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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Centers for Disease Control
National Institute for
Occupational Safety & Health
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Cincinnati OH 45226-1998

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May 22, 1985

Plant Manager
Aerovox Industries, Inc.
P.O. Box B-970
740 Belleville Avenue
New Bedford, Massachusetts 02741

Dear Sir:

I have enclosed a copy of a draft report which is an update of a mortality study of workers exposed to polychlorinated biphenyls. The plant 2 study population are workers from the Aerovox plant. This draft report has been sent out for review. Upon completion of this review, the report will be appropriately revised and submitted for publication in a scientific journal. I welcome any comments you may have.

If you have any questions regarding this report, please call me at 513-841-4203.

Sincerely yours,

David P. Brown

David P. Brown
Assistant Chief
Industrywide Studies Branch
Division of Surveillance, Hazard
Evaluations and Field Studies

Enclosure

MORTALITY OF WORKERS EXPOSED TO POLYCHLORINATED BIPHENYLS - AN UPDATE

DRAFT

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Cincinnati, Ohio

April, 1985

Abstract

A retrospective cohort mortality study of workers exposed to polychlorinated biphenyls (PCB's) in two plants manufacturing electrical capacitors was first reported in 1981. Due to small numbers of deaths and a relatively short observation period that study was considered inconclusive. We have now updated the earlier study by adding seven years of observation. The number of deaths in the study cohort increased during this interval from 163 to 282. We find that a statistically significant excess in deaths for cancer of the liver and biliary passages is now evident (5 observed versus 1.8 expected; $p < 0.05$). Most of this excess in mortality from liver cancer was observed in women employed in one plant; and due to the small numbers of deaths, it remains difficult to interpret these findings in regard to PCB exposure. This excess is of particular interest because PCB's cause liver tumors in exposed animals.

Mortality from cancer of the rectum was also elevated (4 observed versus 1.9 expected), but this finding was not statistically significant. Mortality overall (282 observed versus 311 expected) and mortality of all major anatomical sites was lower than expected, except deaths from diseases of the circulatory system which were slightly elevated over expectation (115 observed versus 112.9 expected).

Introduction

In 1981[1] we reported the results from a retrospective cohort mortality study of 2567 workers employed in two plants where PCB's were used to manufacture electrical capacitors. The purpose of that study was to determine whether occupational exposure to PCB's was associated with long term health effects, particularly cancer. Based on the animal data,[2-9] cancer and more specifically liver cancer were the diseases of most concern. The study population included workers with at least three months of employment in areas of the plants considered to represent the potential for the heaviest occupational exposure to PCBs. The two plants were located in Upper New York State (plant 1) and Massachusetts (plant 2). The results of this study were inconclusive due to the small numbers of total deaths (N-163) and the relatively short time of follow-up, which ended on January 1, 1976. Since seven years of additional follow-up data was available and since the question regarding the long term health effects among workers occupationally exposed to PCB's is still unknown, an update to the original study was conducted to help provide more conclusive results.

For details on the study population, on the two capacitor manufacturing facilities and on the levels of exposure to PCBs at the facilities studied, refer to the original report.[1]

Methods

In the original study, the vital status of the cohort was determined as of January 1, 1976. This update extends the follow-up through December 31, 1982. The vital status follow-up was accomplished by searching the records maintained by the Social Security Administration, the Internal Revenue Service and the National Death Index (NDI). The NDI, which is administered by the National Center for Health Statistics, is a file containing information on all deceased individuals in the United States since 1979. For all those known to be deceased, death certificates were requested from the appropriate State Vital Statistics Office. The underlying cause of death listed on each death certificate was coded by a trained nosologist according to the Revision of the International Classification of Diseases (ICD) in effect at the time of death. Those lost to follow-up (unknown vital status) and those who died subsequent to the closing date of the study, December 31, 1982, were considered alive for purposes of analysis.

Person-years were accumulated for each worker, starting after three months of employment in "PCB exposed" jobs and ending at the date of death or the closing date whichever occurred first. Using a life table analysis system,[10] the person-years for each worker were combined into 5-year calendar time periods and 5-year age groups and multiplied by the corresponding U.S. White Male (for male workers) and U.S. White Female (for female workers) cause-specific mortality rates to yield the expected number of deaths.

At the time of this analysis, the life table analysis system only maintained U.S. mortality rates through 1978, the end of the eighth revision of the ICD. To calculate expected deaths through 1982 for this study, the death rates for the interval 1975-1979 were based on U.S. deaths occurring through 1978, and the death rates for the interval 1980-1982, were assumed to be identical to the previous time period (1975-1979). Since the comparison rates did not include deaths occurring in the ninth revision of the ICD, deaths observed in the study population after 1978 were assigned codes according to the rules of the eighth revision of the ICD. This methodology could yield biased results if the U.S. death rates changed between 1978 and 1982. For liver cancer which was the cause of most concern, the death rates have remained constant.[11]

Person-years were additionally distributed by length of employment in "PCB exposed" jobs and by time since first employment in "PCB exposed" jobs (latency). The observed and expected cause-specific deaths were compared and differences were tested based on the Poisson distribution. The risk is reported as a standardized mortality ratio (SMR), defined as observed/expected deaths x 100.

Results

This update includes a slightly different total number of workers compared to the original cohort. There were 2567 workers in the original study and 2562 in the update. This difference is due to changes in acceptance criteria built into the life table analysis system which has been revised since the initial

analysis. The five individuals excluded did not achieve a full three months of employement in PCB exposed jobs.

The results of the vital status ascertainment through December 31, 1982 are given in Table 1. The update resulted in an additional 119 deaths and added 15,877 person-years to the original study.

The mortality by major cause of death is given in Table 2. Except for diseases of the circulatory system which is slightly elevated (SMR-102) mortality from all other major causes is lower than expected. Compared to the results of the original study there has been little change in the SMRs by major death groupings. The largest change was seen in malignant neoplasms where the SMR dropped from 89 (39 observed and 43 expected) to 78 (61 observed and 78.2 expected). This difference is due primarily to the observation of no additional cancer deaths among Plant 1 males.

In Table 3 the mortality results by cancer site are given. Of particular interest are cancer of the rectum and liver cancer, both of which were elevated in the original study, especially for females in Plant 2. No additional deaths from cancer of the rectum were observed since the original study and the SMR dropped from 336 (4 observed vs 1.19 expected) to 211 (4 observed vs 1.9 expected). On the other hand, two additional deaths from cancer of the liver were observed, both among females in Plant 2. For the whole cohort the SMR for cancer of the liver is 278 (5 observed vs 1.8 expected). The difference between these observed and expected deaths is statistically significant at $p < 0.05$ using a one-sided test of significance.

Since the risk of cancer associated with occupational exposure usually does not occur until a number of years after first exposure has elapsed (latency), an analysis by this variable was conducted for liver cancer and is presented in Table 4. There does not appear to be an increase in risk with an increase in time since first employment in "PCB exposed" jobs. The two additional deaths identified in the updated analysis fall into the greater than 20 year stratum.

The risk from cancer of the liver was also examined by length of employment in "PCB exposed" jobs. This analysis is presented in Table 5. The risk does not increase with an increase in exposure as measured by length of employment in "PCB exposed" jobs.

Both the latency and exposure analysis may be misleading because the two variables are measured in terms of employment in "PCB exposed" jobs only. These jobs were identified as those representing the heaviest and most direct exposure to PCB's and only account for approximately 10% of all jobs at the plants. As documented by industrial hygiene surveys,[1] there was potential exposure throughout the plant; therefore, latency and exposure based on total employment may be more appropriate. For females from plant 2, an analysis calculating observed and expected deaths stratified by length of employment and latency using total work history was conducted and is presented in Tables 6 and 7.

Discussion

The most important finding of this updated study is the significant excess in cancer of the liver. This finding is of particular interest because it is consistent with the animal data where liver tumors have been induced by PCBs in several species of animals.[2-9]

The excess in mortality from liver cancer is primarily restricted to the female workers in Plant 2. This may be due to two reasons: (1) This group accounts for the largest segment of the total cohort - 41% of the person-years and 52% of the person-years over 20 years of latency. (2) Plant 2 airborne exposure levels to PCB's were higher than those measured in Plant 1 during the NIOSH survey in 1977,[1] indicating that the exposures may have been higher historically, as well. However, it can not be determined directly whether the excess risk among the female workers is associated with higher exposures since historical exposure does not exist.

The analysis of liver cancer by length of employment and latency provides limited information, primarily because of the small numbers. Based on the four deaths from plant 2, there is no increase in risk with increase in length of employment. The risk associated with latency is also uninformative, except no deaths occurred prior to ten years from first employment.

Since 1981 two other cohort mortality studies of workers exposed to PCB's have been reported. The first study, by Zack,[12] included workers who were

involved in the manufacturing of PCB's. The study cohort was defined as all workers at the plant employed for at least six months during the period from 1945 to 1965. The cohort was followed through 1977. This study was limited, in that there were only 89 workers included in the cohort which yielded 30 deaths. There were no liver cancers but there were statistically significant increases in circulatory disease, exclusive of arteriosclerotic heart disease, in white males.

The second study, by Bertazzi,[13] included 1310 workers employed for at least 6 months from 1946 to 1970 in a capacitor manufacturing facility located in Italy. Mortality of this cohort was determined from 1954 to 1978. In the original analysis of this data there were only 27 deaths, 14 of which were due to cancer. Two sites of cancer were elevated, digestive organs /peritoneum and lymphatic/hematopoietic. This study was recently updated through 1982 and expanded to include all workers with at least one week of employment, increasing the cohort to 2100 workers.[14] The updated results showed a statistically significant excess in cancer (11 observed vs 5.3 expected) among females with a 3 fold excess (3 observed vs 1.1 expected) of lymphatic/hematopoietic cancer. Among males there was a statistically significant excess in all cancer (14 observed vs 7.6 expected) and in digestive cancer (6 observed vs 2.2 expected); and a non-significant excess in lymphatic/hematopoietic cancer (3 observed vs 1.1 expected). Unfortunately not enough information was given to determine the risk regarding the occurrence of liver cancers.

The results from the studies of Zack and Bertazzi are limited by small numbers of death. At this time, neither study provides convincing evidence regarding the carcinogenicity of PCB's in occupationally exposed workers. Furthermore, there are no corroborative findings between these studies and our study, except for the possibility of digestive system cancer as reported by Bertazzi and liver cancer reported by us.

The update of this study provides additional evidence that occupational exposure to PCB's may be associated with an excess risk of liver cancer mortality. However, the number of liver cancer deaths is small and definitive conclusions are still tentative. Continuing follow-up of this cohort as well as other cohorts exposed to PCB's should be encouraged.

Finally, this study illustrates the importance of periodically updating cohort mortality studies which are inconclusive due to small numbers of deaths and short latency periods. This is a fairly easy task since the demographic and work history data is already collected and computerized. For studies initially followed through 1978, only the National Death Index is necessary for determining the vital status of each cohort member.

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Table 1. Vital Status Ascertainment of Workers Exposed to PCB

	Plant 1			Plant 2			Grand Total (%)
	Males	Females	Total	Males	Females	Total	
Known Alive	504	338	842	584	755	1,339	2,181 (85)
Known Dead	77	36	113	57	112	169	282 (11)
Unknown	5	11	16	29	54	83	99 (4)
Total	586	385	971	670	921	1,591	2,562 (100)
Person-years	11,166	7,600	18,766	13,545	22,583	36,129	54,895

Table 2. Mortality[1] from Major Causes Among Workers Exposed to PCB

Cause of Death (7th Revision ICD No.)	Plant 1		Plant 2		Total	SMR[2]	SMR[3] (observed)
	Males	Females	Males	Females			
All Malignant Neoplasms (140-205)	9/16.9	8/13.3	7/13.6	37/ 34.4	61/ 78.2	78	89 (39)
Nervous System (330-334,345)	2/ 4.7	2/ 3.6	4/ 3.3	12/ 10.4	20/ 22.0	91	88 (11)
Circulatory System (400-468)	42/35.3	15/13.4	27/26.4	31/ 37.8	115/112.9	102	95 (60)
Accidents (800-962)	8/ 8.1	3/ 1.8	6/10.3	3/ 5.2	20/ 25.4	79	71 (13)
All Other Causes	16/19.8	8/ 9.3	13/17.5	29/ 25.9	66/ 72.5	91	89 (40)
All Causes	77/84.8	36/41.4	57/71.1	112/113.7	282/311	91	89 (163)

[1] Mortality is reported as observed/expected deaths
[2] SMR = Observed/expected deaths x 100 - for the updated results
[3] SMR's from the original study. (observed deaths)

Table 3. Mortality (observed/expected deaths) From Malignant Neoplasms Among Workers Exposed to PCB

Cause of Death (7th Revision ICD no.)	Plant 1		Plant 2		Total	SMR[1]	SMR[2] (observed)
	Males	Females	Males	Females			
All Malignant Neoplasms (140-205)	9/16.9	8/13.3	7/13.6	37/34.4	61/78.2	78	89 (39)
Stomach (151)	0/ 0.8	0/ 0.4	1/ 0.6	0/ 1.0	1/ 2.8	36	60 (1)
Intestine except Rectum (152, 153)	1/ 1.5	2/ 1.4	0/ 1.1	5/ 3.6	8/ 7.6	105	99 (4)
Rectum (154)	1/ 0.5	0/ 0.3	0/ 0.3	3/ 0.8	4/ 1.9	211	336 (4)
Liver (155, 156)	1/ 0.4	0/ 0.3	0/ 0.3	4/ 0.8*	5/ 1.8*	278	280 (3)
Pancreas (157)	0/ 0.9	1/ 0.6	1/ 0.7	0/ 1.5	2/ 3.7	54	53 (1)
Respiratory (160-164)	4/ 6.1	2/ 1.7	0/ 4.8	3/ 4.1	9/16.7	54	88 (7)
Urinary (180-181)	2/ 0.9	0/ 0.3	2/ 0.7	0/ 0.9	4/ 2.8	143	not reported
Lymphatic and Hematopoietic (200-205)	0/ 1.8	0/ 1.1	1/ 1.6	4/ 2.9	5/ 7.4	68	46 (2)
Breast (170)	---	1/ 3.2	---	8/ 8.2	9/11.4	79	102 (7)
Female Genital Organs (171-176)	---	1/ 2.2	---	6/ 5.8	7/ 8.0	88	not reported
Other	0/ 4.0	1/ 1.8	2/ 3.5	4/ 4.8	7/14.1	---	---

[1] SMR's from updated study
[2] SMR's from the orginal study (observed deaths)
* Difference between observed and expected deaths is statistically significant $p < 0.05$

Table 4. Mortality From Liver Cancer by Time Since First Employed (latency) in "PCB Exposed" Jobs

Latency (years)	Plant 1		Plant 2		Total		SMR
	O	E	O	E	O	E	
< 10	1	0.2	1	0.2	2	0.4	500
10 - 19	0	0.2	1	0.3	1	0.5	200
≥ 20	0	0.3	2	0.6	2	0.9	222
Total	1	0.7	4	1.1	5	1.8	278

O = Observed deaths
E = Expected deaths

Table 5. Mortality From Liver Cancer by Length of Employment in "PCB Exposed" Jobs

Length of Employment	Plant 1		Plant 2		Total		SMR
	O	E	O	E	O	E	
3 months < 5 years	1	0.5	3	0.8	4	1.3	308
≥ 5 years	0	0.2	1	0.3	1	0.5	200
Total	1	0.7	4	1.1	5	1.8	278

O = Observed deaths
E = Expected deaths

Table 6 - Mortality From Liver Cancer by Time Since First Employed (Latency) at Plant 2 Among Females

Latency (years)	O	E	SMR
< 10	0	0.10	---
10-19	2	0.21	952
≥ 20	2	0.55	364
Total	4	0.86	465

O = Observed deaths
E = Expected deaths

Table 7 - Mortality From Liver Cancer by Length of Employment at Plant 2 Among Females

Length of Employment (years)	O	E
< 5	1	0.15
5- 9	1	0.17
10-14	0	0.20
15-19	1	0.13
20-24	0	0.11
≥ 25	1	0.10
Total	4	0.86

O = Observed deaths
E = Expected deaths