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A Critical Look at Hazards from Benzene in Workplace and Community Air[1]

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Experience in industry over the last half-century suggests that long-term exposure to high concentrations of benzene in the air in the workplace is associated with the occurrence of various blood dyscrasias, including leukemia.

It has been stated that no basis exists for the determination of a dose-response relationship for the leukemogenic action of benzene. A critical review of the literature, however, reveals first, that more cases occur at higher concentrations (Hardy and Elkins, 1948; Schönenberger, 1963; Vigliani, 1976); second, that the incidence drops when the level of exposure is reduced (Yllner, 1976; Ikeda, 1976; Aksoy, 1980); and third and most importantly, that no cases of benzene-induced leukemia have been reported in workers exposed to concentrations that did not exceed 100 and possibly 150 ppm (Jandl, 1977a; Aksoy, 1977; Pagnotto *et al.*, 1979).

There are some flaws in the reports which suggest an association between an excess incidence of leukemia in workers and exposure to low levels of benzene. In the context of this presentation, it is not possible to go into detail criticizing those few reports which do suggest such an association and to which reference has repeatedly been made. This critique has been given elsewhere (Lamm and Tabershaw, 1977; Jandl, 1977b; Van Raalte, 1979). A very relevant comment, however, should be repeated here. The authors of those papers suggesting such an association related the reported effects or responses to an at-times-broad range of concentrations, recorded intermittently, to which the subjects had been exposed. With respect to the concentration at the upper end of the range, this is probably justified. The observed effects are known to be associated with exposures at high levels. An entirely different situation, however, exists with regard to the concentrations at the lower end of the range. These were measured at different times. Because of the fluctuating levels in a "range of concentrations" there were probably occasions when even lower concentrations could have been recorded. In the practice of in-

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TABLE 1

FACTS (NOT OPINIONS OR DEDUCTIONS) THAT EMERGE AFTER CRITICAL EVALUATION OF THE LITERATURE

Level* (ppm)	Hematology	Myelopathy	Leukemia
10	−	−	−
15	−	−	−
20–25	−	−	−
50	+	−	−
100	+	+	±
150	+	+	+

* At the workplace during most of the time.

dustrial medicine and environmental health, the lower point of an exposure range is practically always zero. Thus, the concentrations at the lower end of a range as well as the so-called "mean concentration" become meaningless in dose-response relationships.

In these circumstances, the only meaningful relationships are

(1) an observed effect at a defined upper concentration and.
(2) a no-effect/no-response level *below* a defined upper concentration.

Bearing these comments in mind. particularly point (2), a critical evaluation of the literature reveals the facts as depicted in Table 1.

At lower concentrations no cases of effects have been described or reported that can withstand the acid test of critical validity.

BENZENE AND THE GENERAL PUBLIC

Turning now to the possibility of a leukemia hazard to members of the general public from exposure to benzene in community air, the following established facts are relevant:

(1) No cases in workers have been reported to have occurred at levels of exposure below 100 ppm.

TABLE 2

NORWAY—GASOLINE CONSUMPTION, NUMBER OF DEATHS FROM LEUKEMIA 12 YEARS LATER, AND MORTALITY RATE FROM LEUKEMIA 12 YEARS LATER

Year	Gasoline consumption (tons · 10^3)	Number of deaths from leukemia 12 years later	Mortality rate from leukemia per 100,000 12 years later
1950	322	298	8.3
1952	363	302	8.2
1954	404	322	8.6
1956	453	354	9.9
1958	511	337	a.9
1960	MU	350	a.7
1962	687	340	8.5
1964	806	341	8.5

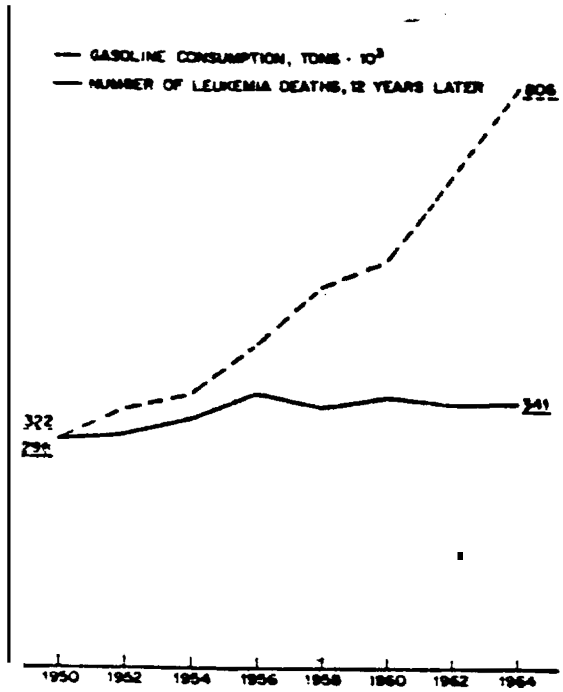

FIG. 1. Annual gasoline consumption from 1950 to 1964 and total number of cases of leukemia 12 years later, 1962 to 1976, in Norway.

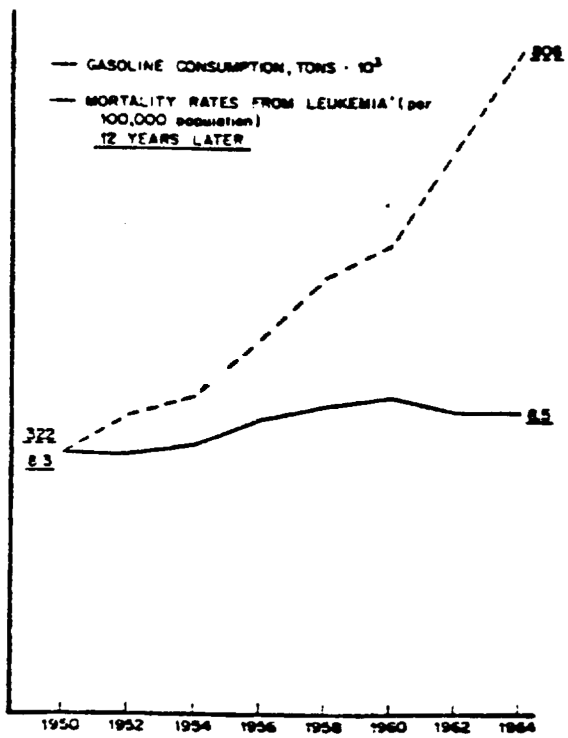

FIG. 2. Annual gasoline consumption from 1950 to 1964 and leukemia mortality rate (per 100,000 12 years later, 1962 to 1976, in Norway.

TABLE 3a

THE NETHERLANDS—GASOLINE CONSUMPTION AND MORTALITY FROM LEUKEMIA: TOTAL NUMBER OF CASES AND NUMBER OF CASES IN MEN ONLY

Year	Gasoline consumption (tons · 10³)	Total number of deaths from leukemia 12 years later	Total number of deaths from leukemia in men 12 years later
1955	888	930	531
1957	977	880	488
1959	1112	819	440
1961	1315	912	520
1962	1427	911	538
1963	1541	912	522
1964	1778	920	518

(2) Exposure of the general public occurs at concentrations at least two to three orders of magnitude lower than have been recorded for industrial situations. Measured concentrations of benzene in community air were reported to range from 0.5 to 16.3 ppb. Thus, in a Frankfurt residential area outside traffic arteries values of 4.62–16.3 ppb were measured (Batelle Institute, 1976); in an urban area in Berlin Dahlem, 0.79–4.38 ppb (Lahman *et al.*, 1978); and in a rural residential and industrial area, 3.08–9.24 ppb (Frohne and Knappe, 1975). These levels are very similar to those reported from the United States, viz., 0.49–12 ppb in 18 cities and towns and 0.49–2 ppb in rural areas (American Petroleum Institute, 1978), an average of 15 ppb with peaks up to 57 in the Los Angeles Basin (Lonneman *et al.*, 1968), and an average of 13 ppb in Toronto (Pilar and Gradon, 1973). This compares favorably to levels reported by Robinson *et al.* (1973) from air in the Amazon Basin: up to 14 ppb.

(3) Experience from Europe shows that the incidence of leukemia does not increase with increasing emissions of benzene in community air.

TABLE 3b

THE NETHERLANDS – STANDARDIZED MORTALITY RATES

Year	Gasoline consumption (tons · 10³)	Standardized mortality rate from leukemia per 100.000	Standardized mortality rate from leukemia per 100.000 males
1955	888	7.1	8.1
1956	989	7.1	8.3
1957	977	6.5	7.3
1958	1037	6.1	7.2
1959	1112	5.8	6.3
1960	1215	6.7	7.7
1961	1315	6.3	7.3
1962	1427	6.2	7.5
1963	1541	6.0	7.2
1964	1778	6.0	7.0

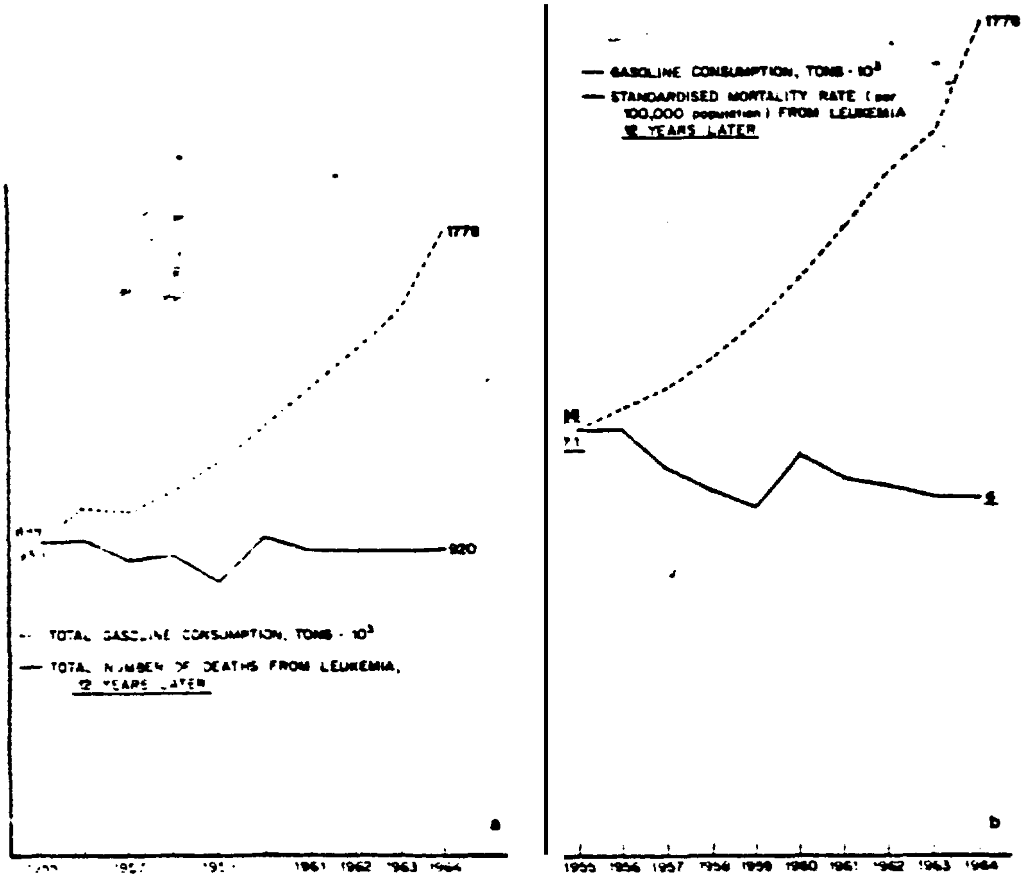

FIG. 3a. Annual gasoline consumption from 1955 to 1964 and total number of deaths from leukemia 12 years later, 1967 to 1976, in The Netherlands.
FIG. 3b. Standardized mortality rates for The Netherlands.

When far-reaching regulations are being discussed, it would seem reasonable—apart from a consideration of assumptions and, at times, acrobatic extrapolations—to take a sober look at facts and figures for what has actually occurred in real life.

GASOLINE CONSUMPTION, MORTALITY RATES, AND INCIDENCE OF LEUKEMIA IN THREE EUROPEAN COUNTRIES

There is no doubt that the greatest single contribution to the presence and concentration of benzene in community air—certainly in Europe—comes from the manufacture, transport, storage, and use of motor gasoline.

An investigation has been carried out of the consumption of motor gasoline and its benzene content in three European countries together with the number of leukemia deaths and the incidence of leukemia over a period of years. Since benzene-induced leukemia may have a latency period of 5 to 15 years, the consumption of gasoline has been correlated with the Occurrence of leukemia 5, 12, and, in one

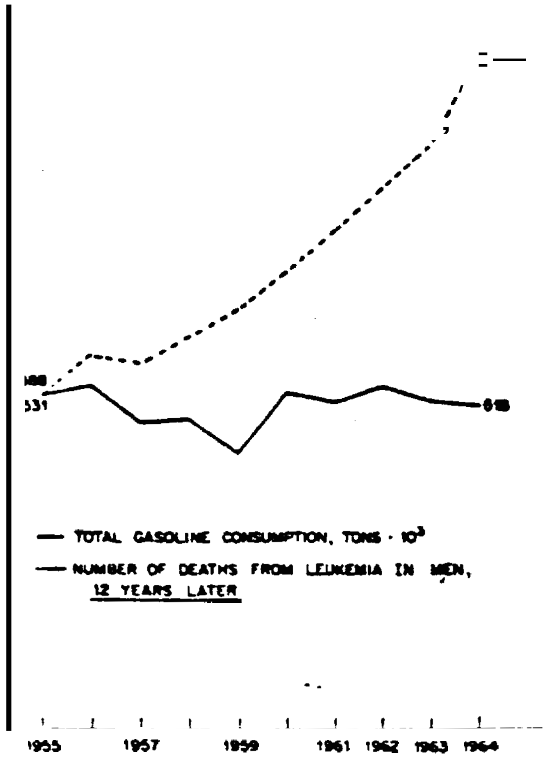

FIG. 4. Annual gasoline consumption from 1955 to 1964 and total number of deaths from leukemia, for *males* only. 12 years later, 1967 to 1976. in The Netherlands.

case. IS years later. The countries involved am Norway, The Netheriands. and Denmark. All three countries have an excellent National Bureau of Statistics which registers both movements in commerce of goods such as gasoline and causes of death from diseases such as leukemia.

TABLE 4a

DENMARK—ACUTE NONLYMPHOCYTIC LEUKEMIA (ANLL): TOTAL NUMBER OF CASES, INCIDENCE PER 100,000 AND GASOLINE CONSUMPTION 15 YEARS PREVIOUSLY

Year	Total cases of ANLL	Incidence per 100,000	Gasoline consumption (tons · 10³) 15 years previously
1968	167	3.4	614
1969	182	3.6	652
1970	158	3.7	690
1971	188	3.8	723
1972	186	3.7	756
1973	153	3.0	790
1974	145	29	852
1975	155	3.1	910
1976	133	2.6	979

TABLE 4b

DENMARK—TOTAL NUMBER OF CASES OF LEUKEMIA AND GASOLINE CONSUMPTION 15 YEARS PREVIOUSLY

Year	Total cases of leukemia	Gasoline consumption (tons · 10^3) 15 years previously
1968	487	614
1969	523	652
1970	484	690
1971	539	723
1972	506	756
1973	444	790
1974	467	852
1975	492	910
1976	438	979

1. Norway[2]

Table 2 and Fig. 1 show the annual gasoline consumption (tons · 10^3) from 1950 to 1364 and the total number of cases of leukemia 12 years later, i.e., from 1962 to 1976.

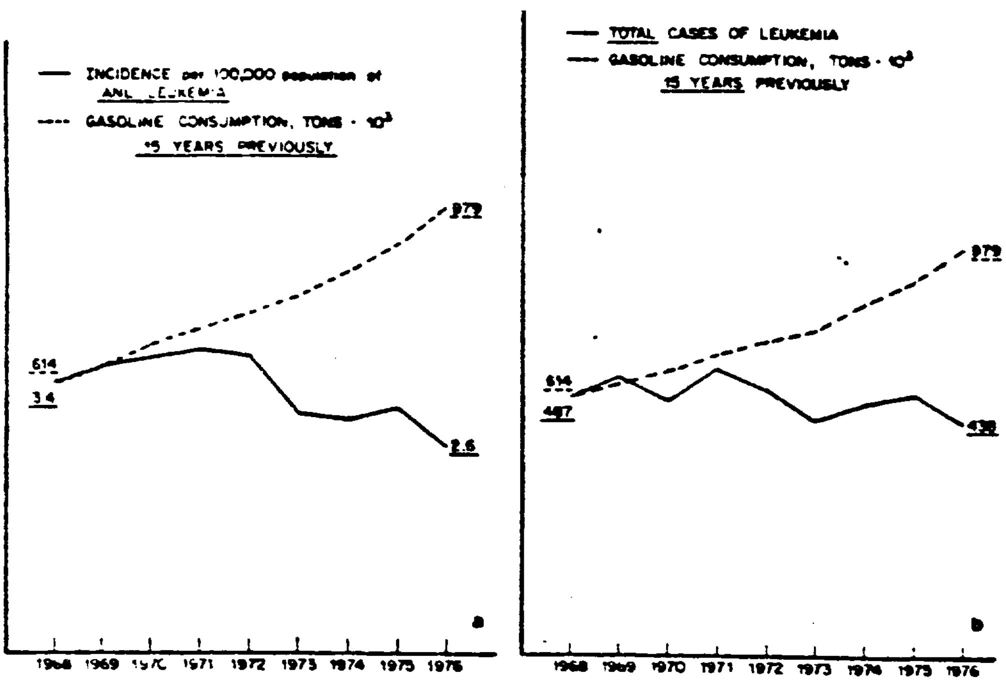

FIG. 5a. Gasoline consumption 15 years previously and incidence per 100,000 of acute nonlymphocytic leukemia in Denmark.

FIG. 5b. Gasoline consumption 15 years previously and total number of cases of all types of leukemia in Denmark.

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[2] *From*: Secretary-General, Norwegian Petroleum Institute and Cancer Registry of Norway, Oslo, 1978: "Incidence of Cancer in Norway."

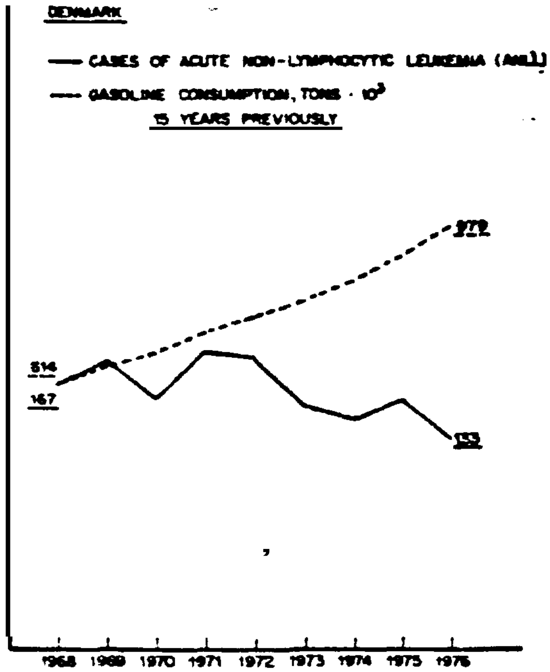

FIG. 6. Gasoline consumption 15 years previously and total number of cases of acute nonlymphocytic leukemia in Denmark.

Since the population of Norway increased considerably during the period which would affect the number of cases of leukemia from other causes, the incidence of leukemia per 100,000 population was also tabulated and this is also shown in Table 2 and Fig. 2.

2. *Netherlands*[3]

Table 3a and Fig. 3a show the total annual gasoline consumption (tons. 10^3) from 1955 to 1964 and the mortality from leukemia expressed as the total number of cases 12 years later, i.e., from 1967 to 1976. Since men would probably be more heavily exposed than women, a similar investigation was carried out for males only (Fig. 4). There is no correlation. The standardized mortality rates have decreased (see Table 3b and Fig. 3b).

3. *Denmark*[4]

Denmark has a very sophisticated cancer registry which enabled tabulation of the acute nonlymphocytic leukemia (ANLL) cases separately. It is this *type* of leukemia which particularly has been associated with exposure lo benzene. Tables 4a and b and Figs. 5a and b and 6 show the number of cases as well as the incidence of ANLL per 100,000 population, together with the gasoline consumption 15 years previously.[5]

[3] *From:* Anonymous (1978); OECD Statistics; and Centraal Bureau Statistiek, Voorburg.
[4] *From:* Danish Institute of Petroleum; Clemmesen (1979).
[5] Table 4b and Fig. 5b show all cases of leukemia.

TABLE 5

DENMARK—TOTAL NUMBER OF CASES OF ANLL IN MALES ONLY AND GASOLINE CONSUMPTION 15 YEARS PREVIOUSLY

Year	Number of cases of ANLL in men	Gasoline consumption (tons · 10^3) 15 years previously
1968	84	614
1969	103	652
1970	91	690
1971	91	723
1972	102	7%
1973	80	790
1974	72	852
1975	82	910
1976	63	979

Table 5 and Fig. 7 show the total number of cases of ANLL in males only and the total gasoline consumption 15 years previously.

The benzene content of motor gasoline in all three countries gradually increased from an average of 1.5% in the midfifties to 3-3.5% (range 2-6%) in the sixties and seventies. For Denmark (Clemmesen, 1979) the absolute number of cases of ANLL remained constant during and after the war.

Gori, deputy director of NCI, emphasizes "the distinction between the practical and the theoretical" (1980). The above figures tend to confirm this and would lead to rhc conclusion that at low concentrations benzene has little or no effect on the incidence of Ieukcmia.

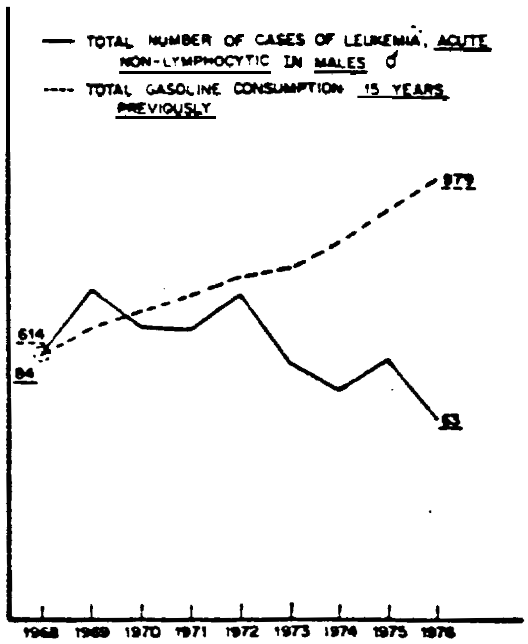

FIG. 7. Gasoline consumption 15 years previously and total number of cases of acute nonlymphocytic leukemia, for *males* only, in Denmark.

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Not a good study

1. No measurement of Benzene Exposure rates

2. Why not ask about who pumped in the gasoline!

3. what about the oil refinery worker?