Monsanto

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MAR 4 1985

Dear David:

Enclosed is a photocopy of the report "Mortality of PCB Workers at the Monsanto Plant in Sauget, Illinois" by Judith Zack and David Musch. As far as I know, this is the final report, although the report was never published in the scientific literature.

It was good hearing from you yesterday. I will be attending the NIOSH Dioxin Registry meeting in Cincinnati on March 14-15, 1985, and I am looking forward to seeing the old crew that is still working at NIOSH.

Sincerely,

Terry L. Leet

Enclosure

cc: W.R. Gaffey

Mortality of PCB Workers at the Monsanto Plant in Sauget, Illinois

Judith A. Zack and David C. Musch
December 14, 1979

Summary

An historical prospective mortality study was conducted on workers exposed to polychlorinated biphenyls at the Monsanto Company plant in Sauget, Illinois. Eighty-nine workers exposed to PCBs for a minimum of six months during the period 1945 to 1965 were followed for their mortality experience. Observed deaths were not statistically different from expected deaths for any of the cancer sites examined. No deaths were observed from cancer of the liver or pancreas or from malignant melanoma. No excess was seen in deaths from liver cancer. A statistically significant excess of circulatory disease, exclusive of arteriosclerotic heart disease, was seen in white males.

Background

The term "polychlorinated biphenyls" (PCBs) describes a group of mixed chlorinated biphenyls which vary in consistency from light free-flowing liquids to crystalline and non-crystalline solids depending on the degree of chlorination. PCBs have been in commerical use since 1929. Their electrical properties, fire resistance, and inertness have made them popular for many applications. They have been used particularly in the production of electric capacitors and transformers and in the insulation of electric cables and wires.

Reports of adverse health effects in man and carcinogenic effects in certain animals species prompted the National Institute of Occupational Safety and Health (NIOSH) to request that epidemiological studies be carried out on PCB-exposed worker populations. In a preliminary study of workers exposed to PCBs at the Mobil Oil Company plant in Pauleboro, New Jersey, Bahn reported an excess of deaths from malignant melanoma and pancreatic cancer among research and production employees.[1] At the same time, Roush reported the findings of a preliminary mortality study of PCB workers at the Monsanto Company plant in Sauget, Illinois (G. Roush, written communication, September 1976). No cases of malignant melanoma or pancreatic cancer were found.

The accidental poisonings with PCBs in Yusho, Japan provide information on the acute toxic effects of PCBs for man. PCB poisoning occurred following the ingestion of Kanemi rice oil contaminated with PCBs. The general symptoms of Yusho disease included neuroendocrine disturbances, abnormal lipid metabolism, disturbances of the respiratory system, acneform eruption, pigmentation, and ocular changes.[2] Yusho disease, however, has also been attributed to the ingestion of polychlorinated dibenzofurans (PCDFs) present in the rice oil as PCB contaminant. The presence of PCDFs obscure the relationship of PCBs to the clinical picture of Yusho disease.

In 1976, the Monroe County Board of Health conducted biochemical tests among Bloomington, Indiana residents exposed to PCBs. Serum levels of gamma glutamyl transpeptidase and plasma triglyceride levels were found to show a direct relationship to serum PCB levels.[3]

In a recent study, Wareham et al. evaluated pulmonary function in 243 workers exposed to PCBs in the manufacture of capacitors.[4] Thirty-four of these workers (14%) were found to have abnormal forced vital capacity measurement. Of these thirty-four, twenty-seven demonstrated a restricted pattern of impairment with virtually no radiographic change. The relationship between restrictive spirometric impairment and duration of PCB exposure was not addressed in this study.

Extensive studies of PCB toxicity for animals have been conducted and have been throughly reviewed.[5] In a two-year chronic oral toxicity test of PCBs, no carcinogenic effects were observed in the rats and beagles tested. Hyperplasia, hypertrophy, extensive fibrosis, and several benign tumors were observed in the livers of the rats, but there was no evidence of malignancy of any of the test animals.[6]

Other investigators have reported liver tissue effects ranging from hyperplasia to well-differentiated hepatocellular carcinomas in rats or mice fed with various PCB-containing diets. Kimbrough fed rats PCBs and observed lipid accumulation, hypertrophy, and adenofibromas, but no maligancies in the livers of the test animals.[7] In a later

experiment, the same researcher reported the induction of hepatocellular carcinomas and neoplastic nodules of the liver.[8]

The literature on PCB toxicity points to several organ sites in man that could potentially incur toxic effects of exposure to PCBs. The present study represents a completed analysis of the preliminary study of Monsanto PCB workers reported in 1976. This study will examine the mortality experience of PCB workers with particular attention given to overall cancer, liver and pancreatic cancer, and malignant melanoma.

Population and Methods

This study focused on workers exposed to polychlorinated biphenyls at the Monsanto plant in Sauget, Illinois. PCBs were manufactured at this plant during the period 1936 to 1977. All male employees from the hourly roll who worked in the PCB department for at least six months between January 1, 1945, and December 31, 1965, were selected for study.

During the period of study, the PCB process remained relatively unchanged The process, in brief, involved the batch chlorination of biphenyls in the presence of iron and iron chloride catalysts. The crude mixture produced in the chlorinators was aerated, distilled, earth treated, filtered and transferred to storage tanks. No industrial hygiene data were available to quantify the PCB exposure levels. Through interviews with plant personnel, it was determined that exposure levels to PCB did not vary considerably within the PCB department. Therefore, all workers in the PCB department were considered to have common exposure level. Other exposures in this department included hydrochloric acid, tri- and tetrachlorobenzene, biphenyl, and chlorine gas.

The PCB worker cohort was identified from the plant's computerized work history system. Eighty-nine male hourly employees met the criteria for inclusion in the study. The vital status of each member was determined as of December 31, 1977, using standard followup techniques. A death certificate was obtained for each person found to be deceased.

The underlying cause of death was coded to the Eighth Revision of the International Classification of Disease, Adapted[8] by an experienced independent nosologist.

The data were analyzed by the modified life table method using the Monson program.[9] Standardized mortality ratios were calculated for nineteen selected cause-of-death categories. Mortality comparisons were made with the general U.S. population. Statistical significance was determined at the 5% level assuming a Poisson distribution.

Results

Eighty-eight of the eighty-nine members of the study cohort were traced. Fifty-eight were verified living and thirty were verified deceased by death certificate. The results of this vital status tracing are shown in Table 1.

The person-years of observation contributed by the eighty-nine member study cohort are shown in Table 2. A total of 1800.1 person-years were observed at all ages. Most of these person-years were observed in the middle-age range with 1333.1 person-years (74%) observed for ages 35-60.

Table 3 categorizes duration of exposure to PCBs by vital status. For both living and deceased workers, the majority were exposed less than three years. The next frequent exposure class was for five or more years of exposure. The least number of workers fell in the three to five years of exposure category. Overall, the average length of exposure for living and deceased workers was similar with deceased workers having 3.7 years of exposure and living workers having slightly less at 3.2 years.

The mortality experience for all males is summarized in Table 4. The mortality of white and nonwhite males is examined separately in Tables 5 and 6. Observed and expected deaths and SMR's are shown for each of the nineteen cause-of-death categories examined.

For all males, there were 30 deaths observed and 22.88 expected (Table 4) The overall SMR was 131. For malignant neoplasms, 8 deaths were observed with 4.46 expected. The SMR for all malignant neoplasm was 179. No deaths were observed from liver or pancreatic cancer or from malignant melanoma. The SMR for lung cancer was high at 278. The only statistically significant difference seen in this table is seen for diseases of the circulatory system, exclusive of arteriosclerotic heart disease. Nine deaths were observed with 3.98 expected, yielding a SMR of 226.

Table 5 shows the overall SMR remains high for white males at 133. There were 4 deaths from cancer with 2.70 expected. None were from liver or pancreatic cancer or from malignant melanoma. The high SMR's seen in Table 4 for lung cancer and the residual diseases of the circulatory system appear to be explained by the high SMR's for these causes in white males. There were 3 deaths observed from lung cancer with 0.94 expected, yielding a SMR of 319. For the category of circulatory disease, exclusive of arteriosclerotic heart disease, the SMR was 526 with 7 observed and 1.83 expected deaths. This difference was the only one of statistical significance in this table.

For nonwhite males, there were no statistically significant differences seen in Table 6. The overall SMR was also high at 128. Four deaths from cancer were observed with 1.76 expected, but none from liver or pancreatic cancer or from malignant melanoma.

Case histories for the eight cancer deaths are summarized in Table 7.

Discussion

The results of this study do not corroborate an excess risk of pancreatic cancer or malignant melanoma among workers exposed to PCBs as reported in the study of Mobil workers. Nor do the results uphold translating to man the outcome of animal tests, in which hepatomas have been associated with long-term PCB exposure. In this study, no deaths were ob-

served from pancreatic or liver cancer or from malignant melanoma.

The SMR for all causes was elevated from what one would expect in an industrial cohort. The high SMR for white males is, for the most part, explained by the excess in deaths from circulatory diseases exclusive of arteriosclerotic heart diseases. This cause-of-death category includes deaths from rheumatic heart disease, cerebrovascular disease, and other forms of heart disease, all of which are unlikely to be related to exposure in the workplace. It is urged that a larger study to be undertaken of the total Krummrich plant population to evaluate the overall risk of death from all causes and from cardiovascular diseases.

References

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Table 1

Polychlorinated Biphenyl Workers -
Results of Tracing as of 12/31/77

Total to be traced	89
Status Known	88
Verified Alive	58
Verified Dead	30
Death Certificate Found	30
Death Certificate Not Found	0
Status Unknown	1

Table 2

Person-Years of Observation Contributed by Workers Exposed to PCB's by Five Year Age Groups

Age in Years	Person-Years of Observation
20-24	11.4
25-29	63.8
30-34	142.6
35-39	222.5
40-44	283.2
45-49	325.3
50-54	294.5
55-59	207.6
60-64	134.0
65+	115.2
Total - All Workers	1800.1

Table 3

Duration of Exposure to PCB's for Workers by Vital Status

Years of Exposure	Living N=58	Deceased N=30	Unknown N=1	Total N=89
< 1 yr.	20	5	1	26
1-3 yrs.	20	12	0	32
3-5 yrs.	6	4	0	10
> 5 yrs.	12	9	0	21
Average Length of Exposure	3.2 yrs.	3.7 yrs.	0.7 yrs.	3.3 yrs.

*Lifetime exposure prior to 1-1-66.

Table 4

Observed and Expected Deaths, All Males

I.C.D. No. (Eighth Rev.)	Cause of Death	Observed	Expected	SMR
	All causes of death	30	22.88	131
140-209	All malignant neoplasms	8	4.46	179
140-149	Buccal cavity and pharynx	0	0.16	-
150-159	Digestive organs and peritoneum	1	1.33	75
155,156	Liver	0	0.10	-
-	All other digestive organs	1	1.23	81
160-163	Respiratory system	4	1.53	261
162,163	Lung	4	1.44	278
-	All other respiratory organs	0	0.09	-
185-189	Genitourinary organs	1	0.51	196
200-209	Lympatic and hematopoietic tissue	1	0.40	250
-	Other sites	1	0.53	189
390-458	Diseases of the circulatory system	16	11.17	143
410-413	Arteriosclerotic heart disease	7	7.19	97
-	All other diseases of the circulatory system	9	3.98	226*
460-519	Diseases of the respiratory system	1	1.27	79
520-577	Diseases of the digestive system	2	1.20	167
-	All other diseases	2	2.40	83
800-998	External causes of death	1	2.38	42

Number of persons observed = 89

* $p < .05$

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Table 5

Observed and Expected Deaths, White Males

I.C.D. No. (Eighth Rev.)	Cause of Death	Observed	Expected	SMR
	All causes of death	18	13.53	133
140-209	All malignant neoplasms	4	2.70	148
140-149	Buccal cavity and pharynx	0	0.09	-
150-159	Digestive organs and peritoneum	0	0.75	-
155,156	Liver	0	0.05	-
-	All other digestive organs	0	0.70	-
160-163	Respiratory system	3	0.94	319
162,163	Lung	3	0.89	337
-	All other respiratory organs	0	0.05	-
185-189	Genitourinary organs	0	0.20	-
200-209	Lymphatic and hematopoietic tissue	0	0.28	-
-	Other sites	1	0.36	278
390-458	Diseases of the circulatory system	11	6.82	161
410-413	Arteriosclerotic heart disease	4	4.99	80
-	All other diseases of the circulatory system	7	1.83	526*
460-519	Diseases of the respiratory system	0	0.73	-
520-577	Diseases of the digestive system	1	0.75	133
-	All other diseases	2	1.10	182
800-998	External causes of death	0	1.43	-

Number of persons observed = 60

*$p < .05$

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Table 6

Observed and Expected Deaths, Nonwhite Males

I.C.D. No. (Eighth Rev.)	Cause of Death	Observed	Expected	SMR
	All causes of death	12	9.35	128
140-209	All malignant neoplasms	4	1.76	227
140-149	Buccal cavity and pharynx	0	0.07	-
150-159	Digestive organs and peritoneum	1	0.58	172
155,156	Liver	0	0.05	-
-	All other digestive organs	1	0.53	189
160-163	Respiratory system	1	0.59	169
162,163	Lung	1	0.55	182
-	All other respiratory organs	0	0.04	-
185-189	Genitourinary organs	1	0.23	435
200-209	Lymphatic and hematopoietic tissue	1	0.12	833
-	Other sites	0	0.17	-
390-458	Diseases of the circulatory system	5	4.35	115
410-413	Arteriosclerotic heart disease	3	2.20	136
-	All other diseases of the circulatory system	2	2.15	93
460-519	Diseases of the respiratory system	1	0.54	185
520-577	Diseases of the digestive system	1	0.45	222
-	All other diseases	0	1.30	-
800-998	External causes of death	1	0.95	105

Number of persons observed = 29

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Table 7

Case Summaries of Cancer Deaths Among PCB Workers

Race	Year of Birth	Year of First Exposure	Year of Death	Duration Ever Exposed to PCB's	Death Certificate Statement of Cause of Death
Nonwhite	1909	1942	1959	1 yr., 1 mo.	Carcinoma of colon (153.8)
Nonwhite	1913	1954	1965	7 yrs., 1 mo.	Carcinomatosis - primary site kidney (189.0)
Nonwhite	1909	1951	1968	2 yrs., 4 mos.	Carcinoma of the lung (162.1)
White	1893	1943	1963	2 yrs., 10 mos.	Carcinoma right lung (162.1)
White	1912	1951	1968	2 yrs., 4 mos.	Cancer of lung (162.1)
White	1916	1951	1977	2 yrs., 9 mos.	Carcinoma of lung (162.1)
Nonwhite	1907	1945	1964	8 mos.	Multiple myeloma (203.0)
White	1906	1940	1957	6 yrs., 7 mos.	Metastatic carcinoma - carcinomatosis (199.0)