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American Petroleum Institute
1220 L Street, Northwest
Washington, D.C. 20005

Robert T. Drew, Ph.D.
Director, Health and
Environmental Sciences
(202) 682-8308
(202) 682-8270 (FAX)

FYI-93-000898
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September 23, 1993

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(Identification no: FYI not assigned) A Nested Case-Control Study of Kidney Cancer, Leukemia and Multiple Myeloma in a Cohort of Land-Based Terminal Workers Exposed To Gasoline in the Petroleum Industry. Document No. 0300-015-015, ENSR Health Sciences.

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Sincerely,

Robert T. Drew, Ph.D.

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American Petroleum Institute

Washington, D. C.

ENSR

A Nested Case-Control Study of Kidney Cancer, Leukemia and Multiple Myeloma in a Cohort of Land-Based Terminal Workers Exposed to Gasoline in the Petroleum Industry

ENSR Health Sciences

August 1993

Document Number 0300-015-015

ENSR

A Nested Case-Control Study of Kidney Cancer, Leukemia and Multiple Myeloma in a Cohort of Land-Based Terminal Workers Exposed to Gasoline in the Petroleum Industry

ENSR Document No. 0300-015-015
September 1993

Prepared for

American Petroleum Institute
Washington, D. C.

by:
Otto Wong, Sc.D., F.A.C.E
Principal Investigator
Chief Epidemiologist
Applied Health Sciences
181 Second Avenue, Suite 628
San Mateo, California 94401

and

Lisa Trent, M.S.
Biostatistician
ENSR Health Sciences

ENSR Health Sciences
1320 Harbor Bay Parkway
Alameda, California 94501

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ACKNOWLEDGEMENTS

The authors of this report (Otto Wong at Applied Health Sciences and Lisa Trent at ENSR Health Sciences) wish to express their appreciation to:

- Professor Thomas J. Smith, University of Massachusetts (now at Harvard University), for providing exposure estimates

- The External Reviewers for comments and suggestions:

  Professor Philip E. Enterline, University of Pittsburgh
  Professor Melvin W. First, Harvard University
  Professor David H. Wegman, University of Massachusetts

- The Task Force Members for valuable support and assistance:

  Mr. William J. Bailey (Co-Chair), Chevron
  Mr. Norman C. Zeiser (Co-Chair), Chevron
  Dr. David M. Batey, Exxon
  Mr. James S. Branham, Exxon
  Dr. Sally R. Cowles, Shell
  Dr. Barbara J. Divine, Texaco
  Ms. Jane E. Keller, Mobil
  Mr. Stephen E. Killiany, Jr., Exxon
  Dr. Gerhard K. Raabe, Mobil
  Mr. Jerry D. Ransdell, Shell
  Ms. Leba Shallenberger, Exxon
  Mr. Wayne J. Skocypec, Mobil

- Mr. David Mongillo, American Petroleum Institute, for administrative support

- American Petroleum Institute for sponsoring the project

- The participating companies for providing data

- ENSR staff, especially Ms. Laura Akin, for administrative and technical support

SUMMARY

This nested case-control study is based on the data in a cohort mortality study of marketing and marine distribution workers with potential exposure to gasoline in the petroleum industry. The original cohort consisted of 18,135 employees from four petroleum companies. The results of the cohort study have been reported elsewhere (Wong and Harris, 1992; Wong, et al., 1993). Four diseases were selected for additional analyses in this case-control study: leukemia (all cell types), acute myeloid leukemia (AML), kidney cancer and multiple myeloma. The case-control study was limited to the land-based workers, because of the availability of quantitative exposure data.

The cases were defined as deceased cohort members whose death certificates listed any one of these diseases either as the underlying cause of death or as a contributory cause of death. Included in the analyses were 35 leukemia cases (all cell types), 13 acute myeloid leukemia cases, 13 kidney cancer cases and 11 multiple myeloma cases. For each case, five individually matched controls were selected, except for one leukemia case the number of eligible controls was only three, and for one AML case no controls could be found.

In the original cohort study, broad generic job categories were used as part of exposure assessment. In the present case-control study, a finer and more homogeneous job classification was developed. In addition to job category, several quantitative gasoline exposure indices were used in the analyses: length of exposure, cumulative exposure (ppm-years in terms of total hydrocarbons) and frequency of peak exposure. Time period of first exposure to gasoline (≤1948 vs. ≥1949) was also included as an exposure index.

Analyses based on the Mantel-Haenszel χ^2 and conditional multiple logistic regression were performed for each of the four diseases. Although statistically nonsignificant excesses were found for some job categories, these excesses did not appear to be related to gasoline exposure. For example, nonsignificant increases of leukemia (all cell types) and kidney cancer were found for the category of "foremen/supervisors," whose job functions entailed relatively low exposure. On the other hand, among the new job categories created, "mechanics" and "maintenance/yard workers" were considered to have higher exposure than the others. Neither of these two groups showed any increased risk. Analyses using logistic regression models based on length of exposure, cumulative exposure, and frequency of peak exposure did not find any increased risk or exposure-effect relationship between these exposure indices and any of the four diseases. Time period of first exposure to gasoline (≤1948 vs. ≥1949) was also found to be unrelated to the four diseases under investigation.

Based on the results of this nested case-control study as well as the findings in the original cohort study, we conclude that exposure to gasoline at the levels experienced by this cohort is not a significant risk factor for leukemia (all cell types), acute myeloid leukemia, kidney cancer or multiple myeloma.

1.0 BACKGROUND

1.1 Summary of the Original Cohort Study

The present nested case-control study is based on the data in a cohort mortality study of marketing and marine distribution workers with potential exposure to gasoline in the petroleum industry. The cohort study has previously been reported in detail elsewhere (Wong and Harris, 1992; Wong et al., 1993), and will not be repeated here. However, for convenience, a brief summary of the cohort study is provided below.

The original cohort consisted of 18,135 distribution employees with potential exposure to gasoline for at least one year at land-based terminals (N = 9,026) or on marine vessels (N = 9,109) between 1946 and 1985. Four companies participated in the study. The primary objective of the cohort study was to determine the relationship, if any, between exposure to gasoline and mortality from kidney cancer or leukemia. Another cause of death of interest was multiple myeloma. The mortality of the cohort was observed through June 30, 1989.

The results of the cohort study indicated that there was no increased mortality from either kidney cancer, leukemia or multiple myeloma among marketing and marine distribution employees who were exposed to gasoline in the petroleum industry, when compared to the general population (Table 1-1). Among the land-based terminal employees, the kidney cancer standardized mortality ratio (SMR) was 65.4 (12 deaths) and leukemia SMR was 89.1 (27 deaths). For the marine cohort, the SMRs were 83.7 for kidney cancer (12 deaths) and 70.0 for leukemia (16 deaths), respectively. More importantly, based on internal comparisons, there was no association between mortality from kidney cancer or leukemia and various indices of gasoline exposure. In particular, neither duration of employment, duration of exposure, age at first exposure, year of first exposure, job category, cumulative exposure, frequency of peak exposures, nor average intensity of exposure had any effect on kidney cancer or leukemia mortality.

TABLE 1-1

Mortality from Kidney Cancer, Leukemia, and Multiple Myeloma for the Combined Cohort of Land-Based Terminal and Marine Employees Exposed to Gasoline

Cause of Death	Land-Based Terminal	Marine	Combined Cohort
Kidney Cancer			
SMR	65.4	83.7	74.0
Observed Deaths	12	12	24
Leukemia (All Cell Types)			
SMR	89.1	70.0	80.3
Observed Deaths	27	16	43
Acute Myeloid Leukemia			
SMR	150.5	74.2	117.1
Observed Deaths	13	5	18
Multiple Myeloma			
SMR	87.0	70.7	79.4
Observed Deaths	10	7	17

In the past, leukemia was considered a single disease in most occupational epidemiologic studies, partly because of the historical nomenclature, unavailability of cell-type specific rates for comparison, and, most importantly, the paucity of cases by cell type in individual studies. It has now been recognized that the diseases collectively known as leukemia are several distinct malignancies characterized by different patterns of age, sex, race, and ethnicity, and have dissimilar secular trends and different etiologic factors (Linet, 1985). The diversity of cell-type specific leukemias has long been noted by pathologists and hematologists (Wintrobe, et al., 1981). Because of this cell-type difference and the relationship between benzene and acute myeloid leukemia, the latter was also analyzed as a separate entity in the cohort study.

For acute myeloid leukemia (AML), a non-significant mortality increase was found in land-based terminal employees (SMR = 150.5, 13 deaths), but no trend was detected when the data were analyzed by various gasoline exposure indices. Most of the acute myeloid leukemia deaths occurred among land-based terminal employees hired prior to 1948. On the other hand, a deficit of mortality from acute myeloid leukemia was observed among marine employees (SMR = 74.2, 5 deaths). For the two cohorts combined, SMR for acute myeloid leukemia was 117.1 based on 18 deaths (Table 1-1).

We did not find any relationship in our cohort study between gasoline exposure and mortality from multiple myeloma. In the original cohort study, analysis was performed with the use of the University of Pittsburgh OCMAP program (Marsh and Preininger, 1980), and multiple myeloma was analyzed as part of the category "cancer of other lymphatic tissue." No mortality excess or exposure pattern was detected for this heterogeneous category of diseases. Subsequently, a separate analysis for multiple myeloma alone indicated that the SMRs were 87.0 and 70.7 for the land-based terminal and the marine cohort, respectively. For the combined cohort, the multiple myeloma SMR was 79.4, based on 17 deaths (Table 1-1).

1.2 Rationale for the Case-Control Study

In the original study design, it was proposed that case-control analyses on two diseases (such as leukemia and kidney cancer) be performed in addition to the cohort analyses. The rationale for this approach was to provide some additional in-depth analyses that were considered impractical in the cohort study at that time. In particular, a detailed exposure assessment for the cohort was not part of the original study plan. The original strategy was to perform some overall analyses on the cohort data, without the benefit of a detailed exposure profile for every cohort member. According to the original strategy, once the cohort analyses had been completed, then detailed case-control analyses of selected diseases could be performed on a limited number of study subjects. Since the number of study subjects in a case-control study would be much smaller, it would be much more efficient and practical to develop detailed individual exposures. Mantel (1973) was among the first to suggest such an approach.

However, the exposure assessment effort in the cohort study turned out to be much more extensive than originally anticipated (T. J. Smith et al., 1992 and 1993). As a result, we were able to develop for each cohort member an individual gasoline exposure profile in terms of both 8-hour time-weighted average (TWA) of total hydrocarbons and a peak exposure. In the cohort analyses (based on both SMR and the Cox's proportional hazards model), we made extensive use of these quantitative exposure profiles. These cohort analyses based on detailed exposure assessment lessened the need for the originally planned case-control study.

For simplicity and data manageability, the exposure assessment developed in the cohort study was necessarily based on broad generic job categories. Therefore, the case-control study would provide us with an opportunity to re-assess these broad generic job categories, and to possibly develop finer, and presumably more homogeneous, job classifications. Other benefits of the case-control study would include detailed analyses of both acute myeloid leukemia and multiple myeloma, which were part of larger disease categories in the cohort analyses.

Another benefit of the case-control study is that it is based on internal comparisons, which alleviates the potential problems of relying on an external comparison population. However, it must be pointed out that stratified analyses based on SMRs and analyses based on proportional hazards models in the cohort study were not influenced by the choice of an external comparison population either.

2.0 MATERIALS AND METHODS

2.1 Selection of Cases and Controls

In the nested case-control study, cases were identified through the use of death certificates obtained in the cohort study. Both the underlying and contributory causes of death were used in the selection of cases. The four causes of death included in the case-control study and their corresponding 8th Revision of International Classification of Diseases (ICD) codes were as follows:

Disease Category	8th Revision ICD Code
Leukemia (all cell types)	204 - 207
Acute myeloid leukemia	205.0
Kidney cancer	189
Multiple myeloma	203

For each disease of interest, a control group consisting of workers free from the disease was selected as a baseline against which the cases were compared in terms of gasoline exposure. For a proper comparison, controls should be similar to the cases with respect to historical potential for occupational gasoline exposure. In other words, in the absence of a disease-exposure association, the controls and the cases should have had an equal opportunity for exposure.

For each case, five controls were selected from the rest of the cohort; i.e., among workers who were still alive at the end of study and deceased workers whose death certificates did not mention any of these four diseases. The 1:5 case-to-control ratio was chosen based on a consideration of efficiency. According to Ury (1975) and Breslow and Patton (1979), the efficiency of a case-control study with a 1:C ratio, relative to one where an arbitrarily large number of controls is used, is given by: efficiency = C/(C+1). The following table presents the relative efficiency for several case-to-control ratios:

Number of Controls Per Case	Relative Efficiency
1	50%
2	67%
3	75%
4	80%
5	83%
6	86%
7	88%
unlimited number	100%

Thus, a reasonable choice would be 1:5, which would provide an efficiency of 83%. Larger ratios would result in a diminishing return for effort expended.

Controls were randomly selected with the following restrictions. To ensure an equal opportunity for potential exposure, the controls must be alive at the time of death of the corresponding case. Furthermore, they were individually matched to the corresponding case according to the following criteria:

- same company
- date of birth (within 2 years)
- same sex

Each case together with the corresponding matched controls would constitute a matched set, which formed the unit of statistical analysis (see below).

2.2 Exposure Assessment in the Case-Control Study

The major refinement in exposure assessment in the case-control study was the development of more specific and more homogeneous job categories. After the cases and the controls had been selected, a list of all their jobs, arranged alphabetically and without revealing the case/control status, was created. This list was reviewed by the exposure assessment team (Dr. Thomas Smith with assistance from company industrial hygienists and epidemiologists). Although both land-based terminal and marine jobs were re-examined, only three new marine job categories were suggested, and very few workers were classified in these new categories (pumpers, captains and masters). For this reason as well as the fact that no quantitative exposure estimates were made for the marine cohort, it was determined that no new information would result from case-control analyses of the marine cohort. Thus, the case-control study was limited to the land-based terminal workers only.

The review by the exposure assessment team of the jobs of the cases and controls resulted in the following new categories for land-based terminal jobs:

Generic Jobs	New Categories
Terminal Operator	plantmen warehousemen laborers mechanics
Drivers	drivers
Loaders	loaders
Other Terminal Jobs	clerks/office workers foremen supervisors maintenance/yard workers other jobs

In addition to the above job categories, other gasoline exposure indices were also used in the case-control analyses: length of employment, length of exposure, cumulative exposure (concentration and duration of exposure expressed as ppm-years in terms of total hydrocarbons), cumulative frequency of peak exposure (a peak exposure was defined as an episode of exposure in excess of 500 ppm lasting 15 to 90 minutes), and year of first exposure (before 1949 vs. in and after 1949). The interest in year of first exposure stems from the observation that the recommended standard for benzene before 1947 was 100 ppm, which was reduced to 50 ppm in 1947, and further reduced to 35 ppm in 1948. Thus, over a short period of two years immediately before 1949, the recommended benzene standard underwent a considerable reduction. Several studies have reported that year of first exposure was found to be an important variable in assessing the health effects of benzene exposure in the petroleum industry (Wong et al., 1986; Wong and Raabe, 1989).

2.3 Statistical Methods

Two standard statistical techniques were used in analyzing the data: the Mantel-Haenszel χ^2 and the conditional multiple logistic regression. The Mantel-Haenszel (1959) procedure was used to analyze job categories and year of first exposure. In this procedure, each matched set was treated as a 2x2 table. The analysis for each job category or year of first exposure consisted of a series of such tables. The Mantel-Haenszel procedure was used to summarize these tables. The summary χ^2 with one degree of freedom tested the hypothesis whether the disease outcome was related to a particular job category or time period of first exposure. The Mantel-Haenszel procedure also provided an estimate of the relative risk (odds ratio).

The second statistical technique used was the conditional multiple logistic regression. The technique was used to analyze continuous variables such as years of exposure and cumulative exposure. In using such a parametric technique, it was not necessary to categorize interval data such as cumulative exposure (ppm-years) into arbitrary discrete groups. Furthermore, using these logistic regression models, it was also computationally less cumbersome to simultaneously analyze several variables. More importantly, when the number of cases was small, stratification by more than one or two variables would not be a viable option.

The multivariate technique was based on the statistical model that an individual's risk of developing a certain disease depended on the logit transformation of the independent variables (such as cumulative exposure), and the dependence assumed the form of a linear multiple regression (Prentice, 1976; Prentice and Pyke, 1979). The slope of the regression line, the regression coefficient β, could be used to calculate the relative risk (RR) between exposure levels x_1 and x_2 through the following formula: $RR = \exp\{\beta^*(x_2 - x_1)\}$. Also provided in the analysis was a χ^2, which tested the null hypothesis: $\beta = 0$, or, equivalently, $RR = 1$.

In the analyses, exposures of the controls were truncated at the time of death of the corresponding case. On a relative basis, this approach tended to slightly under-estimate the exposure of the controls, which would in turn produce a slightly larger relative risk.

3.0 RESULTS

3.1 Descriptive Statistics

Table 3-1 presents the numbers of cases and controls for each of the four diseases of interest. The numbers of cases of kidney cancer, leukemia (all cell types) and multiple myeloma were slightly higher than the corresponding numbers of observed deaths reported in the cohort study. The differences were due to several death certificates mentioning these diseases as contributory causes.

TABLE 3-1

Distribution of Cases and Controls by Disease

Disease	Cases	Controls
Leukemia (all cell types)	35*	168
Acute Myeloid Leukemia	13*	60
Kidney Cancer	13	65
Multiple Myeloma	11	55
Total	59	288

* One case has no controls.

For most cases, we were able to select 5 matched controls. For one acute myeloid leukemia case, no eligible control could be found. This individual was born in 1884, and was first employed in an exposed job in 1919. His cumulative gasoline exposure was rather low, 144 ppm-years. He died from acute myeloid leukemia at age 95. Although this case was left in the data, it did not contribute any information to statistical analyses since there were no controls in the matched set. For the remaining 12 acute myeloid leukemia cases, 5 controls were selected for each.

For leukemia (all cell types), in addition to the one AML case with no controls, one case had only 3 controls. Five controls were selected for each of the remaining leukemia cases. For both kidney cancer and multiple myeloma, five controls were selected for each case.

Tables 3-2 through 3-5 present the frequency distributions of cases and controls who were ever in a particular job category for each of the diseases of interest. It should be noted that an individual could appear in more than one category in these tables.

TABLE 3-2

Distribution by Terminal Job Categories (Ever/Never) of Leukemia Cases and Controls

Job Category * (Ever/Never)	Cases N (%)	Controls N (%)	Total N (%)
1 Plantmen	15 (42.9)	80 (47.6)	95 (46.8)
2 Warehousemen	2 (5.7)	17 (10.1)	19 (9.4)
3 Laborers	3 (8.6)	15 (8.9)	18 (8.9)
4 Mechanics	5 (14.3)	28 (16.7)	33 (16.3)
5 Clerks/Office Workers	4 (11.4)	33 (19.6)	37 (18.2)
6 Foremen/Supervisors	9 (25.7)	34 (20.2)	43 (21.2)
7 Maintenance/Yard Workers	0 (0.0)	12 (7.1)	12 (5.9)
8 Drivers	24 (68.6)	124 (73.8)	148 (72.9)
9 Loaders	1 (2.9)	6 (3.6)	7 (3.5)
10 Other Terminal Jobs	12 (34.3)	62 (36.9)	74 (36.5)
Total N	35	168	203

* Individuals may appear in more than one job category
( ) Column Percentage

TABLE 3-3

Distribution by Terminal Job Categories (Ever/Never) of Acute Myeloid Leukemia Cases and Controls

Job Category * (Ever/Never)	Cases N (%)	Controls N (%)	Total N (%)
1 Plantmen	7 (53.9)	30 (50.0)	37 (50.7)
2 Warehousemen	0 (0.0)	4 (6.7)	4 (5.5)
3 Laborers	1 (7.7)	2 (3.3)	3 (4.1)
4 Mechanics	2 (15.4)	10 (16.7)	12 (16.4)
5 Clerks/Office Workers	1 (7.7)	12 (20.0)	13 (17.8)
6 Foremen/Supervisors	4 (30.8)	17 (28.3)	21 (28.8)
7 Maintenance/Yard Workers	0 (0.0)	4 (6.7)	4 (5.5)
8 Drivers	7 (53.9)	44 (73.3)	51 (69.9)
9 Loaders	0 (0.0)	3 (5.0)	3 (4.1)
10 Other Terminal Jobs	4 (30.8)	25 (41.7)	29 (39.7)
Total N	13	60	73

* Individuals may appear in more than one job category
( ) Column Percentage

TABLE 3-4

Distribution by Terminal Job Categories (Ever/Never) of Kidney Cancer Cases and Controls

Job Category * (Ever/Never)	Cases N (%)	Controls N (%)	Total N (%)
1 Plantmen	4 (30.8)	23 (35.4)	27 (34.6)
2 Warehousemen	2 (15.4)	6 (9.2)	8 (10.3)
3 Laborers	2 (15.4)	6 (9.2)	8 (10.3)
4 Mechanics	0 (0.0)	5 (7.7)	5 (6.4)
5 Clerks/Office Workers	4 (30.8)	22 (33.9)	26 (33.3)
6 Foremen/Supervisors	5 (38.5)	15 (23.1)	20 (25.6)
7 Maintenance/Yard Workers	1 (7.7)	4 (6.2)	5 (6.4)
8 Drivers	9 (69.2)	43 (66.2)	52 (66.7)
9 Loaders	2 (15.4)	2 (3.1)	4 (5.1)
10 Other Terminal Jobs	8 (61.5)	30 (46.2)	38 (48.7)
Total N	13	65	78

* Individuals may appear in more than one job category
( ) Column Percentage

TABLE 3-5

Distribution by Terminal Job Categories (Ever/Never) of Multiple Myeloma Cases and Controls

Job Category * (Ever/Never)	Cases N (%)	Controls N (%)	Total N (%)
1 Plantmen	4 (36.4)	28 (50.9)	32 (48.5)
2 Warehousemen	2 (18.2)	6 (10.9)	8 (12.1)
3 Laborers	0 (0.0)	5 (9.1)	5 (7.6)
4 Mechanics	1 (9.1)	10 (18.2)	11 (16.7)
5 Clerks/Office Workers	1 (9.1)	14 (25.5)	15 (22.7)
6 Foremen/Supervisors	3 (27.3)	9 (16.4)	12 (18.2)
7 Maintenance/Yard Workers	0 (0.0)	3 (5.5)	3 (4.6)
8 Drivers	8 (72.7)	41 (74.6)	49 (74.2)
9 Loaders	1 (9.1)	5 (9.1)	6 (9.1)
10 Other Terminal Jobs	4 (36.4)	23 (41.8)	27 (40.9)
Total N	11	55	66

* Individuals may appear in more than one job category
( ) Column Percentage

Tables 3-6 through 3-9 and Tables 3-10 through 3-13 present similar frequency distributions of cases and controls who were in a particular job category for at least 5 years and for at least 10 years, respectively. These tables do not seem to indicate any major differences in job categories between the cases and controls, with the possible exception of "foremen/supervisors" for leukemia (all cell types) and kidney cancer. A formal relative risk analysis by job category is given in Section 3.2 below.

TABLE 3-6

Distribution by Terminal Job Categories (5+ Years) of Leukemia Cases and Controls

Job Category * (5+ Years)	Cases N (%)	Controls N (%)	Total N (%)
1 Plantmen	5 (14.3)	42 (25.0)	47 (23.2)
2 Warehousemen	0 (0.0)	6 (3.6)	6 (3.0)
3 Laborers	1 (2.9)	1 (0.6)	2 (1.0)
4 Mechanics	3 (8.6)	15 (8.9)	18 (8.9)
5 Clerks/Office Workers	1 (2.9)	11 (6.6)	12 (5.9)
6 Foremen/Supervisors	7 (20.0)	20 (11.9)	27 (13.3)
7 Maintenance/Yard Workers	0 (0.0)	3 (1.8)	3 (1.5)
8 Drivers	17 (48.6)	104 (61.9)	121 (59.6)
9 Loaders	0 (0.0)	1 (0.6)	1 (0.5)
10 Other Terminal Jobs	7 (20.0)	37 (22.0)	44 (21.7)
Total N	35	168	203

* Individuals may appear in more than one job category
( ) Column Percentage

TABLE 3-7

Distribution by Terminal Job Categories (5+ Years) of Acute Myeloid Leukemia Cases and Controls

Job Category * (5+ Years)	Cases N (%)	Controls N (%)	Total N (%)
1 Plantmen	3 (23.1)	12 (20.0)	15 (21.0)
2 Warehousemen	0 (0.0)	2 (3.3)	2 (2.7)
3 Laborers	0 (0.0)	0 (0.0)	0 (0.0)
4 Mechanics	1 (7.7)	5 (8.3)	6 (8.2)
5 Clerks/Office Workers	0 (0.0)	5 (8.3)	5 (6.9)
6 Foremen/Supervisors	3 (23.1)	11 (18.3)	14 (19.2)
7 Maintenance/Yard Workers	0 (0.0)	1 (1.7)	1 (1.4)
8 Drivers	5 (38.5)	36 (60.0)	41 (56.2)
9 Loaders	0 (0.0)	1 (1.7)	1 (1.4)
10 Other Terminal Jobs	3 (23.1)	16 (26.7)	19 (26.0)
Total N	13	60	73

* Individuals may appear in more than one job category
( ) Column Percentage

TABLE 3-8

Distribution by Terminal Job Categories (5+ Years) of Kidney Cancer Cases and Controls

Job Category * (5+ Years)	Cases N (%)	Controls N (%)	Total N (%)
1 Plantmen	3 (23.1)	11 (16.9)	14 (18.0)
2 Warehousemen	1 (7.7)	4 (6.2)	5 (6.4)
3 Laborers	0 (0.0)	0 (0.0)	0 (0.0)
4 Mechanics	0 (0.0)	4 (6.2)	4 (5.1)
5 Clerks/Office Workers	2 (15.4)	9 (13.9)	11 (14.1)
6 Foremen/Supervisors	5 (38.5)	11 (16.9)	16 (20.5)
7 Maintenance/Yard Workers	0 (0.0)	2 (3.1)	2 (2.6)
8 Drivers	6 (46.2)	30 (46.2)	36 (46.2)
9 Loaders	0 (0.0)	0 (0.0)	0 (0.0)
10 Other Terminal Jobs	7 (53.9)	24 (36.9)	31 (39.7)
Total N	13	65	78

* Individuals may appear in more than one job category
( ) Column Percentage

TABLE 3-9

Distribution by Terminal Job Categories (5+ Years) of Multiple Myeloma Cases and Controls

Job Category * (5+ Years)	Cases N (%)	Controls N (%)	Total N (%)
1 Plantmen	0 (0.0)	17 (30.9)	17 (25.8)
2 Warehousemen	1 (9.1)	1 (1.8)	2 (3.0)
3 Laborers	0 (0.0)	1 (1.8)	1 (1.5)
4 Mechanics	0 (0.0)	3 (5.5)	3 (4.6)
5 Clerks/Office Workers	0 (0.0)	4 (7.3)	4 (6.1)
6 Foremen/Supervisors	1 (9.1)	5 (9.1)	6 (9.1)
7 Maintenance/Yard Workers	0 (0.0)	1 (1.8)	1 (1.5)
8 Drivers	7 (63.6)	32 (58.2)	39 (59.1)
9 Loaders	0 (0.0)	1 (1.8)	1 (1.5)
10 Other Terminal Jobs	2 (18.2)	14 (25.5)	16 (24.2)
Total N	11	55	66

* Individuals may appear in more than one job category
( ) Column Percentage

TABLE 3-10

Distribution by Terminal Job Categories (10+ Years) of Leukemia Cases and Controls

Job Category * (10+ Years)	Cases N (%)	Controls N (%)	Total N (%)
1 Plantmen	2 (5.7)	19 (11.3)	21 (10.3)
2 Warehousemen	0 (0.0)	1 (0.6)	1 (0.5)
3 Laborers	0 (0.0)	0 (0.0)	0 (0.0)
4 Mechanics	1 (2.9)	7 (4.2)	8 (3.9)
5 Clerks/Office Workers	1 (2.9)	6 (3.6)	7 (3.5)
6 Foremen/Supervisors	5 (14.3)	9 (5.4)	14 (6.9)
7 Maintenance/Yard Workers	0 (0.0)	3 (1.8)	3 (1.5)
8 Drivers	16 (45.7)	88 (52.4)	104 (51.2)
9 Loaders	0 (0.0)	1 (0.6)	1 (0.5)
10 Other Terminal Jobs	6 (17.1)	28 (16.7)	34 (16.8)
Total N	35 (100.0)	168 (100.0)	203 (100.0)

* Individuals may appear in more than one job category
( ) Column Percentage

TABLE 3-11

Distribution by Terminal Job Categories (10+ Years) of Acute Myeloid Leukemia Cases and Controls

Job Category * (10+ Years)	Cases N (%)	Controls N (%)	Total N (%)
1 Plantmen	1 (7.7)	5 (8.3)	6 (8.2)
2 Warehousemen	0 (0.0)	0 (0.0)	0 (0.0)
3 Laborers	0 (0.0)	0 (0.0)	0 (0.0)
4 Mechanics	0 (0.0)	2 (3.3)	2 (2.7)
5 Clerks/Office Workers	0 (0.0)	4 (6.7)	4 (5.5)
6 Foremen/Supervisors	2 (15.4)	4 (6.7)	6 (8.2)
7 Maintenance/Yard Workers	0 (0.0)	0 (0.0)	0 (1.4)
8 Drivers	5 (38.5)	30 (50.0)	35 (48.0)
9 Loaders	0 (0.0)	1 (1.7)	1 (1.4)
10 Other Terminal Jobs	2 (15.4)	11 (18.3)	13 (17.8)
Total N	13 (100.0)	60 (100.0)	73 (100.0)

* Individuals may appear in more than one job category
( ) Column Percentage

TABLE 3-12

Distribution by Terminal Job Categories (10+ Years) of Kidney Cancer Cases and Controls

Job Category * (10+ Years)	Cases N (%)	Controls N (%)	Total N (%)
1 Plantmen	1 (7.7)	4 (6.2)	5 (6.4)
2 Warehousemen	1 (7.7)	2 (3.1)	3 (3.9)
3 Laborers	0 (0.0)	0 (0.0)	0 (0.0)
4 Mechanics	0 (0.0)	3 (4.6)	3 (3.9)
5 Clerks/Office Workers	1 (7.7)	6 (9.2)	7 (9.0)
6 Foremen/Supervisors	3 (23.1)	8 (12.3)	11 (14.1)
7 Maintenance/Yard Workers	0 (0.0)	1 (1.5)	1 (1.3)
8 Drivers	6 (46.2)	23 (35.4)	29 (37.2)
9 Loaders	0 (0.0)	0 (0.0)	0 (0.0)
10 Other Terminal Jobs	6 (46.2)	20 (30.8)	26 (33.3)
Total N	13 (100.0)	65 (100.0)	78 (100.0)

* Individuals may appear in more than one job category
( ) Column Percentage

TABLE 3-13

Distribution by Terminal Job Categories (10+ Years) of Multiple Myeloma Cases and Controls

Job Category * (10+ Years)	Cases N (%)	Controls N (%)	Total N (%)
1 Plantmen	0 (0.0)	7 (12.7)	7 (10.6)
2 Warehousemen	0 (0.0)	0 (0.0)	0 (0.0)
3 Laborers	0 (0.0)	0 (0.0)	0 (0.0)
4 Mechanics	0 (0.0)	2 (3.6)	2 (3.0)
5 Clerks/Office Workers	0 (0.0)	2 (3.6)	2 (3.0)
6 Foremen/Supervisors	1 (9.1)	3 (5.5)	4 (6.1)
7 Maintenance/Yard Workers	0 (0.0)	1 (1.8)	1 (1.5)
8 Drivers	7 (63.6)	28 (50.9)	35 (53.0)
9 Loaders	0 (0.0)	0 (0.0)	0 (0.0)
10 Other Terminal Jobs	2 (18.2)	8 (14.6)	10 (15.2)
Total N	11 (100.0)	55 (100.0)	66 (100.0)

* Individuals may appear in more than one job category
( ) Column Percentage

Four key exposure variables (length of employment, length of exposure, cumulative exposure and frequency of peak exposure) were compared between the cases and controls by matched set for the four disease categories in Tables 3-14 through 3-17. For leukemia (all cell types), acute myeloid leukemia and kidney cancer, the cases consistently had either similar or slightly lower averages for these four exposure variables than the controls (Tables 3-14 through 3-16). For multiple myeloma, the average length of employment was identical between the cases and controls (Table 3-17). The multiple myeloma cases had a shorter average length of exposure and a lower average cumulative exposure than their controls. However, the controls had fewer numbers of peak exposure than their cases.

TABLE 3-14

Comparison of Exposure Indices Between Leukemia Cases and Controls

Matched Set		Length of Employment (Years)	Length of Exposure (Years)	Cumulative Exposure (ppm-Years)	Peak Exposure (Cumulative Frequency)
1	Case	45.0	45.0	1,448.0	22,613.0
	Controls	25.6	23.0	449.2	1,374.2
2	Case	3.0	3.0	41.0	264.0
	Controls	11.0	9.4	370.0	612.6
3	Case	12.0	4.0	335.0	454.0
	Controls	31.8	29.0	634.0	4,310.8
4	Case	17.0	17.0	900.0	7,168.0
	Controls	35.4	29.4	983.6	10,211.4
5	Case	4.0	4.0	180.0	0.0
	Controls	21.8	20.8	356.6	1,235.4
6	Case	21.0	21.0	294.0	671.0
	Controls	28.0	27.6	828.8	7,971.2
7	Case	32.0	26.0	1,714.0	10,601.0
	Controls	29.8	27.0	831.0	12,024.8
8	Case	27.0	24.0	1,013.0	7,506.0
	Controls	36.2	32.0	625.0	3,436.6
9	Case	26.0	26.0	391.0	72.0
	Controls	31.8	27.0	669.0	1,552.0
10	Case	14.0	14.0	110.0	0.0
	Controls	6.0	3.0	293.7	852.3
11	Case	39.0	8.0	262.0	3,220.0
	Controls	32.2	31.6	670.0	8,272.0
12	Case	36.0	22.0	750.0	13,415.0
	Controls	28.0	22.2	1,003.6	9,790.4
13	Case	34.0	33.0	717.0	1,827.0
	Controls	30.2	27.8	881.0	8,151.6

TABLE 3-14 (Cont'd)

Comparison of Exposure Indices Between Leukemia Cases and Controls

Matched Set		Length of Employment (Years)	Length of Exposure (Years)	Cumulative Exposure (ppm-Years)	Peak Exposure (Cumulative Frequency)
14	Case	24.0	24.0	754.0	5,613.0
	Controls	34.6	28.2	1,104.4	7,779.6
15	Case	32.0	31.0	333.0	1,676.0
	Controls	20.0	13.2	486.4	1,742.4
16	Case	25.0	21.0	2,047.0	12,787.0
	Controls	25.0	17.4	827.4	4,476.6
17	Case	34.0	22.0	192.0	39.0
	Controls	30.0	28.0	1,284.0	6,782.0
18	Case	43.0	41.0	2,776.0	24,338.0
	Controls	33.4	33.2	1,376.4	16,212.4
19	Case	22.0	22.0	1,204.0	3,647.0
	Controls	32.2	28.6	1,426.6	7,996.6
20	Case	25.0	25.0	1,278.0	10,956.0
	Controls	30.2	28.0	1,008.2	6,726.8
21	Case	32.0	31.0	418.0	1,277.0
	Controls	28.6	21.6	1,014.6	8,032.6
22	Case	16.0	16.0	756.0	172.0
	Controls	22.2	21.2	701.8	2,007.2
23	Case	13.0	7.0	82.0	0.0
	Controls	37.6	33.6	864.4	7,477.0
24	Case	32.0	32.0	676.0	287.0
	Controls	39.8	18.4	209.8	2,416.2
25	Case	20.0	20.0	283.0	0.0
	Controls	29.8	22.6	563.0	7,728.4
26	Case	25.0	15.0	652.0	818.0
	Controls	33.8	29.6	967.6	7,937.6

TABLE 3-14 (Cont'd)

Comparison of Exposure Indices Between Leukemia Cases and Controls

Matched Set		Length of Employment (Years)	Length of Exposure (Years)	Cumulative Exposure (ppm-Years)	Peak Exposure (Cumulative Frequency)
27	Case	40.0	38.0	2,148.0	18,801.0
	Controls	33.4	30.0	1,127.8	8,772.4
28	Case	44.0	39.0	1,169.0	16,797.0
	Controls	31.2	26.4	1,447.8	7,653.8
29	Case	38.0	37.0	1,215.0	10,400.0
	Controls	29.0	23.2	710.8	7,483.6
30	Case	31.0	31.0	911.0	1,239.0
	Controls	21.8	17.2	780.6	2,088.2
31	Case	34.0	32.0	1,278.0	6,668.0
	Controls	31.0	23.2	709.8	2,040.4
32	Case	21.0	20.0	1,342.0	8,140.0
	Controls	25.4	19.8	846.4	5,609.6
33	Case	1.0	1.0	48.0	42.0
	Controls	11.0	10.0	377.4	602.4
34	Case	25.0	12.0	101.0	236.0
	Controls	30.0	26.2	1,439.2	6,349.6
35	Case	28.0	18.0	144.0	208.0
	Controls	NA	NA	NA	NA
Average	Cases	25.6	21.8	814.2	5,832.6
	Controls	27.9	24.4	819.8	6,074.6

TABLE 3-15

Comparison of Exposure Indices Between Acute Myeloid Leukemia Cases and Controls

Matched Set		Length of Employment (Years)	Length of Exposure (Years)	Cumulative Exposure (ppm-Years)	Peak Exposure (Cumulative Frequency)
1	Case	13.0	7.0	82.0	0.0
	Controls	37.6	33.6	864.4	7,477.0
2	Case	32.0	32.0	676.0	287.0
	Controls	39.8	18.4	209.8	2,416.2
3	Case	20.0	20.0	283.0	0.0
	Controls	29.8	22.6	563.0	7,728.4
4	Case	25.0	15.0	652.0	818.0
	Controls	33.8	29.6	967.6	7,937.6
5	Case	40.0	36.0	2,148.0	18,801.0
	Controls	33.4	30.0	1,127.8	8,772.4
6	Case	44.0	39.0	1,169.0	16,797.0
	Controls	31.2	26.4	1,447.8	7,653.8
7	Case	38.0	37.0	1,215.0	10,400.0
	Controls	29.0	23.2	710.8	7,483.6
8	Case	31.0	31.0	911.0	1,239.0
	Controls	21.8	17.2	780.6	2,088.2
9	Case	34.0	32.0	1,278.0	6,668.0
	Controls	31.0	23.2	709.8	2,040.4
10	Case	21.0	20.0	1,342.0	8,140.0
	Controls	25.4	19.8	846.4	5,609.6
11	Case	1.0	1.0	48.0	42.0
	Controls	11.0	10.0	377.4	602.4
12	Case	25.0	12.0	101.0	236.0
	Controls	30.0	26.2	1,439.2	6,349.6
13	Case	28.0	18.0	144.0	208.0
	Controls	NA	NA	NA	NA
Average	Cases	27.1	23.2	773.0	4,895.1
	Controls	29.5	23.4	837.1	5,513.3

TABLE 3-16

Comparison of Exposure Indices Between Kidney Cases and Controls

Matched Set		Length of Employment (Years)	Length of Exposure (Years)	Cumulative Exposure (ppm-Years)	Peak Exposure (Cumulative Frequency)
1	Case	44.0	44.0	275.0	6,101.0
	Controls	41.8	41.8	673.8	6,131.4
2	Case	13.0	11.0	199.0	432.0
	Controls	31.2	24.6	669.4	1,704.8
3	Case	10.0	10.0	138.0	0.0
	Controls	15.6	15.4	448.0	1,049.4
4	Case	28.0	27.0	570.0	2,210.0
	Controls	30.2	28.0	1,049.8	6,335.6
5	Case	26.0	26.0	550.0	2,923.0
	Controls	22.2	17.0	298.0	537.6
6	Case	14.0	13.0	1,192.0	3,251.0
	Controls	23.6	20.8	391.8	316.6
7	Case	11.0	11.0	99.0	0.0
	Controls	26.0	23.2	678.0	5,800.4
8	Case	25.0	24.0	931.0	1,607.0
	Controls	25.4	18.4	1,298.2	4,935.2
9	Case	28.0	19.0	600.0	8,121.0
	Controls	29.4	24.0	698.8	6,173.2
10	Case	37.0	33.0	947.0	10,486.0
	Controls	30.6	28.2	2,050.2	1,762.4
11	Case	42.0	38.0	2,006.0	7,797.0
	Controls	33.8	31.4	1,933.0	10,536.4
12	Case	16.0	16.0	96.0	989.0
	Controls	4.8	4.6	123.6	354.6
13	Case	31.0	31.0	442.0	1,014.0
	Controls	31.0	24.6	957.0	2,477.2
Average	Cases	25.0	23.3	618.9	3,456.2
	Controls	26.6	23.2	866.9	3,701.1

TABLE 3-17

Comparison of Exposure Indices Between Multiple Myeloma Cases and Controls

Matched Set		Length of Employment (Years)	Length of Exposure (Years)	Cumulative Exposure (ppm-Years)	Peak Exposure (Cumulative Frequency)
1	Case	37.0	37.0	1,080.0	20,350.0
	Controls	31.2	31.0	704.0	7,114.0
2	Case	35.0	26.0	46.0	0.0
	Controls	20.4	20.0	676.6	2,082.6
3	Case	31.0	11.0	740.0	4,521.0
	Controls	31.8	19.8	743.4	5,171.4
4	Case	31.0	31.0	990.0	15,798.0
	Controls	35.4	34.6	1,320.4	14,012.4
5	Case	25.0	22.0	1,255.0	6,415.0
	Controls	20.8	19.8	503.0	3,179.6
6	Case	28.0	23.0	605.0	8,866.0
	Controls	31.2	26.2	835.2	5,722.6
7	Case	28.0	19.0	233.0	0.0
	Controls	26.6	25.8	495.8	6,136.2
8	Case	6.0	3.0	304.0	284.0
	Controls	30.8	30.4	634.2	4,206.0
9	Case	29.0	29.0	849.0	13,153.0
	Controls	30.0	25.8	1,440.4	7,886.2
10	Case	32.0	32.0	1,216.0	20,562.0
	Controls	28.8	27.0	869.0	11,047.4
11	Case	25.0	6.0	83.0	13.0
	Controls	19.8	17.4	587.6	3,655.0
Average	Cases	27.9	21.7	672.8	8,178.4
	Controls	27.9	25.3	800.9	6,383.0

3.2 Mantel-Haenszel χ^2 Procedure

Table 3-18 shows the Mantel-Haenszel relative risks for leukemia by "ever/never" job category. No significantly increased leukemia risk was detected for any job category in Table 3-18. The category "foremen/supervisors" showed a RR of 1.36 (not significant) based on 9 cases. No increases were seen for any other job categories. Table 3-19 shows similar results for AML. Except for the category "laborers," which consisted of only one case, no job category showed an AML excess. The job category "foremen/supervisors" showed a nonsignificant increase of kidney cancer (RR=2.08, p>0.05; Table 3-20). For "loaders," the kidney cancer RR was 5.73 based on only two cases, and it was not statistically significant (p>0.05).

TABLE 3-18

Mantel-Haenszel Relative Risk of Leukemia by Terminal Job Categories (Ever/Never)

Job Category (Ever/Never)	Cases	Controls	RR	95% CI	χ^2	p
1 Plantmen	15	80	0.83	(0.40 - 1.72)	0.263	0.608
2 Warehousemen	2	17	0.54	(0.12 - 2.40)	0.659	0.417
3 Laborers	3	15	0.96	(0.26 - 3.51)	0.005	0.946
4 Mechanics	5	28	0.83	(0.30 - 2.34)	0.120	0.729
5 Clerks/Office Workers	4	33	0.53	(0.18 - 1.58)	1.305	0.253
6 Foreman/Supervisors	9	34	1.36	(0.59 - 3.18)	0.520	0.470
7 Maintenance/Yard Workers	0	12	0.00	-	2.644	0.104
8 Drivers	24	124	0.77	(0.35 - 1.71)	0.400	0.527
9 Loaders	1	6	0.79	(0.09 - 6.82)	0.044	0.834
10 Other Terminal Jobs	12	62	0.89	(0.41 - 1.92)	0.086	0.770

TABLE 3-19

Mantel-Haenszel Relative Risk of Acute Myeloid Leukemia by Terminal Job Categories (Ever/Never)

Job Category (Ever/Never)	Cases	Controls	RR	95% CI	χ^2	p
1 Plantmen	7	30	1.17	(0.35 - 3.91)	0.062	0.803
2 Warehousemen	0	4	0.00	-	0.904	0.342
3 Laborers	1	2	2.42	(0.21 - 27.35)	0.508	0.476
4 Mechanics	2	10	0.91	(0.17 - 4.80)	0.013	0.911
5 Clerks/Office Workers	1	12	0.33	(0.04 - 2.62)	1.091	0.296
6 Foreman/Supervisors	4	17	1.12	(0.30 - 4.18)	0.031	0.861
7 Maintenance/Yard Workers	0	4	0.00	-	0.904	0.342
8 Drivers	7	44	0.42	(0.13 - 1.44)	1.901	0.168
9 Loaders	0	3	0.00	-	0.669	0.414
10 Other Terminal Jobs	4	25	0.62	(0.17 - 2.25)	0.523	0.470

TABLE 3-20

Mantel-Haenszel Relative Risk of Kidney Cancer by Terminal Job Categories (Ever/Never)

Job Category (Ever/Never)	Cases	Controls	RR	95% CI	χ^2	p
1 Plantmen	4	23	0.81	(0.22 - 2.95)	0.101	0.751
2 Warehousemen	2	6	1.79	(0.32 - 9.95)	0.440	0.507
3 Laborers	2	6	1.79	(0.32 - 9.95)	0.440	0.507
4 Mechanics	0	5	0.00	-	1.055	0.304
5 Clerks/Office Workers	4	22	0.87	(0.24 - 3.16)	0.046	0.831
6 Foreman/Supervisors	5	15	2.08	(0.60 - 7.26)	1.328	0.249
7 Maintenance/Yard Workers	1	4	1.27	(0.13 - 12.51)	0.042	0.837
8 Drivers	9	43	1.15	(0.32 - 4.19)	0.046	0.831
9 Loaders	2	2	5.73	(0.88 - 37.33)	3.330	0.068
10 Other Terminal Jobs	8	30	1.87	(0.54 - 6.29)	1.013	0.314

TABLE 3-21

Mantel-Haenszel Relative Risk of Multiple Myeloma By Terminal Job Categories (Ever/Never)

Job Category (Ever/Never)	Cases	Controls	RR	95% CI	χ^2	p
1 Plantmen	4	28	0.55	(0.15 - 2.10)	0.765	0.382
2 Warehousemen	2	6	1.82	(0.32 - 10.39)	0.448	0.503
3 Laborers	0	5	0.00	-	1.066	0.302
4 Mechanics	1	10	0.45	(0.05 - 3.81)	0.537	0.464
5 Clerks/Office Workers	1	14	0.29	(0.04 - 2.28)	1.376	0.241
6 Foreman/Supervisors	3	9	1.92	(0.43 - 8.59)	0.722	0.395
7 Maintenance/Yard Workers	0	3	0.00	-	0.619	0.431
8 Drivers	8	41	0.91	(0.21 - 3.96)	0.016	0.901
9 Loaders	1	5	1.00	(0.11 - 9.51)	0.000	1.000
10 Other Terminal Jobs	4	23	0.80	(0.21 - 3.06)	0.111	0.739

With respect to multiple myeloma, no significant excess was found for any job category (Table 3-21). However, those who were ever foremen or supervisors, their relative risk was 1.92 (based on 3 cases, p>0.05).

Similarly, Tables 3-22 through 3-25 show the Mantel-Haenszel relative risks for each disease by job category with a minimum length of 5 years. As indicated in Table 3-22, for leukemia (all cell types), the category "foremen/supervisors" (5+ years) continue to show a modest, nonsignificant increase (RR=1.85, p>0.05, based on 7 cases). For AML (Table 3-23), the RR for this job category with 5+ years was lower (RR=1.34, p>0.05, based on 3 deaths) than the "ever/never" category. A RR of 3.07 (p>0.05) for kidney cancer was detected for those who had been in the "foremen/supervisors" category for at least 5 years. Table 3-24 indicates that those with at least 5 years in the broad category "other terminal jobs" experienced a modest, nonsignificant excess of kidney cancer (RR=1.99, p>0.05, based on 7 cases). The results for multiple myeloma are presented in Table 3-25. No significant excess was reported for multiple myeloma.

TABLE 3-22

Mantel-Haenszel Relative Risk of Leukemia by Terminal Job Categories (5+ Years)

Job Category (5+ Years)	Cases	Controls	RR	95% CI	χ^2	p
1 Plantmen	5	42	0.50	(0.19 - 1.35)	1.86	0.17
2 Warehousemen	0	6	0.00	-	1.282	0.258
3 Laborers	1	1	4.91	(0.39 - 62.11)	1.512	0.219
4 Mechanics	3	15	0.96	(0.26 - 3.51)	0.005	0.946
5 Clerks/Office Workers	1	11	0.42	(0.06 - 3.18)	0.706	0.401
6 Foreman/Supervisors	7	20	1.85	(0.72 - 4.75)	1.638	0.201
7 Maintenance/Yard Workers	0	3	0.00	-	0.631	0.427
8 Drivers	17	104	0.58	(0.28 - 1.21)	2.128	0.145
9 Loaders	0	1	0.00	-	0.208	0.648
10 Other Terminal Jobs	7	37	0.89	(0.36 - 2.19)	0.070	0.792

TABLE 3-23
Mantel-Haenszel Relative Risk of Acute Myeloid Leukemia by Terminal Job Categories (5+ Years)

Job Category (5+ Years)	Cases	Controls	RR	95% CI	χ^2	p
1 Plantmen	3	12	1.20	(0.28 - 5.09)	0.061	0.805
2 Warehousemen	0	2	0.00	-	0.439	0.507
3 Laborers	0	0	-	-	-	-
4 Mechanics	1	5	0.92	(0.10 - 8.71)	0.006	0.940
5 Clerks/Office Workers	0	5	0.00	-	1.147	0.284
6 Foreman/Supervisors	3	11	1.34	(0.31 - 5.71)	0.153	0.696
7 Maintenance/Yard Workers	0	1	0.00	-	0.217	0.642
8 Drivers	5	36	0.42	(0.12 - 1.41)	1.986	0.159
9 Loaders	0	1	0.00	-	0.217	0.642
10 Other Terminal Jobs	3	16	0.83	(0.20 - 3.41)	0.071	0.791

TABLE 3-24

Mantel-Haenszel Relative Risk of Kidney Cancer By Terminal Job Categories (5+ Years)

Job Category (5+ Years)	Cases	Controls	RR	95% CI	χ^2	p
1 Plantmen	3	11	1.47	(0.35 - 6.26)	0.275	0.600
2 Warehousemen	1	4	1.27	(0.13 - 12.51)	0.042	0.837
3 Laborers	0	0	-	-	-	-
4 Mechanics	0	4	0.00	-	0.832	0.362
5 Clerks/Office Workers	2	9	1.13	(0.21 - 6.03)	0.021	0.885
6 Foreman/Supervisors	5	11	3.07	(0.87 - 10.81)	3.043	0.081
7 Maintenance/Yard Workers	0	2	0.00	-	0.405	0.524
8 Drivers	6	30	1.00	(0.30 - 3.30)	0.000	1.000
9 Loaders	0	0	-	-	-	-
10 Other Terminal Jobs	7	24	1.99	(0.60 - 6.59)	1.279	0.258

TABLE 3-25

Mantel-Haenszel Relative Risk of Multiple Myeloma by Terminal Job Categories (5+ Years)

Job Category (5+ Years)	Cases	Controls	RR	95% CI	χ^2	p
1 Plantmen	0	17	0.00	-	4.510	0.034
2 Warehousemen	1	1	5.40	(0.40 - 72.19)	1.625	0.202
3 Laborers	0	1	0.00	-	0.200	0.655
4 Mechanics	0	3	0.00	-	0.619	0.431
5 Clerks/Office Workers	0	4	0.00	-	0.839	0.360
6 Foreman/Supervisors	1	5	1.00	(0.11 - 9.51)	0.000	1.000
7 Maintenance/Yard Workers	0	1	0.00	-	0.200	0.655
8 Drivers	7	32	1.26	(0.33 - 4.85)	0.111	0.739
9 Loaders	0	1	0.00	-	0.200	0.655
10 Other Terminal Jobs	2	14	0.65	(0.13 - 3.39)	0.260	0.610

Similar analyses were performed for each disease by job category with a minimum length of 10 years. The results are presented in Tables 3-26 through 3-29. Overall, the results are similar to those for job categories defined as "ever/never" or "at least 5 years." In particular, no significant increase was observed for any job category. The category "foremen/supervisors" continued to show a nonsignificant increase in leukemia of all cell-types combined.

TABLE 3-26

Mantel-Haenszel Relative Risk of Leukemia by Terminal Job Categories (10+ Years)

Job Category (10+ Years)	Cases	Controls	RR	95% CI	χ^2	p
1 Plantmen	2	19	0.48	(0.11 - 2.08)	0.973	0.324
2 Warehousemen	0	1	0.00	-	1.208	0.648
3 Laborers	0	0	-	-	-	-
4 Mechanics	1	7	0.68	(0.08 - 5.64)	0.131	0.713
5 Clerks/Office Workers	1	6	0.79	(0.09 - 6.82)	0.044	0.834
6 Foreman/Supervisors	5	9	2.94	(0.96 - 9.01)	3.579	0.059
7 Maintenance/Yard Workers	0	3	0.00	-	0.631	0.427
8 Drivers	16	88	0.77	(0.37 - 1.59)	0.513	0.474
9 Loaders	0	1	0.00	-	0.208	0.648
10 Other Terminal Jobs	6	28	1.03	(0.39 - 2.73)	0.005	0.945

TABLE 3-27

Mantel-Haenszel Relative Risk of Acute Myeloid Leukemia by Terminal Job Categories (10+ Years)

Job Category (10+ Years)	Cases	Controls	RR	95% CI	χ^2	p
1 Plantmen	1	5	0.92	(0.10 - 8.71)	0.006	0.940
2 Warehousemen	0	0	-	-	-	-
3 Laborers	0	0	-	-	-	-
4 Mechanics	0	2	0.00	-	0.439	0.507
5 Clerks/Office Workers	0	4	0.00	-	0.904	0.342
6 Foreman/Supervisors	2	4	2.55	(0.43 - 15.05)	1.062	0.303
7 Maintenance/Yard Workers	0	0	-	-	-	-
8 Drivers	5	30	0.63	(0.18 - 2.14)	0.562	0.453
9 Loaders	0	1	0.00	-	0.217	0.642
10 Other Terminal Jobs	2	11	0.81	(0.16 - 4.22)	0.063	0.802

TABLE 3-28

Mantel-Haenszel Relative Risk of Kidney Cancer by Terminal Job Categories (10+ Years)

Job Category (10+ Years)	Cases	Controls	RR	95% CI	χ^2	p
1 Plantmen	1	4	1.27	(0.13 - 12.51	0.042	0.837
2 Warehousemen	1	2	2.63	(0.24 - 29.23)	0.616	0.433
3 Laborers	0	0	-	-	-	-
4 Mechanics	0	3	0.00	-	0.616	0.433
5 Clerks/Office Workers	1	6	0.82	(0.09 - 7.52)	0.031	0.860
6 Foreman/Supervisors	3	8	2.14	(0.49 - 9.31	1.024	0.312
7 Maintenance/Yard Workers	0	1	0.00	-	0.200	0.655
8 Drivers	6	23	1.57	(0.47 - 5.22)	0.531	0.466
9 Loaders	0	0	-	-	-	-
10 Other Terminal Jobs	6	20	1.93	(0.58 - 6.44)	1.139	0.286

TABLE 3-29

Mantel-Haenszel Relative Risk of Multiple Myeloma by Terminal Job Categories (10+ Years)

Job Category (10+ Years)	Cases	Controls	RR	95% CI	χ^2	p
1 Plantmen	0	7	0.00	-	1.542	0.214
2 Warehousemen	0	0	0.00	-	-	-
3 Laborers	0	0	-	-	-	-
4 Mechanics	0	2	0.00	-	0.406	0.524
5 Clerks/Office Workers	0	2	0.00	-	0.406	0.524
6 Foreman/Supervisors	1	3	1.73	(0.17 - 18.25)	0.210	0.647
7 Maintenance/Yard Workers	0	1	0.00	-	0.200	0.655
8 Drivers	7	28	1.69	(0.44 - 6.44)	0.587	0.444
9 Loaders	0	0	-	-	-	-
10 Other Terminal Jobs	2	8	1.31	(0.24 - 7.25)	0.093	0.761

The results of the Mantel-Haenszel analysis by year of first exposure to gasoline are presented in Table 3-30. The frequency of cases and controls by year of first exposure is presented in Table 3-31. As discussed earlier, based on a consideration of the reduction in recommended benzene standards in 1947 and 1948, the risk of developing the four diseases among those first exposed before 1949 was compared to that among those exposed thereafter. No difference in risk in any of these four diseases was detected by year of first exposure. In particular, the AML risk was similar regardless whether first exposure occurred before or after 1949 (RR=0.92).

TABLE 3-30

Mantel-Haenszel Relative Risk of Leukemia, Acute Myeloid Leukemia, Kidney Cancer, and Multiple Myeloma by Year of First Exposure (≤1948 vs ≥1949)

Disease	Cases	Controls	RR	95% CI	χ^2	p
Leukemia	25	130	0.73	(0.32 - 1.66)	0.566	0.452
Acute Myeloid Leukemia	10	47	0.92	(0.22 - 3.89)	0.012	0.912
Kidney Cancer	7	45	0.52	(0.16 - 1.73)	1.139	0.286
Multiple Myeloma	9	42	1.39	(0.27 - 7.33)	0.153	0.696

TABLE 3-31

Distribution by Year of First Exposure Among Cases and Controls

	Year of First Exposure	
Disease Category	≤1948	≥1949
Leukemia		
Cases	9	2
Controls	42	13
Acute Myeloid Leukemia		
Cases	10	3
Controls	47	13
Kidney Cancer		
Cases	7	6
Controls	45	20
Multiple Myeloma		
Cases	25	10
Controls	130	38

3.3 Conditional Multiple Logistic Regression

Five key exposure variables were included in the conditional logistic regression analyses: length of employment, length of exposure, cumulative exposure, frequency of peak exposure, and year of first exposure. As discussed earlier, the regression coefficient, β, is a measure of association between a particular exposure variable and the disease.

Results based on univariate conditional logistic regression are shown in Tables 3-32 through 3-35 by disease category, respectively. In these univariate analyses, only one exposure variable was in the logistic model. None of the β's presented in Tables 3-32 through 3-35 was significantly different from 0. In other words, based on these univariate models, no association was found between any of the five exposure variables and any of the four diseases.

TABLE 3-32

Univariate Conditional Logistic Regression Analysis for Leukemia

Model	Variable in the Model	β	SE(β)	χ^2	p	RR*
1	Length of Employment (yr)	-0.026112	0.020450	1.631	0.202	0.97
2	Length of Exposure (yr)	-0.013375	0.018340	0.532	0.466	0.99
3	Cumulative Exposure (ppm-yr)	-0.000003	0.000318	0.000	0.993	1.00
4	Frequency of Peak Exposure	-0.000006	0.000034	0.028	0.868	1.00
5	Year of First Exposure (≤1948 v. ≥1949)	-0.549856	0.553380	0.987	0.320	0.58

* Relative Risk corresponding to an increment of 1-unit of the independent variable

TABLE 3-33

Univariate Conditional Logistic Regression Analysis for Acute Myeloid Leukemia

Model	Variable in the Model	β	SE(β)	χ^2	p	RR*
1	Length of Employment (yr)	-0.031112	0.034410	0.818	0.366	0.97
2	Length of Exposure (yr)	0.002738	0.029530	0.009	0.926	1.00
3	Cumulative Exposure (ppm-yr)	-0.000032	0.000527	0.004	0.951	1.00
4	Frequency of Peak Exposure	-0.000007	0.000055	0.015	0.901	1.00
5	Year of First Exposure (≤1948 v. ≥1949)	-0.315322	0.948050	0.111	0.739	0.73

* Relative Risk corresponding to an increment of 1-unit of the independent variable

TABLE 3-34

Univariate Conditional Logistic Regression Analysis for Kidney Cancer

Model	Variable in the Model	β	SE(β)	χ^2	p	RR*
1	Length of Employment (yr)	-0.027584	0.039670	0.484	0.487	0.97
2	Length of Exposure (yr)	0.001030	0.035180	0.001	0.977	1.00
3	Cumulative Exposure (ppm-yr)	-0.000477	0.005243	0.827	0.363	1.00
4	Frequency of Peak Exposure	-0.000011	0.000066	0.028	0.867	1.00
5	Year of First Exposure (≤1948 v. ≥1949)	-1.115231	0.815680	1.869	0.172	0.33

* Relative Risk corresponding to an increment of 1-unit of the independent variable

TABLE 3-35

Univariate Conditional Logistic Regression Analysis for Multiple Myeloma

Model	Variable in the Model	β	SE(β)	χ^2	p	RR*
1	Length of Employment (yr)	0.000244	0.038260	0.000	0.995	1.00
2	Length of Exposure (yr)	-0.038776	0.034580	1.257	0.262	0.96
3	Cumulative Exposure (ppm-yr)	-0.000536	0.000732	0.536	0.464	1.00
4	Frequency of Peak Exposure	0.000046	0.000052	0.790	0.374	1.00
5	Year of First Exposure (≤1948 v. ≥1949)	0.644938	1.125110	0.329	0.567	1.91

* Relative Risk corresponding to an increment of 1-unit of the independent variable

Results of the multivariate conditional logistic regression analyses are presented in Tables 3-36 through 3-39. In these models, various combinations of two exposure variables were used, such as length of exposure and frequency of peak exposure, cumulative exposure and frequency of peak exposure, etc. In one model, three exposure variables were analyzed simultaneously: cumulative exposure, frequency of exposure, and year of first exposure. No significant association was detected between the exposure variables and any of the diseases in the multivariate logistic regression models.

TABLE 3-36

Multivariate Conditional Logistic Regression Analysis for Leukemia

Model	Variables in the Model	β	SE(β)	χ^2	p	RR*
1	Length of Employment	-0.028628	0.021500	1.774	0.183	0.97
	Cumulative Exposure	0.000127	0.000330	0.148	0.700	1.00
2	Length of Exposure	-0.015262	0.019680	0.601	0.438	0.98
	Cumulative Exposure	0.000089	0.000332	0.071	0.789	1.00
3	Length of Exposure	-0.016621	0.022130	0.564	0.453	0.98
	Peak Exposure	0.000011	0.000041	0.071	0.790	1.00
4	Cumulative Exposure	0.000093	0.000328	0.080	0.777	1.00
	Year of First Exposure	-0.601892	0.586200	1.054	0.305	0.55
5	Cumulative Exposure	0.000031	0.000362	0.007	0.933	1.00
	Peak Exposure	-0.000007	0.000039	0.035	0.852	1.00
6	Peak Exposure	0.000005	0.000036	0.022	0.882	1.00
	Year of First Exposure	-0.580452	0.592170	0.961	0.327	0.56
7	Cumulative Exposure	0.000089	0.000365	0.059	0.808	1.00
	Peak Exposure	0.000001	0.000041	0.001	0.978	1.00
	Year of Exposure	-0.605765	0.603110	1.009	0.315	0.55

* Relative Risk corresponding to an increment of 1-unit of the independent variable

TABLE 3-37

Multivariate Conditional Logistic Regression Analysis for Acute Myeloid Leukemia

Model	Variables in the Model	β	SE(β)	χ^2	p	RR*
1	Length of Employment Cumulative Exposure	-0.031395 0.000029	0.034770 0.000507	0.815 0.003	0.367 0.955	0.97 1.00
2	Length of Exposure Cumulative Exposure	0.003672 -0.000053	0.031160 0.000562	0.014 0.009	0.906 0.924	1.00 1.00
3	Length of Exposure Peak Exposure	0.006950 -0.000014	0.035440 0.000066	0.038 0.046	0.845 0.831	1.01 1.00
4	Cumulative Exposure Year of First Exposure	0.000010 -0.320016	0.000542 0.983630	0.000 0.106	0.986 0.745	1.00 0.73
5	Cumulative Exposure Peak Exposure	0.000000 -0.000007	0.000602 0.000063	0.000 0.012	1.000 0.914	- 1.00
6	Peak Exposure Year of First Exposure	-0.000002 -0.306216	0.000058 0.997490	0.001 0.094	0.977 0.759	1.00 0.74
7	Cumulative Exposure Peak Exposure Year of Exposure	0.000021 -0.000003 -0.310769	0.000605 0.000065 1.007420	0.001 0.002 0.095	0.972 0.967 0.758	1.00 1.00 0.73

* Relative Risk corresponding to an increment of 1-unit of the independent variable

TABLE 3-38

Multivariate Conditional Logistic Regression Analysis for Kidney Cancer

Model	Variables in the Model	β	SE(β)	χ^2	p	RR*
1	Length of Employment	-0.022300	0.040470	0.304	0.582	0.98
	Cumulative Exposure	-0.000434	0.000515	0.710	0.399	1.00
2	Length of Exposure	0.007465	0.035870	0.043	0.835	1.01
	Cumulative Exposure	-0.000502	0.000550	0.831	0.362	1.00
3	Length of Exposure	0.003560	0.037650	0.009	0.925	1.00
	Peak Exposure	-0.000013	0.000070	0.036	0.850	1.00
4	Cumulative Exposure	-0.000347	0.000523	0.440	0.507	1.00
	Year of First Exposure	-0.940683	0.832270	1.277	0.258	0.39
5	Cumulative Exposure	-0.000510	0.000566	0.810	0.368	1.00
	Peak Exposure	0.000012	0.000069	0.033	0.857	1.00
6	Peak Exposure	0.000009	0.000065	0.021	0.885	1.00
	Year of First Exposure	-1.146254	0.847470	1.829	0.176	0.32
7	Cumulative Exposure	-0.000409	0.000571	0.513	0.474	1.00
	Peak Exposure	0.000026	0.000068	0.142	0.706	1.00
	Year of Exposure	-0.995804	0.851270	1.368	0.242	0.37

* Relative Risk corresponding to an increment of 1-unit of the independent variable

TABLE 3-39

Multivariate Conditional Logistic Regression Analysis for Multiple Myeloma

Model	Variables in the Model	β	SE(β)	χ^2	p	RR*
1	Length of Employment	0.010532	0.040450	0.068	0.795	1.01
	Cumulative Exposure	-0.000600	0.000779	0.594	0.441	1.00
2	Length of Exposure	-0.033747	0.038630	0.763	0.382	0.97
	Cumulative Exposure	-0.000218	0.000755	0.083	0.773	1.00
3	Length of Exposure	-0.098083	0.052870	3.441	0.064	0.91
	Peak Exposure	0.000153	0.000089	2.980	0.084	1.00
4	Cumulative Exposure	-0.000651	0.000761	0.732	0.392	1.00
	Year of First Exposure	0.949287	1.301220	0.532	0.466	2.58
5	Cumulative Exposure	-0.001226	0.001040	1.381	0.240	1.00
	Peak Exposure	0.000088	0.000065	1.850	0.174	1.00
6	Peak Exposure	0.000042	0.000053	0.624	0.430	1.00
	Year of First Exposure	0.468231	1.153240	0.165	0.685	1.60
7	Cumulative Exposure	-0.001323	0.001060	1.565	0.211	1.00
	Peak Exposure	0.000085	0.000065	1.708	0.191	1.00
	Year of Exposure	0.916341	1.501540	0.372	0.542	2.50

* Relative Risk corresponding to an increment of 1-unit of the independent variable

4.0 DISCUSSION

The original objective of the case-control study was to perform additional analyses on data derived from the original cohort study using a more detailed exposure assessment. As stated earlier however, a detailed exposure assessment was developed in the cohort study, which lessened the need for a case-control study. In the case-control analyses, the same quantitative exposure indices were used to characterize exposure. In addition, a more detailed job classification was developed.

Analysis by job category did not find any significantly increased risk for any of the diseases of interest: leukemia (all cell types), acute myeloid leukemia, kidney cancer and multiple myeloma. However, statistically nonsignificant excesses were detected for some job categories. In particular, nonsignificant excesses were found for the category of "foremen/supervisors" for leukemia, kidney cancer and multiple myeloma:

Relative Risks and 95% C. I. for "Foremen/Supervisors"

Disease	Ever/Never	5+ Years	10+ Years
Leukemia	1.36 (0.59 - 3.18)	1.85 (0.72 - 4.75)	2.94 (0.96 - 9.01)
AML	1.12 (0.30 - 4.18)	1.34 (0.31 - 5.71)	2.55 (0.43 - 15.05)
Kidney Cancer	2.08 (0.60 - 7.26)	3.07 (0.87 - 10.81)	2.14 (0.49 - 9.31)
Multiple Myeloma	1.92 (0.43 - 8.59)	1.00 (0.11 - 9.51)	1.73 (0.17 - 18.25)

For overall leukemia and AML, the relative risks increased with a longer duration in this job category. On the other hand, for kidney cancer and multiple myeloma, no trend was observed for relative risk by duration. Although the increases were not statistically significant (i.e., they could have been due to chance), the consistency of the relative risks for overall leukemia and AML merits discussion.

From the exposure point of view, the category "foremen/supervisors" is considered a group with low exposure, at least on a time-weighted average basis. On the other hand, among the new job categories created, "mechanics" and "maintenance/yard workers" were considered to have higher exposure than the others. Neither of these two groups showed an excess in leukemia or kidney cancer. Thus, the excesses found among "foremen/supervisors" could not be explained in terms of their average level of exposure.

In general, the job functions of foremen and supervisors would not entail much exposure to gasoline on a continuous basis. However, they might be required to perform certain tasks that could result in intermittent exposures, which would have been characterized by peak exposure. A review of the employment histories of the leukemia cases among foremen and supervisors did not reveal any unusual pattern. In particular, their frequency of peak exposure was not higher than their controls. Although some of the "foremen/supervisors" had held other jobs in the past, we could not identify any unusual pattern of previous jobs. Neither did their location of work suggest any "clustering." Thus, the observed nonsignificant increases in leukemia and kidney cancer risk did not seem to be related to gasoline exposure, a conclusion supported by the logistic regression analyses based on cumulative and peak exposure.

In addition to "foremen/supervisors," a few other groups were also found to have elevated relative risks. However, none of these relative risks were statistically significant, and all were based on very small numbers. For example, a multiple myeloma relative risk of 5.40 was found for those who had been "warehousemen" for more than 5 years. However, this relative risk was based on only 1 case, making any interpretation of this statistical finding extremely difficult.

In addition to job categories, other exposure variables were used in the case-control analyses. Included in the logistic regression analyses were several quantitative exposure indices: length of exposure, cumulative exposure and frequency of peak exposure. Exposure characterization in epidemiologic studies is dictated by the availability of historical data and limited by budgetary constraints. Outlined below is a general hierarchy of exposure classification which can be a useful guide in evaluating the relative merits of various exposure indices in occupational epidemiologic studies (Checkoway, 1986; Wegman, 1991):

1. Employment in the industry.
2. Length of employment.
3. Job categories (qualitative).
4. Job categories ordered by exposure intensity.
5. Quantitative exposure.
6. Quantitative dose (delivered to the target site).

Therefore, according to the above hierarchy, analyses based on quantitative exposure indices (such as cumulative exposure in ppm-years) should carry more weight than analyses based on job categories.

Analyses based on univariate logistic regression did not indicate any relationship between the diseases of interest and quantitative gasoline exposure indices (length of exposure, cumulative exposure, peak exposure). Since these exposure indices correlated with one another, multiple logistic regression models were also used. For example, cumulative exposure was highly dependent on length of exposure. In one of the models, both cumulative exposure and length of exposure were analyzed simultaneously. Again, no association between any of the four disease categories and any of the exposure indices was found. These case-control analyses based on logistic regression confirmed the findings based on subcohort SMR analyses and proportional hazards models reported in the original cohort study.

In the original cohort study, a modest increase in acute myeloid leukemia (SMR=150.5, nonsignificant) was reported among the land-based terminal workers. A review of the work histories of the 13 AML deaths indicated that 9 were first exposed before 1949. As discussed earlier, the recommended standard for benzene underwent a considerable reduction between 1947 and 1949. Assuming a similar reduction of benzene exposure in the industry, a comparison of AML risk by year of first exposure (≤1948 v. ≥1949) would be informative.

A comparison of AML risk by year of first exposure based on either the Mantel-Haenszel χ^2 or the conditional logistic regression did not find any significant difference. Several explanations are possible. First, the modest increase in AML observed in the cohort study might not be related to occupational exposure in general or to gasoline exposure in particular. Furthermore, exposure to benzene among distribution workers was not as high as levels reported previously for other chemical workers. There might not be any effects at low exposure levels such as those observed in our studies. This explanation was supported by the lack of an exposure-effect relationship based on the proportional hazards analyses in the cohort study and the conditional logistic regression analyses in the case-control study.

Second, AML as a single disease category may not be as homogeneous as once thought to be, especially for etiologic investigations. Recent research suggests that, at the molecular and cytogenetic levels, AML may be considered a heterogenous disease (M. T. Smith, et al., 1992). Similarly, in a recently published epidemiologic study, the first of its kind, using *ras* mutation-positive (*ras*-positive) AML as a molecular subtype, Taylor et al. (1992) reported that *ras*-positive AML was associated with various occupational exposures but not *ras*-negative AML. The occupational association reported by Taylor et al. (1992) would not have been detected had *ras*-positive and *ras*-negative AML patients been analyzed as a single group. Thus, cytogenetic information may increase the specificity of disease classification, which in turn may substantially enhance the sensitivity of epidemiologic studies.

Third, the hematopoietic toxicity of benzene is believed to be attributed to covalent DNA-binding of its toxic metabolites produced through bioactivation mediated by enzymes (P-450) in the body (Snyder, et al., 1981; Bauer, et al., 1989). Since gasoline is a complex mixture of aliphatic and aromatic hydrocarbons (with 2% to 3% benzene), many other components of gasoline may compete with benzene for metabolism-bioactivation and thereby modify its toxicity. For example, animal studies (Andrews, et al., 1977; Sato and Nakajima, 1979) have demonstrated that toluene, which is present in gasoline, can act as an inhibitor of the metabolism of benzene. This competitive inhibition or antagonism can reduce the metabolite-mediated toxicity of benzene.

Thus, the complex toxicological relationship between various components of gasoline is not accurately reflected in a single index based on total hydrocarbons. In other words, the exposure indices based on air concentrations of total hydrocarbons may not accurately reflect the actual "dose" of benzene-metabolites available for covalent binding with DNA at the target site. Indeed, continuing to improve exposure assessment (such as the incorporation of pharmacokinetic or toxicokinetic models) will remain a challenge for epidemiologists, industrial hygienists and environmental scientists in the future.

Before closing, some potential limitations of the case-control study should be pointed out. For certain job categories, the number of available cases was too small for a definitive analysis. For example, both "mechanics" and "maintenance/yard workers" categories were created for the case-control analyses to capture their intermittent exposure patterns. However, the numbers of cases in these categories were too small for any definitive analysis.

Exposure information in the case-control analyses was limited to employment in the petroleum industry. No information on lifestyle, previous medical histories, or information on employment outside the petroleum industry was available to control potential confounding effects. Many substances have been reported to be associated with an increased risk of the diseases under investigation. For example, gamma radiation (Flodin, et al., 1981) and cigarette smoking (Severson, et al., 1990) have been linked to an increased risk of AML. For kidney cancer, cigarette smoking (Doll and Peto, 1976; McLaughlin, et al., 1983) and dietary fat and cholesterol (Wynder, et al., 1974) have been found to be risk factors in epidemiologic studies. Cigarette smoking (Mills, et al., 1990), use of laxatives (Linet et al., 1987), a history of diabetes (Boffetta, et al., 1989) and a history of musculo-skeletal diseases (Doody, et al., 1992) have been linked to multiple myeloma. It was beyond the scope of this case-control study to collect information on these potential confounding factors.

Finally, although an extensive effort has been made to characterize gasoline exposure in this study, the indices based on total hydrocarbons may not reflect accurately the biological "dose" of various components of the complex mixture of gasoline.

5.0 CONCLUSION

In this nested case-control study, a finer and more homogeneous job classification than the one used in the original cohort study was developed. In addition to job category, several quantitative gasoline exposure indices were used in the analyses: length of exposure, cumulative exposure (ppm-years) and frequency of peak exposure. Time period of first exposure to gasoline (≤1948 vs. ≥1949) was also included as an exposure index.

Analyses based on the Mantel-Haenszel χ^2 and conditional multiple logistic regression were performed for four disease categories: leukemia (all cell types), acute myeloid leukemia, kidney cancer and multiple myeloma. Although some nonsignificant excesses were found for some job categories, these excesses did not appear to be related to gasoline exposure. Analyses based on logistic regression did not find any increased risk or exposure-effect relationship between the exposure indices and any of the four diseases. Time period of first exposure to gasoline (≤1948 vs. ≥1949) was also found to be unrelated to the four diseases under investigation.

Based on the results of this case-control study as well as the findings in the original cohort study, we conclude that exposure to gasoline at the levels experienced by this cohort is not a significant risk factor for leukemia (all cell types), acute myeloid leukemia, kidney cancer, or multiple myeloma.

6.0 REFERENCES

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