, and lymphocytosis.^{1,2} A previous study³ demonstrated no long-term effects, although skin sensitization has been reported in a human experiment.⁴ Furthermore, on the basis of extrapolation from animals to humans, earlier authors have speculated on the genetic risk to man due to ethylene oxide exposure.^{5,6}

Two recent studies have shown an increased risk of leukemia following occupational exposure to ethylene oxide. Three cases of leukemia occurred in a small group of Swedish workers using ethylene oxide for the sterilization of hospital equipment.⁷ The expected number of leukemia cases based on national incidence rates was 0.2.

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This study was performed by SRI International under a contract with Texaco Inc.

The time-weighted average ethylene oxide concentration was 20 ± 10 ppm.

Another study of mortality and cancer incidence in a cohort of workers with full-time exposure to ethylene oxide at a Swedish company engaged in the production of ethylene oxide since the early 1940s found 23 observed deaths with 13.5 deaths expected.⁸ Observed numbers of deaths were elevated for malignant neoplasms (9 observed vs. 3.4 expected), cancer of the stomach (3 observed vs. 0.4 expected), leukemia (2 observed vs. 0.14 expected), and diseases of the circulatory system (12 observed vs. 6.3 expected). Among 89 maintenance workers with intermittent exposure there were 3 observed deaths from malignant neoplasms with 3.4 expected and 1 death each from stomach cancer (expected deaths = 0.4) and leukemia (expected deaths = 0.13). There were 8 deaths from diseases of the circulatory system with 6.6 expected. Total deaths for maintenance workers were 14 with 13.5 expected. Most exposures to ethylene oxide were below 14 ppm, although much higher peaks occurred.

For 66 other workers never exposed to ethylene oxide, there were 10 deaths with 8.3 expected. There was only 1 death from malignant neoplasms with 2.0 expected deaths. Among these 66 men, there were also 6 deaths from diseases of the circulatory system and 3.5 expected deaths.

The Texaco Chemical Company Plant (formerly Jefferson Chemical Company Plant) in Port Neches, Tex., has been in continuous production of ethylene oxide since 1948. The plant occupies 1,100 acres. An industrial hygiene survey of this plant was performed in July 1977 by SRI International. At that time there were 750 persons employed; 100 of these workers were potentially exposed to ethylene oxide, with about 60 of the workers being directly involved in the production of ethylene oxide. There is an accurate up-to-date service recordkeeping system for all active and past hourly and salaried employees. Plant records date back to 1948, the year the plant began operation, and include records of employees working in 1955 or hired thereafter. The records of employees who terminated prior to 1955, however, have been purged from the files.

Table 1. — Observed and Expected Deaths and SMRs in Males Exposed to Ethylene Oxide.

Cause	Deaths Observed	Deaths Expected	SMR (x100)	95% Confidence Limits of SMR (x100)	
				Lower	Upper
All causes	46	80.00	58	42	77
All malignant neoplasms	11	15.24	72	36	129
Pancreatic cancer	3	0.80	377	76	1102
Bladder cancer	1	0.31	322	4	1794
Brain and CNS cancer	2	0.70	285	32	1030
Hodgkin's disease	2	0.35	570	64	2058
Leukemia	0	0.70	0	0	523
Allergic, endocrine, and metabolic diseases	0	1.47	0	0	249
All circulatory causes	20	31.36	64	39	99
All respiratory causes	1	3.58	28	0	106
All digestive diseases	1	4.87	21	0	118
All genitourinary diseases	1	0.89	112	1	622
All external causes	6	14.68	41	15	89
Unknown	4				

At the time of the industrial hygiene survey, detailed notes were made concerning the job classifications of all workers potentially exposed to ethylene oxide. Environmental sampling of the ethylene oxide production units that were operating and of the oxide derivative units was performed using the Century Organic Vapor Analyzer, Model 128. Pump, valve, pipe flanges, spigots and gauges in the production area were monitored. The instrument detected virtually no ethylene oxide in the area; where there was an indication, the gas chromatograph was used to quantitate the concentration. All readings at these sources were less than 10 ppm ethylene oxide. Only at the tank car loading operations did the instrument detect an elevated reading, approximately 6,000 ppm, escaping from a leak on the slip tube used to gauge the level of ethylene oxide in the car. This leak was stopped by tightening the packaging around the gauging tube. All other readings observed during the walk-through survey of the operating units were well below the Occupational Safety and Health Administration limits of 50 ppm for an eight-hour time-weighted averaged exposure. The precautions taken in the handling of ethylene oxide were, therefore, effective in maintaining the concentration well below the current federally mandated standards.

The industrial hygiene walk-through survey at this plant was performed as part of an industry-wide industrial hygiene study concerning ethylene oxide. Survey results for all of the visited sites were similar. The low levels of ethylene oxide found throughout the plants can be attributed to three major factors: (1) a completely closed system is used for the storage, transferral, and production of ethylene oxide; (2) the many precautionary measures and design considerations intended to prevent fire danger also reduce the potential exposure to workers in the area; and (3) ethylene oxide reaction systems are out-of-doors so that great natural air volume and movement disperse any leaking gas quickly.

Methods

This paper describes the mortality experience of a population of employees potentially exposed to ethylene

oxide at the Texaco Chemical Company Plant in Port Neches, Tex. The work history records of these employees were screened at the plant by SRI's research staff in October 1978. To be accepted as an eligible cohort member, an individual had to have worked at the plant between January 1955 and December 31, 1977, and to have been employed for at least five years. Records of eligible individuals were microfilmed.

Texaco Chemical Company personnel determined whether an individual was potentially exposed or unexposed to ethylene oxide based on his work history. Vital status was determined from plant records, personal knowledge, and telephone follow-up.

Demographic information for each cohort member — including name, race, sex, Social Security number, employment and vital status, and birth, hire, and termination dates — and potential exposure data were coded. Vital status could not be determined for less than 5% of the cohort. If a cohort member died within the study dates, SRI searched for and obtained the death certificate. Death certificates for 4 of the 46 dead in the exposed male population could not be located. Three deaths occurred in the unexposed male population.

The date of death, age at death, and underlying cause of death were coded by a trained nosologist. Deaths occurring before 1968 were coded by the 7th Revision of the International Classification of Diseases; all deaths occurring after 1967 were coded by the 8th Revision, then converted to the 7th Revision.

Analysis

A modified life table program⁹ was used to compare the mortality experience of ethylene oxide workers with the pattern expected on the basis of U.S. vital statistics. The experience of all 850 workers was analyzed, with separate analyses for all 812 males (49 deaths), and 767 males exposed to ethylene oxide (46 deaths) and the 38 females (no deaths). Only results for the exposed males are included in this paper, although the complete results are available upon request.

Table 1 shows the mortality experience for selected

Table 2. — Observed and Expected Deaths and SMRs in Males Exposed to Ethylene Oxide SMRs Corrected for Unknown Cause of Death.

Cause	Deaths Observed	Deaths Expected	SMR (x100)	95% Confidence Limits of SMR (x100)	
				Lower	Upper
All causes	46	80.00	58	42	77
All malignant neoplasms	11	15.24	79	41	138
Pancreatic cancer	3	0.80	411	94	1149
Bladder cancer	1	0.31	353	15	1847
Brain and CNS cancer	2	0.70	313	45	1074
Hodgkin's disease	2	0.35	626	90	2147
Leukemia	0	0.70	0	0	523
Allergic, endocrine, and metabolic diseases	0	1.47	0	0	249
All circulatory causes	20	31.36	70	44	106
All respiratory causes	1	3.58	31	1	160
All digestive diseases	1	4.87	22	1	118
All genitourinary diseases	1	0.89	123	5	643
All external causes	6	14.68	45	17	94
Unknown	4				

causes of death for males characterized as exposed. Because death certificates could not be obtained for nearly 10% (i.e., 4 out of 46) of the deaths among these individuals, Table 2 shows the same results under the assumption that these deaths from unknown causes are distributed by cause in the same manner as the 42 deaths with known cause. This slightly raises the standardized mortality ratios (SMRs) for these causes but has little effect on the findings.

The specific causes presented in these tables include cancers of several sites, including all those with elevated SMRs. Major nonneoplastic categories of causes of death with relatively large expected numbers of deaths also are presented. A complete listing of observed and expected deaths and SMRs for all causes analyzed by the modified life table program is available upon request.

The tables illustrate a greatly reduced overall mortality, with an SMR of 58 and an upper 95% confidence limit of 77. The only excesses seen are those in a few cancers (pancreas, bladder, brain, and Hodgkin's disease). Each of these SMRs is based on 3 or fewer observed deaths and has a lower 95% confidence limit under 100, that is, not statistically significantly elevated. Only one death from cancer of the lung is seen, and, except for the two deaths from Hodgkin's disease, there are no deaths from cancer of the lymphatic and hematopoietic system. There is no increased risk of death from any of the nonneoplastic causes.

Although no increased risk of leukemia was seen, the cohort size was small. A calculation of the amount of excess risk that could be detected was performed. Based on the sample size of this cohort (13,969 person-years of observation for the exposed male population), an excess of leukemia deaths as small as 10.5-fold could be detected at the 95% confidence level with a power of 80%.¹⁰

Summary and Conclusions

Although it is difficult to make a definitive conclusion in the face of small numbers, it is clear that there is no

major mortality excess among ethylene oxide workers although this group of workers appeared, at least recently, to have only minimal exposure. Because this plant is one of the largest and oldest producers of ethylene oxide in the United States, any excess risk of leukemia due to ethylene oxide exposure might be expected to appear here first. The number of expected deaths due to leukemia was less than one so the occurrence of no deaths was not unexpected. However, it does not appear from the results that ethylene oxide is a strong leukemogen.

Indeed, these workers appear to enjoy a mortality rate less than expected, for both cancer and noncancerous causes. The possible exceptions to this could be cancers of the pancreas, bladder and brain, and Hodgkin's disease where the SMRs all exceed 250, albeit with very small numbers. Although there is a considerable likelihood that this could be due to chance, the possibility of a causal workplace exposure cannot be dismissed.

The elevated SMR for cancer of the pancreas is interesting because several other recent studies of occupational groups have shown similar results. Li et al¹¹ found an increased risk of pancreatic cancer (PMR = $p < 0.01$) among members of the American Chemical Society who died between 1948 and 1967. No specific chemicals were implicated. Thomas et al¹² found an excess proportionate mortality ratio (PMR = 338, $p < 0.05$) for pancreatic cancer among deceased Texas Oil, Chemical and Atomic Workers' Union members who were engaged in petroleum refining and production of petrochemicals. The PMRs were higher among workers with fewer than 10 years of union membership, but because the union was not formed until the 1940s, all early deaths are necessarily in this category. Pickle and Gottlieb¹³ investigated high pancreatic cancer mortality among white males in a cluster of Louisiana parishes. Using occupation as recorded on the death certificate, they found an odds ratio of 2.11 for those in oil refining industries, although the odds ratio was not statistically significant, and they found a slightly elevated odds ratio for residents near refineries.

Buffler¹⁴ studied the association between cancer of the pancreas and employment at selected chemical companies in Orange and Jefferson counties, Texas, and found that the subjects with cancer were more than twice as likely as the controls to have been employed by the participating companies.

The other cancers for which the SMRs are elevated are also among those that have been associated with occupation. For these reasons, Texaco intends to continue monitoring the mortality experience of persons potentially exposed to ethylene oxide.

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John Fitzgerald Kennedy

It can be said of him, as of few men in a like position, that he did not fear the weather, and did not trim his sails, but instead challenged the wind itself, to improve its direction and to cause it to blow more softly and more kindly over the world and its people.

— E. B. White, The J. F. Kennedy Memorial, Boston.