

Epidemiologic Survey of Leukemia in Persons Potentially Exposed to Benzene

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A review of the literature on the epidemiology of leukemia in persons exposed to benzene reveals a lack of broad based population studies. Browning¹ in 1965 reported a total of 61 cases of various types which had been reported between 1897 and the early 1960's. The majority of these were single cases, with seven being the largest number in any one series.

The lack of data on the 1897 case makes the diagnosis doubtful and according to Dameshek and Gunz² the first clearly established case of leukemia in a benzol worker was published in 1928 and the second in 1932. Vigliani and Saita³ in 1964 reported that they had seen 47 cases of benzene hemopathy between 1942 and 1963 at the Clinica del Lavoro — six of these had leukemia. During the period 1960 to 1963 the neighboring Institute of Occupational Health in Pavia observed five cases of leukemia. All the rest of Italy reported 13 cases during the period 1941 to 1963. The majority of these were workers in small plants or cottage industries where solvents or glues containing up to 60% benzene were used and the exposures were apparently high, although no exact measurements were made. The duration of exposure ranged from 4 to 20 years. Vigliani also cites Cavignaux⁴ who reported on 42 cases of benzene myelopathy occurring in France during the years 1960 to 1961, six of these were cases of leukemia.

Aksoy⁵ in 1972 reported the deaths

from leukemia of four Turkish shoemakers who worked for periods of 6 to 14 years in unhygienic conditions where air concentrations between 150 and 210 ppm were measured. Although the fact of excessive benzene exposure appeared evident in all of these cases there was little, if any, indication of the total number of workers at risk. In an earlier work by the same group of investigator⁶ however, they had reported a study which conforms more closely to a true epidemiological investigation. They compared the hematological findings in a control group of 100 males with those in 217 apparently healthy males employed in a number of poorly ventilated shoe shops where benzene solvents were used. Benzene exposures ranged between 30 and 210 ppm for periods of three months to 17 years. Although 51 (23.5%) of the exposed workers showed hematological abnormalities, consisting of leucopenia, thrombocytopenia or pancytopenia, no cases of leukemia were observed. Mild to moderate hypochromic or normochromic anemia was present in the exposed group but was also noted in 21% of the controls, so the authors were hesitant about ascribing this abnormality solely to benzene.

One other fairly large scale study in the field was reported in 1971 by Ishimaru et al⁷ as part of the follow-up work done in Japan by the Atomic Bomb Casualty Commission. The major work of this group has been related to the correlation of the radiation dose received and the development of pathological changes in various organ systems. In particular their work has shown that an

increase in leukemia incidence can be related to a single dose of 100 RADS or more, that the modal incubation time is about five years and that approximately 90% of cases will occur within ten years of the exposure.

In the work referred to here however, Ishimaru and his co-workers attempted to evaluate occupational and other environmental factors in relation to the incidence of leukemia in persons exposed to the radiation from single atomic bomb blasts in Hiroshima and in Nagasaki in 1945. In 303 pairs of adult leukemia cases and controls, the risk was approximately 2.5 times higher among those with a history of probable occupational exposure to benzene or its derivatives and medical x-ray. Unfortunately, the retrospective nature of the study, the fact that the environmental exposure data in many cases had to be obtained from relatives or close friends of the leukemia victims and a lumping together of occupations where solvents probably containing benzene were used with those where medical x-ray exposure existed, make it impossible to really isolate the benzene effect.

This somewhat confusing situation is not clarified by the fact that experimental attempts to induce leukemia in animals have not been uniformly successful.⁸ Thus, while there are a number of cases where exposure to high levels of benzene is followed by marked hematopoietic changes, including acute leukemia, there is less than solid scientific evidence for attributing leukemia to exposure to low levels of benzene.⁸

The comments by an official of a European government agency that data

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from medical records of a company such as Exxon might influence their action in recommending a ceiling limit on benzene provided the incentive for undertaking this study. Eight European affiliates were asked to participate and all responded generously and enthusiastically to our request for assistance.

Methodology

The eight affiliates chosen were selected because past experience had indicated they had a fairly broad based experience with the manufacture, transportation and marketing of petroleum or chemical products containing benzene for at least ten years. They also had well organized periodic examination and absentee data collection for their entire population for a similar period.

The participating affiliates were: (1) AIS Norske Esso; (2) Esso A.C.; (3) Esso Belgium S.A.; (4) Esso Italiana; (5) Esso Nederland N.V.; (6) Esso Petroleum Co. Ltd.; (7) Esso Standard S.A.F.; and (8) Esso (Switzerland).

Our original proposal was purposely rather general in nature, particularly with respect to the diagnostic categories included. Figure 1 shows the form sent to the cooperating affiliates:

As the completed forms were returned it became obvious that entities such as aplastic anemia were not frequent enough to have any statistical validity or the diagnostic terminology did not permit comparison with statistics reported for the general population. For these

reasons it was decided to confine the study to leukemia.

Certain methodological problems were recognized from the onset of the study. They were: (1) Low incidence of leukemia in the general population; (2) The validity of the diagnosis of the cases of leukemia reported; (3) The quantitative definition of the extent of exposure to benzene of the population under study; (4) The inadequacy of follow-up on annuitants; and (5) Incomplete occupational histories on individuals with the diagnosis of leukemia.

The problems listed above may be amplified as follows:

1. The incidence of leukemia in the general population with an age distribution similar to that under study is very low — about three to eight cases per 100,000 population. This makes meaningful evaluation of the occurrence of an odd case or two in a small company or unit difficult. To overcome this problem we have used the "person-years" concept. This involved cumulating the population of each af-

filiate for the 10-year period 1962 to 1971 chosen for study. This gave us a reasonably large denominator for calculating incidence rates. We were able to obtain the total employee population figure from all of the affiliates for the years in question and the annuitant totals from six of the eight. The age breakdown for the entire population for each year of the 10-year period was unobtainable. We were, however, able to obtain this data on employees for 1971 from Esso Europe. This information plus the use of the percentage age distribution from general census data for 1971 applied to the annuitant person years yielded an age distribution population which we believe to be reasonably accurate.

2. The validity of the diagnosis of leukemia. The majority of the cases of leukemia were identified by a review of the annual absence data (which also includes deaths). Many of these were under the care of their own physicians and we had no means of verifying the laboratory or necropsy data which formed the basis for the diagnosis.

3. The quantitative definition of the extent of exposure to benzene of the population under study is admittedly inexact. While data exist regarding certain jobs primarily related to the handling of benzene containing products (operators in benzene extraction plants, barge operators, tank truck operators, etc.) these are necessarily "spot" observations. Sherwood⁹ in 1971 summarized the results of personal air sampling from routine operations in an aromatics plant (Table 1).

In 1972 the same author¹⁰ reported observations on two loaders and one weigher at a loading rack where petrol containing 2.7% and 4.5% benzene by weight was handled (Table 2).

An Institute of Petroleum study group headed by G. S. Parkinson reported results of a survey of retail filling stations

Table 1. — Results: Personal Air Sampling From Routine Operations.

Plant	Operation	Season	Concentration (ppm)	Duration (min)
Aromatics production	Plant sampling	Winhr	4	10
	Plant sampling	Summer	20	10
	Tank dipping	Summer	3	10
Benzene feedstock	Plant sampling	Summer	<0.05 to 0.5	6
	Tank dipping	Summer	2.4	6
	Draining water from tank	Summer	3A	5

Fig 1. — Leukemia epidemiological study.

YEAR	RANGE OF % BENZENE (BY VOL) IN PRODUCTS HANDLED IN -				TOTAL CO POP (ACTIVE EMPL + LIVING ANNUITANTS)	TOTAL NO OF CASES* OF (EMPL & ANNUITANTS)			NO OF EYPL & ANNUITANTS WITH EXPOSURE TO MORE THAN 1% OF BENZENE FOR 5 YEARS IN:	3 OF CASES OF BLOOD DISCRASIAS IN EYPL ANNUITANTS WITH EXPOSURE TO MORE THAN 1% OF BENZENE FOR 5 YRS
	REFINERIES	CHEMICAL PLANTS	TRANSPORTATION	MARKETING		LEUKEMIA	APLASTIC ANEMIA	OTHER BLOOD DISCRASIAS		
1962										
1963										
1964										
1965										
1966										
1967										
1968										
1969										
1970										
1971										

* PLEASE INDICATE NUMBER OF DEATH CASES IN THIS TOTAL BY ()

Table 2. — Summary of Air Sampling Results.

	Loader 1	Loader 2	Weigher
Number of samples	22	17	23
Total sampling period (min)	328	246	342
Exposure (ppm-hours)	8.7	10.2	114
(Morning work only)	(5.6)	(9.7)	(99)
Mean concentration (ppm)	1.6	2.5	20

and normal gasoline transport operations in 1971.¹¹ The survey which was carried out in August and September 1969 included nine filling stations, one road car loading station studied for two days, two rail car loading stations studied for six days and the loading of benzene enriched gasolines for three days at each of three locations. The following con-

people with a potential exposure to 1% or more benzene over a 5-year period. Another way in which we approached the problem was to solicit available information on the percentage of benzene in products handled in the major functional units of each affiliate. From this we derived a "benzene exposure index" which gives a very crude exposure com-

Table 3. — Leukemia Epidemiological Study
Distribution of Cases
of Leukemia by Affiliate.

Esso A.G.	3
Esso Petroleum Co. Ltd.	2
Esso Standard S.A.F.	6
Esso (Switzerland)	1

leukemia. Although the last job category of most of the cases of leukemia reported was available, a number had inadequate histories of what jobs they had held in the past or if they had any benzene exposure during a significant part of their working career.

Results

cases
period

cases

cases

two

more

cases

cases

loading installations did not indicate any significant exposure to benzene."

Until the 1950's employees tended to remain in specific job assignments in given locations in a plant for many years. With the introduction of manpower reduction and efficiency improvement programs in many company locations the concept of mobility or flexibility of job assignment developed. In some instances process operators did unit mechanical work and specific craft assignments gave way to the refinery mechanic concept, so that employees might work near a pump or line containing benzene one or two days and then might be in a benzene free area for days or weeks. Only in locations where highly concentrated benzene was manufactured or transported are assignments reasonably constant and medical controls in effect.

Our approach to this question was to

Table 4. — Leukemia Epidemiological Study — Summary of 18 Cases of Leukemia by Sex, Age at Death (or 1971), Last Job Assignment and Type of Leukemia.

Sex	Age at Death	Last Job Assignment	Type of Leukemia
F	19	Clerk, Head Office	Leukemia, Type?
M	26	Engineer, Refinery	Leukemia, Type?
M†	33	Passenger Car Driver (Tank Truck Driver 1960-66)	Chronic Myeloid Leukemia
M†	36	Mechanic in Refinery	Leukemia, Type?
Y†	40	Plant Operator, Refinery	Myeloid Leukemia
M†	41	Fitter, Refinery	Acute Leukemia
M	42	Kerosene Truck Driver, Airport	Leukemia, Type?
M	46	Mathematician, Head Office	Leukemia, Type?
M†	60	Marketing Superintendent	Leukemia, Type?
M	61	Industrial Assistant Dealer	Leukemia, Type?
M	62*	Carpenter, Refinery	Leukemia, Type?
M†	66	Truck Driver, Marketing	Leukemia, Type?
M	68	Commercial Clerk, Head Office	Leukemia, Type?
M	68*	Clerk Chauffeur, Refinery	Leukemia, Type?
M	69	Clerk, Head Office	Chronic Myeloid Leukemia
M†	70	Process Operator, Refinery	Leukemia, Type?
M	71	Manager, Head Office	Acute Myeloblastic Leukemia
M†	73*	Mechanic, Marketing Repair Shop	Chronic Lymphatic Leukemia

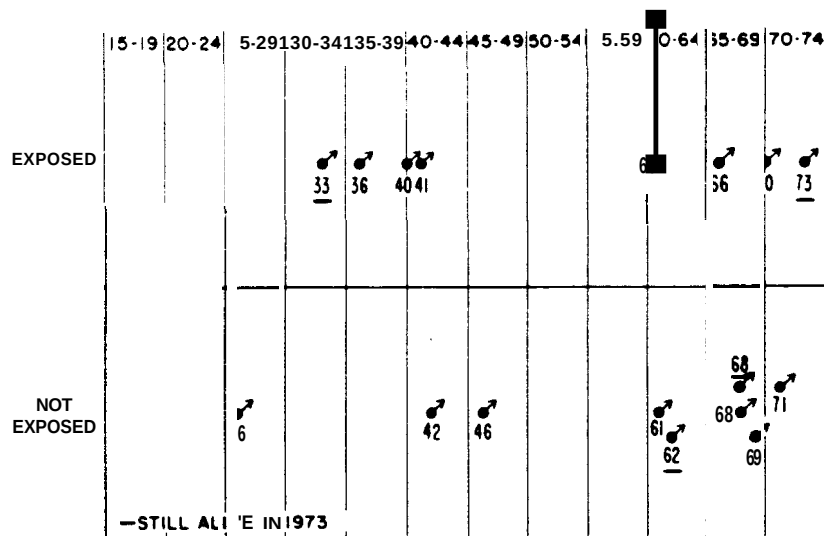


Fig 2 — Age distribution of 18 cases of leukemia (age at death or Dec. 1971).

type of leukemia is given in Table 4.

Figure 2 shows the cases distributed by 5-year age groups in the two major subdivisions "Exposed" and "Not Exposed". As previously noted under Methodology we defined the "exposed" group as those individuals who worked for five or more years in jobs where there was a potential exposure to 1% or more benzene. While we received numbers for this category from all affiliates, the physicians who reported them were well aware that this data was not as exact as it might appear. Some indicated that they were reasonably confident that the jobs included in this category did have an associated benzene exposure, usually at a low level, but the fact that one employee stayed in a particular job five or more years was more difficult to establish. Other medical directors indicated that the number reported in the "exposed" category was more indirectly derived: The number of people in administrative/clerical jobs in headquarters or in the plants was subtracted from the total population and the difference was considered to represent the "exposed" group. What we have in Figure 2 then is, in effect, probably a spectrum extending from an occasional benzene exposure of unknown degree and duration down to absolutely no exposure.

Table 5 recapitulates the jobs considered to be in the "Exposed" and "Not Exposed" categories and reinforces what has just been said about the difficulty in making a sharp distinction between the two. Under the indirect method of calculating exposure one would probably consider the refinery carpenter

and the kerosene truck driver as exposed. It so happened that the physician reporting these cases could categorize them as not having had any benzol exposure.

An attempt to analyze the reported cases of leukemia by various pathological types was unsuccessful as shown in Table 6.

Table 5. — Job Titles of Cases of Leukemia in "Exposed" and "Not Exposed" Categories.

Exposed			Not Exposed		
Job Title	No. of Cases	Age	Job Title	No. of Cases	Age
Tank Truck Driver	2	33, 66	Clerk, Head Office	1	19, 68, 69
Refinery Mechanic	2	36, 41	Manager, Head Office	1	71
Refinery Operator	2	40, 70	Refinery Engineer	1	26
Marketing Repair Mechanic	1	73	Mathematician, Head Office	1	46
Marketing Superintendent	1	70	Refinery Carpenter	1	62
			Refinery Clerk	1	68
			Ind'l Assistant Dealer	1	61
			Kerosene Truck Driver, Airport	1	42

While understandable in a retrospective study reaching back more than ten years, it is unfortunate that we can only be specific about 3 of the 18 cases Vigliani³ has said

We have never seen a case of chronic myeloid or lymphatic leukemia in workers poisoned with benzene all cases seen by us and at the Institute of Pavia in which harmful and prolonged exposure to benzene vapors was ascertained, were hemocytoblastic in type. Whether chronic types of leukemia can be induced by benzene is still an open question, but we must emphasize our view that in some of these cases reported in the literature the occupational history was not con-

vincing. The number of persons occasionally exposed to benzene or exposed to very low benzene concentrations was so high that some cases of chronic leukemia could have occurred among them as among any other working population.

If the data were available and Vigliani is correct we might have had another parameter available by which to evaluate the relationship of the disease to possible exposure.

Turning to the comparison of the experience of the eight affiliates in the study with that of the general population in the same geographical area, Table 7 shows the cumulative employee plus annuitant man-years and the number of cases of leukemia reported.

To make a valid comparison of the leukemia mortality experience between a population of 383,276 and that of the eight European countries involved with a total population many times greater, we chose to compare the "observed" with the "expected" number of deaths. This required apportioning the man-years experience into the same 5-year age classes used to report WHO mortality data. This could be done for the age groups 15

through 69 by multiplying the total employee man-years (321,840) by the percentage distribution in each 5-year class reported to us by Esso Europe for 1971

Table 6. — Types of Leukemia Reported

Type	No.
Chronic Lymphatic Leukemia	1 ^{xx}
Chronic Myeloid Leukemia	2 ^{xx}
Myeloid Leukemia	1 ^{xx}
Acute Myeloblastic Leukemia	1
Acute Leukemia	1 ^{xx}
Leukemia, Type Unspecified	12

^{xx} In "Exposed" Group

When we sought a similar allocation of the 58,436 annuitant man-years we did not have an exact percentage distribution by age groups available within the region so we had to resort to an indirect approach. Utilizing the population of the U.K. (where 37% of our employee population is located) as recorded in the U.N. Demographic Year Book of 1971 for the 5-year age classes 55 through 85 and over, we applied the proportion of the general population in those age groups to our annuitant total. Table 8 shows the estimated age adjusted population arrived at after the above calculations. The "expected" number of deaths was calculated from the age specific mortality rates in the WHO data for 1966 (mid-point of the study).

This information may be summarized by the Standardized Mortality Ratio (SMR):

$$SMR = \frac{\text{Observed No. of Deaths}}{\text{Expected No. of Deaths}}$$

$$SMR = \frac{18}{23.23} = 0.77 = 77\%$$

Since the incidence of leukemia is low, and the study population is relatively small, chance factors may have produced an SMR in this study which is quite different from what might have been found if the study population had been infinitely large. Therefore, before any conclusions can be drawn about the significance of the SMR, we must estimate the most likely values of the true SMR. This must be done in two steps:

1. The Standard Error (SE) has to be calculated by the following formula:

$$SE = \frac{SMR \text{ Expressed as } \% \times 100}{\text{No. of Expected Deaths}}$$

$$SE_{SMR} = \frac{\sqrt{77 \times 100}}{23.23} = 18.21$$

2. A confidence interval (CI) must be calculated. This is an interval which we can say with 95% confidence includes the true SMR, and utilizes the following formula:¹²

$$CI = SMR \pm (1.96 \times SE_{SMR})$$

$$CI = 77 \pm (1.96 \times 18.21) = 113\% \\ 77 - (1.96 \times 18.21) = 41\%$$

Since the interval within which we are 95% confident that the true SMR lies also includes the value 100, we cannot with confidence rule out the possibility that the true SMR is in fact equal to 100. For

Table 7. — Employee & Annuitant Man-Years and Cases of Leukemia.

Affiliate	Man-Years	No. of Leukemia Cases
A/S Norske Esso	13,439	0
Eno A.G.	74,419	3
Esso Belgium	16,606	0
* Esso Italiana	38,092	0
* Esso Nederlands N.V.	17,807	0
Esso Petroleum Co. Ltd.	143,554	8
Esso Standard S.A.F.	74,299	6
Esso (Switzerland)	5,060	1
Total	383,276†	18

* Does not include annuitants

† Includes 58,436 Annuitant Man-Years (15% of Total)

this reason, instead of saying that our leukemia experience is better than the general population we prefer simply to say that it is probably no worse than one would find in the same age span of the population as a whole.

The next question that arises is whether this "normal" mortality experience for the disease under suspicion (leukemia) could be unremarkable when the total European experience is considered and still conceal an abnormal figure in a given location. If we look at Table 7 again we see that four of the affiliates have no cases, one has one case and another has three cases. By inspection we can say that these six do not

have an abnormal mortality experience. This leaves Esso Petroleum Company Ltd. with eight cases and Esso Standard S.A.F. with six to be evaluated. Table 9 summarizes the results of tedious calculations utilizing employee-annuitant person-years and the 1966 WHO Age Specific Mortality Rates for these two affiliates.

This close approximation of observed to expected deaths is of particular interest in the case of Esso Petroleum. This affiliate has been keeping good follow-up records on annuitant deaths since 1964 (8 of the 10 years included in the study) which gives us reasonable confidence that the observed number of

Table 1. — Expected vs. Observed Deaths From Leukemia in 8 European Affiliates 1962 - 1971.

Age at Time of Death	Estimated Age Adjusted Total Person Years	Age Specific* Mortality Rates (WHO-1966)	Expected No. of Deaths	Observed No. of Deaths
15-19	3,283	2.2	0.07	1
20-24	15,592	1.7	0.26	0
25-29	36,707	2.7	0.99	1
30-34	49,051	2.1	1.03	1 (1) ^{xx}
35-39	47,102	3.0	1.41	1
40-44	51,000	3.4	1.73	3
45-49	48,726	4.6	2.24	1
50-54	37,681	6.1	2.30	0
55-59	38,049	8.0	3.04	0
60-64	25,960	12.4	3.22	3 (1) ^{xx}
65-69	11,519	16.8	1.94	4 (1) ^{xx}
70-74	8,064	20.6	1.66	3 (1) ^{xx}
75-79	5,610	28.5	1.60	0
80-84	3,214	37.1	1.21	0
a5 And Over	1,753	30.0	0.53	0
Total All Ages	383,276		23.23	18

* The Age Specific Mortality Rates shown were taken from those of the country (or average of the countries) reporting the cases in the Esso population.

Cases shown ()^{xx} are still living but for these calculations were assumed to have died at their age in 1971 (see text).

Table 9. — Expected vs. Observed Deaths From Leukemia and SMR's for Esso Petroleum and Esso Standard S.A.F.

Affiliate	Person Years	Expected No. of Deaths	Observed No. of Deaths	SMR
Esso Pet. Co. Ltd.	143,554	8.94	8	89.5
Esso Std. S.A.F.	74,299	5.56	6	107.7

ukemia deaths is correct. Our overall appraisal of the data for the eight individual affiliates is that there is no abnormal concentration of leukemia in any one geographic location.

Since we were unable to demonstrate any meaningful difference in the leukemia mortality experience in one affiliate compared to the others, we decided to test the experience of the "exposed" versus the "non-exposed" fractions of the total population. Unfortunately we did not have the age distribution of these two groups for Europe as a whole to calculate "expected" vs. "observed" deaths in the same way we did for the total employee-annuitant population. A simple calculation can be made using the total age adjusted "expected" deaths (23.23) multiplied by the fraction: "Exposed" person years/Total person years and "Non-exposed" person years/Total person years with the results shown in Table 10.

Although this indicates a slight preponderance of "observed" over "expected" deaths in the exposed group, the CI extends from 37 to 205, which translated in terms of expected deaths gives a range of 2.5 to 13.5 hence the observed difference is not significant.

One final attempt was made to determine whether there was a difference between the exposed and non-exposed categories. Esso Petroleum Company

Table 10. — Expected vs Observed Leukemia Deaths in Exposed and Non-Exposed Groups.

	Exposed	Non-Exposed
Expected No. of Deaths	6.6	16.7
Observed No. of Deaths	8.0	10.0
S.M.R.	121.	60

Table 11. — Expected vs Observed Deaths From Leukemia in "Exposed" and "Non-Exposed" Portions of Esso Pet Co. Ltd. Population

	Exposed	Non-Exposed
Expected No. of Deaths	4.62	4.33
Observed No. of Deaths	5	3
SMR	108	69

which, as we have noted, probably has the most accurate figure for leukemia deaths has exposed and non-exposed populations which are approximately equal ("exposed" = 70,570 person years; "non-exposed" = 72,984 person years). We assumed that all person years in the age groups 15 to 19 and 20 to 24 were "unexposed" since our criteria for exposure included at least 5 years in an "exposed" job. We then allocated the person years for the age groups 25 to 85 plus in the ratio 70,570 63,349::exposed: non-exposed, using the age distribution for the entire company. The calculations for the "expected" number of leukemia deaths and their SMR's were made as previously described. Table 11 shows the results of this calculation.

Our conclusion is that we could not prove that the number of observed leukemia deaths exceeded the expected number in the exposed group at the 95% confidence level.

Although we had no convincing evidence that the leukemia mortality in the 8 affiliates in the study was abnormal we attempted to relate the observed mortality rates to the potential benzene exposure in the group. Since we lacked information of the exposure levels measured by multiple sampling we approached this indirectly. In our original questionnaire we had requested data on the percentage of benzene in products processed or handled in various types of operations - i.e. refining, transportation etc. Table 12 shows the form in which this data was reported by one affiliate:

In a number of the affiliates this information was much more varied. We attempted to reduce this complex mass of information to relatively simple terms by using a Benzene Index as shown in Table 13.

Table 14 shows the Benzene Index and the crude mortality rate for leukemia in each affiliate.

If this data is plotted with the Crude Mortality rate on the ordinate and the Benzene Index on the abscissa there is no demonstrable relationship between the two (Figure 3).

One conclusion is that low levels of

potential benzene exposure are unrelated to leukemia mortality. Other possible explanations are (1) The amount of benzene handled in our operations is not related to the actual exposure of employees (2) The criteria for estimating exposure are not uniform from one affiliate to another. This emphasizes the point that more data are needed from our industrial hygienists to classify job exposures to potentially hazardous materials.

Discussion and Conclusions

Despite the problems of data collection outlined in the early part of this presentation, the resultant necessity for making a number of assumptions and recourse to what some may consider "statistical manipulation", we believe that this effort was worth the time and energy on the part of all concerned. We believe that two objectives were attained:

1. The demonstration that the occurrence of leukemia in a population of 38,000 working in a variety of petroleum and petrochemical operations, some of whom were exposed to low levels of benzene over a 10-year period was not abnormal compared to the general population in the countries concerned.

2. The demonstration of the need for improvement in the recording and storage in a readily accessible form of biological observations, job histories, occupational exposures and demographic data. In practical terms this means:

A. The adoption of a form for recording the results of periodic examinations, the causes of sickness disability and death of employees which can be entered and stored in a computer system. In order for this information to be collected centrally where it can be of maximal value the information collection system should be uniform or at least compatible.

B. The development of a method for acquiring information on the cause of death of annuitants. In affiliates where the company is paying all or part of an annuity there must be some mechanism whereby the Employee Relations Department is notified of the death of such individuals. If possible there should be a requirement that the company receive a death certificate. If so, a copy should be forwarded to the Medical Department where immediate follow-up can be made with the attending physician to

verify (and clarify) the diagnosis. This is particularly important where the possibility of a neoplasm exists, (as demonstrated in our present study by our limited information regarding the type of leukemia)

Where the annuitant has no continuing contact with the company, strong efforts should be made to enlist the cooperation of public health authorities to obtain a periodic report of annuitant deaths. This should not be an impossible task if a social security number identity system is in effect.

It is recognized that in some countries current laws forbid the transmittal of medical information to the company. In view of the current interest in the epidemiology of occupational disease the reversal of bureaucratic attitudes may be a less formidable task than we have believed to date. Efforts in this direction should certainly be made.

C. In a number of affiliates there has been a program to develop personnel data banks. Medical Directors and Advisors should consult with their managements about the possibility of entering good job histories and potential hazardous exposures into this system. Observations of the industrial hygienist might well form part of the input into this data bank.

D. Computer soft-wear programs should be developed to obtain yearly summaries of the distribution of the employee and annuitant population in 5-year classes which correspond with those used for reporting census figures and WHO mortality data.

While this concept of improving information storage and retrieval may appear unduly idealistic and expensive we are convinced that it is essential and a sound investment for the future. We are in the early stages of increased government and public health interest in regulating worker exposure to a multitude of environmental factors. In many instances regulations are proposed on highly theoretical considerations. We may expect that unrealistic regulations will be passed if there is no sound information available in the formative stage of such laws or decrees. The chief source of such data with long term statistical validity will be industries or companies such as ours which have had good medical programs for years. The irony of the present situation is that we probably have literally tons of data in

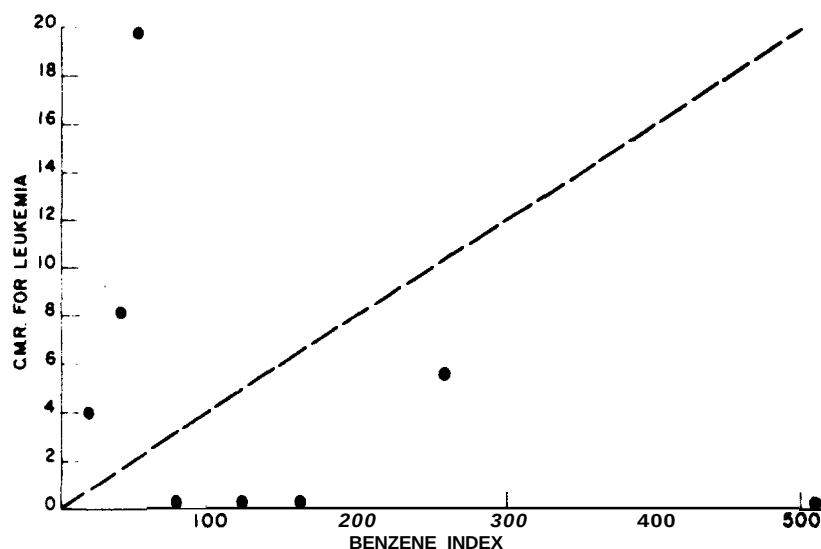


Fig 3. — Benzene index vs. crude leukemia mortality rate.

Table 12. — Range of % Benzene (by vol) in Products Handled by Esso Nederlands NV.

Year	Refining %	Chemicals %	Transportation %	Marketing %
1962	2-10	—	1-10	1-5
1963	2-30	—	1-30	1-5
1964	2-30	5-100	1-30	1-5
1965	2-30	5-100	1-30	1-5
1966	2-30	5-100	1-30	1-5
1967	2-30	5-100	1-10	1-5
1968	2-30	5-100	1-30	1-5
1969	2-30	5-100	1-30	1-5
1970	2-30	5-100	1-30	1
1971	2-30	5-100	1-30	1

Table 13. — Calculation of the Benzene Index.

Type Operation	Ave. % Benzene Handled	Population at Risk Expressed as % of Total Affiliate Population
Refining	A	I
Chemicals	A	x
Transportation	A	I
Marketing	A	u
		$B = AB$
		$B = AB$
		$B = AB$
		$B = AB$
		ΣAB
Benzene Index for Affiliate = ΣAB		

Table 14. — Benzene Index and Crude Mortality Rate for Leukemia in 8 Esso Affiliates.

Affiliate	Benzene Index	Crude Leukemia Mort. Rate
A/S Norske Esso	125	0
Esso A.G.	20	4.0
Esso Belgium SA	509	0
Esso Italiana	81	0
Esso Nederlands NV	164	0
Esso Pet. Co. Ltd.	259	5.6
Esso Standard SAF	42	8.1
Esso (Switzerland)	54	19.8

our records but no practical way to find or analyze it without the expenditure of thousands of man-hours and the loss of time at critical periods. We believe this situation can and should be improved.

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References

1. Browning E: Toxicity and metabolism of industrial solvents. Amsterdam, Elsevier, 1965.
2. Dameshek W, Gunz F: Leukemia. New York, Grune & Stratton, 1959.
3. Vigliani EC, Saita G: Benzene and leukemia. *N Engl J Med* 271:872-876, 1964.
4. Cavignaux L: Les intoxications confirmées. *Cah Med Interprof* 2:28-31, 1962.
5. Aksoy M, et al: Acute leukemia due to chronic exposure to benzene. *Am J Med* 52:160-166, 1972.
6. Aksoy M, et al: Haematological effects of chronic benzene poisoning in 217 workers. *Brit J Ind Med* 28:296-302, 1971.
7. Ishimaru T, et al: Occupational factors in the epidemiology of leukemia in Hiroshima and Nagasaki. *Am J Epidemiol* 93:157-165, 1971.
8. Cronkite EP: Evidence for radiation and chemicals as leukemogenic agents. *Arch Environ Health* 3:297-303, 1961.
9. Sherwood RJ: Occupational hygiene in aromatics plants. *Ann Occup Hyg* 14:125-135, 1971.
10. Sherwood RJ: Evaluation of exposure to benzene vapour during the loading of petrol. *Brit J Ind Med* 29:65, 1972.
11. Parkinson CS: Benzene in motor gasoline - an investigation into possible health hazards in and around filling stations and in normal transport operations. *Ann Occup Hyg* 14:145-153, 1971.
12. W. Caffey: Personal Communication who derived it from a paper by CL Chiang: Standard Error of the Age - Adjusted Death Rate Vital Statistics Special Report 47:275-285, 1961.