

Excess Leukemia in a Refinery.. Population

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A retrospective follow-up mortality study of white male employees of an oil refinery located in southern Illinois revealed a statistically significant excess number of deaths due to leukemia compared with the experience of U.S. white males (standardized mortality ratio [SMR] = 213; 95% confidence interval [CI], 117 to 358). The excess was due mainly to acute myeloid leukemia (AML) (SMR = 394; 95% CI, 172 to 788). From 1973 to 1982, fourteen leukemia deaths were identified; eight of the cancers were of the AML cell type. The work histories of the decedents were examined for the potential for benzene exposure. Although specificity of the work histories was limited, the investigation has shown that the subjects did not work in jobs identified as having the highest benzene exposures. At this time, the excess leukemia remains unexplained.

Exposure to benzene at high levels is associated with an increased risk of acute myeloid leukemia (AML) development.^{1,2} Although many petroleum refinery workers have had some exposure to benzene, mortality studies of these workers have not shown a pattern of excess leukemia.³ This report presents the results of a study of refinery workers in whom an excess leukemia was found.

Methods

The Wood River Refinery located in southern Illinois began operations in 1918 and currently produces a full line of refinery products. A research laboratory operated on the site from 1933 to 1975.

The study population consisted of all white male employees (salaried and hourly) who had worked at the Wood River Refinery for at least one day during the 10-year period, Jan. 1, 1973, through Dec. 31, 1982, and retirees whose

last work location was the study refinery and who were alive as of Jan 1, 1973.

Vital status as of Jan. 1, 1983, was determined for all employees and retirees in the study group by the company's pension and life insurance departments. For employees who terminated employment for reasons other than retirement, vital status information was not obtained. These individuals thus are treated as lost to follow-up.

Because a death certificate is required as proof of death before the payment of benefits to a surviving spouse, most certificates are received by the company. Those not received were requested from the appropriate state vital statistics departments. For each death certificate, the underlying cause of death was coded to the eighth revision of the International Classification of Diseases by a trained nosologist.*

A person entered the study on Jan. 1, 1973, if he began employment on or before that date. Otherwise, he entered the study the day employment started. Person-years were accumulated from the entry date to the date of death, the date of termination, or the study end date, whichever came first. Standardized mortality ratios (SMRs) adjusted for age using the U.S. white male death rates as the standard were calculated.¹⁰ (Leukemia rates for the county in which the refinery is located were virtually the same as U.S. rates.) An additional analysis of cell-type-specific SMRs was done using the Surveillance, Epidemiology and End Results mortality rates for white males, all regions combined, 1973 to 1977.¹¹ The 95% confidence intervals (CIs) of the SMRs were also estimated.¹²

The employment history of each person who died of leukemia was also investigated. Employment history before working at Wood River Refinery was identified from pre-employment application forms. A work history record, kept for payroll purposes, listed department and job title by time period.

Results

The study population included 3,976 white men. About half of the cohort began employment before 1948, and 68% of the cohort had become pensioners before the end of the study period. The mean age of the population on the day of entry into the cohort was 49 years.

Eight percent of employees left employment for reasons

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Table 1—Numbers of Observed and Expected Deaths and SMRs According to Cause*

Cause of Death	Observed	Expected	SMR	95% CI
All causes	640	637.6	76†	71-83
All malignant neoplasms	161	177.0	91	77-106
Leukemia/leukemia	14	6.6	213†	117-358
Lymphosarcoma and reticulosarcoma	0	28	0	<130
Hodgkin's disease	2	1.0	200	22-722
Cancer of other lymphatic tissue	6	4.8	126	46-274
Other malignant neoplasms	139	161.8	86	72-101
All diseases of the blood and blood-forming organs	2	1.8	111	13-402
All diseases of the circulatory system	361	470.0	77†	69-85
All respiratory tract diseases	28	64.2	44†	29-63
All diseases of the digestive system	15	30.6	49†	27-81

* U.S. white males is the comparison population

† An SMR is statistically significant at $p < .05$ if the 95% CI does not include 100

Table 2—Leukemia Cell-Specific SMRs for Specific Forms of Leukemia.

Form	Observed	Expected	SMR	95% CI
Acute lymphatic	1	0.3	340	4-1,854
Chronic lymphatic	1	1.3	74	1-428
Acute myeloid	8	2.0	394†	172-788
Chronic myeloid	1	0.8	121	2-696
Acute monocytic	1	0.2	661	6-2,782
Other and Nonspecified	2	2.0	100	11-361

* Surveillance. Epidemiology and End Results white males, all regions combined. is the comparison population

† An SMR is statistically significant at the $p < .05$ level if the 95% CI does not include 100

other than retirement and were therefore lost to follow-up. At the time of their leaving, 94% of this lost to follow-up group was under 40 years of age and 73% had five years or less of employment.

There were 640 deaths from all causes with 838 expected, an overall SMR of 76. Table 1 lists the SMRs for major causes of death and for leukemia. The SMRs for all causes, all diseases of the circulatory system, all diseases of the respiratory system, and all diseases of the digestive system are lower than expected, with the differences statistically significant.

For leukemia, there were 14 deaths observed with 6.6 expected, an SMR of 213 with a 95% CI of 117 to 358. In 12 cases cell type was specified on the death certificate and, of these, eight were of the acute myelogenous cell type (AML). Two deaths from AML were expected; thus, the SMR for AML is 394 (95% CI, 172 to 788). Similar increases in acute lymphatic and acute monocytic leukemia

were observed but are based on numbers too small to be interpretable (Table 2). No lymphosarcoma or reticulosarcoma was seen even though 28 cases were expected.

Three of the leukemia patients had held laboratory jobs. Five spent most of their careers as maintenance workers, but it is not known if they were ever assigned to benzene units. None of the case subjects was an operator in the benzene units or a loader in the dispatching department. Six subjects (two draftsmen, a patrolman, and three compounders) probably had no benzene exposure above refinery background level. According to the company's employment application forms, two had worked at other oil companies before being employed at the Wood River Refinery.

Discussion

The identification of excess leukemia deaths in an oil refinery population prompted a retrospective follow-up study. A twofold increase in leukemia was observed. Virtually all of the excess number of leukemia cases were of the AML type.

US males seem an appropriate comparison population since the proportion of deaths from leukemia is 0.80% for the United States, 0.80% for Illinois, and 0.84% for Madison County, the county in which the refinery is located. Leukemia probably is not overdiagnosed in this region and overdiagnosis of AML is unlikely.

At the Wood River Refinery, the concentration of benzene in refinery streams did not exceed 5% until 1942 when the toluene units were built with one stream of 5% to 10% benzene. Subsequently, several units with benzene streams from 5% to 100% were constructed. These included a cumene unit (operating from 1943 to 1945), a dodecyl benzene unit (1950 to 1954), benzene extraction units (1960 to present), and catalytic reforming units (1960 to present).

Benzene, as well as other solvents, was used both in the quality-control laboratory (1941 to present) and in the research laboratory (1933 to 1975) in several tests and intermittently in the cleaning of glassware. Benzene and benzene-containing compounds were transferred to barges and tank cars and to and from trucks in the dispatching department. Purchases of coal-derived benzene used in refinery processes were made periodically from 1943 to the present.

What might account for the differences between this study and other studies of refinery workers? Although refineries are basically similar, we do not have the specific information necessary to compare the operations at the Wood River Refinery with the operations in other refineries that have been studied. In addition, the Wood River Refinery purchased both finished and crude coal-derived benzene.

A recent study of rubber workers found a stronger association between coal-derived solvents and lymphocytic leukemia than between petroleum-derived solvents and lymphocytic leukemia."

Another difference between the present study and others is the cell-specific analysis. The SMR for leukemia as a whole is modest when compared with that for AML. It is possible that other refinery studies could have an elevation in AML that is diluted by the summary SMR for all cell types of leukemia combined.

Since AML has been associated with benzene exposure, work histories of the case subjects were reviewed with company industrial hygienists to assess potential for exposure. While individual exposures cannot be defined completely by this preliminary study, it was determined that the subjects had not been assigned to jobs deemed to have the highest potential for exposure, i.e., processes involving high concentrations of benzene. Efforts are under way to provide a more definitive assessment of the effects of past exposures.

At this time, the excess of leukemia remains unexplained.

Acknowledgments

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Medicine: The Icy Science?

The other day, my doctor sat at my bedside just to talk. He assured me my physical complaints will be eased and that he will be in regular attendance. We talked frankly of the dying process and the need of living as I am dying: living to fully appreciate every moment of life. I liked our conversation, but it is hard to come by. Most physicians have lost the pearl that was once an intimate part of medicine, and this is humanism. Medicine is now an icy science; its charm belongs to another age. The dying man can get little comfort from the mechanical doctor.

—From "Thoughts of a Dying Physician" by F. Stenn in *Forum on Medicine*. Vol. 3:718-719, 1979.