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Cancer Morbidity in Lamp Manufacturing Workers

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A historical prospective study of cancer in lamp manufacturing workers in one plant was conducted. All men and women who worked for a total of at least 6 months and were employed at some time between 1960 and 1975 were included. Work histories were abstracted and subjects were divided according to whether they had worked in the coiling and wire drawing area (CWD). Cancer morbidity from 1964 to 1982 was ascertained via the provincial registry, and was compared with the site-specific incidence in Ontario, adjusting for age, sex and calendar period. Of particular interest were primary breast and gynecological cancers in women.

The cancers of a priori concern were significantly increased in women in CWD, but not elsewhere in the plant. The excess was greatest in those with more than 5 yr exposure (in CWD) and more than 15 yr since first working in CWD, with eight cases of breast and gynecological cancers observed in this category compared with 2.67 expected. Only three cancers occurred in men in CWD.

Environmental measurements had not been made in the past and little information was available on substances used in the 1940s and 1950s, the period when the women with the highest excess began employment. It is known that methylene chloride and trichlorethylene have been used, but not enough is known about the dates and patterns of use to draw any conclusions about their relationship with the increase in disease.

Key words: breast cancer, gynecological cancers, incidence, historical prospective study, cluster

INTRODUCTION

Anecdotal reports from the coiling and wire-drawing area (CWD) of the lamp manufacturing department of Canadian General Electric indicated that a number of women who worked there had developed tumors. To some the number seemed excessive given the size of the employee population. (Of the five, four subsequently proved to be benign; there were two hysterectomies for benign conditions, one ovarian cyst and one benign breast lump. The fifth was a breast cancer.) Thus particular attention focused on tumors of the breast and female reproductive system. Following a preliminary investigation it was decided that a more detailed study should be conducted. While men were to be included,

special interest would be placed on the cancers noted above. No known carcinogens were believed to be present in the working environment. The study team reported directly to the plant's Health and Safety Committee.

METHODS AND MATERIALS

Site of Study

The study was of workers at the Dufferin St., Toronto, location of Canadian General Electric. The company manufactures electric lighting equipment including incandescent, discharge, and fluorescent lighting. In 1985, the CWD operation was relocated.

Coiled filaments for incandescent lamps are made in the CWD. Tungsten and molybdenum wires are reduced to the required thickness by passing them through various dies. The reduced wire is then coiled. The coiled filament ("single coil") is formed by winding the wire on a mandrel of steel or molybdenum in a continuous process. The coil, with the mandrel still in place, is heat treated (annealed), cut into desired lengths, sintered, and immersed in an acid bath to dissolve the mandrel out of the coil. The process of making doubled coil (or coiled coil) is essentially the same as for the single coil filament except that the single coil with the mandrel is bound on another mandrel which is later retracted or removed mechanically. A process called 'pico-resin dip' was introduced in 1959 whereby the coil with the mandrel was dipped in the resin to retain the mandrel in coil legs after dissolving. Methylene chloride has been used in this operation to dissolve the resin away.

Study Population

The basic design was a historical prospective morbidity study. The subjects were all men and women at the lamp department, including office workers, who had at least 6 months' cumulative employment at the plant and who worked there at some time between January 1, 1960 and December 31, 1975. This included those who had started work before 1960.

The criterion of at least 6 months' work was chosen to exclude short-term employees. The dates 1960 to 1975 were selected to ensure that some employees would have a reasonably long time since first employment in the department, while those with only very short follow-up were excluded. Those who left before 1960 and would have been difficult to trace were excluded. Preliminary estimates suggested that the power of the study in CWD using a one-sided alpha of 0.05 would be over 80% for the cancers noted above if the relative risk were two or more.

Personal identifying data and detailed work histories were extracted from company records. The completeness of the study population was confirmed by comparison of the list of subjects with union seniority lists at four dates between 1960 and 1975.

Exposure

Since no known carcinogen had been identified and hygiene measurements had not been made in the past, no direct measures of exposure were available. Length of exposure in each area thus served as a proxy for specific quantitative data. Employment was divided into two categories: work in CWD and work elsewhere in the plant.

In 1983 some sampling was conducted by the Ontario Ministry of Labour following the initial reports of a cancer "cluster". Table I shows the results, and the Threshold Lim-

TABLE I. Summary of Airborne Concentrations in CWD in 1983*

Substances measured	No. of samples	Sampling time in minutes	Airborne minimum	Concentration in mg/m ³		TLV 1986 ACGIH threshold limit values in mg/m ³
				Maximum	Mean	
Arsenic	6	365-369	<0.001	0.001	0.001	0.2
Chromium	6	365-369	<0.001	0.0001	0.0001	0.5
Lead	6	365-369	<0.001	<0.001	<0.001	0.15
Molybdenum	6	365-369	<0.001	0.001	0.001	5.0
Selenium	6	365-369	<0.001	0.003	0.002	0.2
Tungsten	6	365-369	<0.001	0.004	0.002	5.0

*Source: Ontario Ministry of Labour sampling reports.

TABLE II. Substances and Amounts Purchased for use in the Coiling and Wire Drawing Area, 1984*

Nitric acid	50,000 kg
Sulphuric acid	52,000 kg
Muriatic acid	5,100 kg
Caustic soda 50% (inc. caustic flakes)	56,000 kg
Aquadag—mostly graphite	140 kg
Ammonia hydroxide	32 liters
Bee hive corn syrup	24 liters
Propanol	60 liters
Javel water (clorox)	100 liters
Methanol	340 liters
Tungsten wire	5,900 kg
Molybdenum wire	4,900 kg
Steel wire	400 kg
Hydrogen	200 × 10 ⁶ m ³
Tergitol anionic—4	210 kg
Methylene chloride	170 liters
4% Tungsten resinate	84 g
Houghton safe 620—hydraulic fluid	200 liters
502 Suntac oil	60 liters
Esso nuto A22 oil	(No purchase in 1984)
GR2B } Retardant grease	6 liters
GR2E }	
GR2D }	
Diamond powder or paste	3 g
Ammonium crystals } Bifloride A664 }	40 kg
Trisodium phosphate	
Covil 10 oil	200 kg
Tellus 10 oil	100 liters
Tellus 30 oil	20 liters

*Source: Canadian General Electric.

it Values for those substances measured [ACGIH, 1986]. Concentrations obtained were very low. The company also provided a list of materials used in CWD and the approximate annual quantity ordered (Table II). It is uncertain if methylene chloride was used before 1959, although there are suggestions it may have been as a general purpose clean-

er. An engineering instruction sheet dated 1955 stated the degreasing solvent was "Blacosolv," or trichloroethylene.

Previous studies [see, e.g., IARC, 1979], including reports on mortality [Friedlander *et al.*, 1978; Hearne *et al.*, 1981; Ott *et al.*, 1983], had not shown methylene chloride to be a human cancer hazard, although it had been found to be a mutagen [IARC, 1979]. However, only Ott's study included women and had very limited power to observe any excess disease from cancers with long latency periods.

Morbidity Ascertainment

The original plan was to trace members of the cohort, send them a questionnaire asking about diagnosed cancers, and confirm the replies with physicians. Supplementary data would be obtained from the cancer registry. Tracing was highly successful (over 90%), but the response rate to the questionnaire, even with reminder letters, was very poor (less than 20%) and an alternative approach was needed.

We therefore sent the list of subjects, without stating their exposure status, to the population-based, provincial cancer registry at the Ontario Cancer Treatment and Research Foundation (OCTRF). This source would have been used under our original plan to determine cancer morbidity in untraced or non-responding subjects. Very good quality information is available from 1964 onwards, and we followed subjects to the end of 1982, except for a small percentage who had left the province. The search provided the sites of primary cancers and dates of diagnosis for subjects matched on the two files. Matching decisions were made blind to exposure status. Imperfect matches were resolved using additional information if available, and we accepted matches only if we were certain they were correct. Thus we were more likely to under- rather than over-estimate the number of cancers.

Analysis

Person-years were calculated by age, sex, and calendar period for the two categories after 6 months' employment. Using cancer rates for the province of Ontario supplied by OCTRF, the expected numbers of cancers were calculated and Standardized Morbidity Ratios (SMbRs) estimated. Internal comparisons were made by examining SMbRs in the two exposure categories, to determine if any excesses or deficits at some sites were unique to one of the categories. Some employees had worked in CWD and in other jobs. When work in other areas preceded CWD work, person-years at risk for the "other work" category were censored at the date of first work in CWD. Once a subject had worked in CWD, person-years were added only to that category.

To conform with the protocol, statistical tests were one-sided using a significance level of 0.05 to compare observed and expected cancers. For expected numbers less than five, the Poisson distribution was used; otherwise, the normal approximation was assumed. Two-sided confidence intervals were estimated under the same criteria.

RESULTS

The eligible subjects were 1,044 women and 826 men. Of these, 203 and 46, respectively, had worked in CWD.

For women born before 1940, the distributions in CWD and non-CWD were very similar (Table VIII). Thus, since these women are the ones at high risk for the cancers of

interest, the comparison of SMbRs in CWD and non-CWD areas was valid. The mean duration of employment in CWD (over 8 yr) was longer than for other areas.

The initial tracing had apparently been successful. The proportions of subjects untraced were 6.0% and 7.2% in CWD and non-CWD workers, respectively. In addition, 1.6% and 1.7%, respectively, were stated to have left the province. This suggests there was little bias between CWD and non-CWD in using only the Ontario registry to ascertain cancer cases.

Malignant neoplasms were recorded in 58 women and 40 men (Table III). In CWD, there was a statistically significant increase in the a priori sites ($p = 0.2$), while there was a slight deficit in the rest of the cohort. For men (Table IV), the major sites of cancer showed no significant increases, although there were seven cancers of the prostate compared with 4.48 expected (SMbR = 1.56, $p = 0.17$), but the SMbRs for this cause showed no consistent pattern with duration of and time since first exposure. Only three cancers were found in men who worked in CWD, so further analysis focused on women.

The increase in the a priori sites was examined in more detail by dividing the data simultaneously by the time since first exposure and length of exposure (Table V). The cut-points were decided before any examination of the data. The pattern is consistent with an occupational cause, with a three-fold risk of the disease in the longer exposure/longer latency subgroup. The major component of the increase was breast cancer and a similar breakdown showed essentially the same pattern for this cause separately, with five cases in the longer exposure/longer latency category compared with 1.55 expected (SMbR = 3.23, 95% confidence limits = 105,753). Most cases in the "over five years' exposure in CWD" category worked considerably more than five years in that area (Table VI).

DISCUSSION

The study was undertaken because workers in CWD noticed that an apparently excessive number of breast and gynecological tumors had been found in women employed in the area. We have confirmed the existence of an excess for these cancers and now discuss the evidence with respect to the hypothesis that the excess is related to work in CWD.

The pattern of SMbRs for the sites of interest by length of exposure and time since first exposure is consistent with an occupational link. The SMbRs increase with both these variables. While the numbers were relatively small, the overall SMbR was statistically significant.

The incidence of cancers in other areas of the plant was very close to that expected. This implies good accuracy of follow-up by OCTRF.

All but one of the tumors that prompted the study were benign. Thus the cases found in this study are largely independent of the original cluster. We have thus used new data to test a previously generated hypothesis. (Even if we had excluded the a priori case the increase would still have been statistically significant.) Indeed, the methodology we used deals with the problems of investigating occupational cancer clusters noted by Schulte *et al.* [1987] and Rothman [1987].

It might also be thought that breast and reproductive cancers should not have been grouped. However, cancers of the breast, uterus, and ovary are all believed to be related to hormonal factors and are adenocarcinomas. Cervical cancers might not have been included. If so, the SMbR in the other a priori sites would have been even greater.

TABLE III. Observed and Expected Numbers of Cancers in Female Lamp Manufacturing Workers, 1964-82, and SMBRs for Selected Sites with 95% Confidence Limits*

Site of Cancer	Coiling/wire drawing				Other areas			
	Observed	Expected	SMBR*	95% C.L.*	Observed	Expected	SMBR*	95% C.L.*
Breast	8	3.92	204	88,402	13	13.40	97	57,166
Cervix uteri	1	0.95	105	3,586	4	3.45	116	32,297
Body of uterus	2	0.94	214	26,760	0	3.06	0	0,121
Ovary	1	0.68	147	4,819	2	2.41	83	10,300
All gynecological & breast	12	6.68	180	103,314	19	23.05	82	53,129
All other sites	7	5.55	126	61,260	20	20.01	100	64,154

*SMBR: Standardized Morbidity Ratio = Observed/Expected \times 100; 95% C.L. = 95% confidence limits.

TABLE IV. Observed and Expected Numbers of Cancers in Male Lamp Workers, 1964–82, and SMbRs for Major Sites With 95% Confidence Limits*

Site of cancer	Observed	Expected	SMbR	95% CL
Stomach/colon/rectum	9	8.49	106	56,201
Pancreas	0	1.56	0	0,237
Lung	6	10.30	58	27,127
Prostate	7	4.48	156	63,322
Bladder	3	3.22	93	19,272
Other sites	15	17.89	84	50,138
Total	40	45.94	87	64,119

*SMbR: Standardized Morbidity Ratio = Observed/Expected \times 100; 95% C.L. = 95% Confidence Limits.

Methylene chloride, a solvent, was on the list of materials used in CWD in 1984. A NIOSH Intelligence Bulletin [NIOSH, 1986], issued shortly after our preliminary analysis, reported recent animal studies in which Fischer 344 rats exposed to methylene chloride in air developed fibromas and fibroadenomas of the mammary glands and Sprague-Dawley rats similarly exposed developed fibromas, fibroadenomas, and tumors of the mammary glands. Although studies of mice did not show such an increase, these reports provided biological plausibility for methylene chloride as the cause of the excess. Unfortunately, records of substances used are kept by the company for only 5 yr and purchase records are retained for 10 yr [H.R. Hosein, personal communication]. Table VII shows details for methylene chloride. The current process was introduced in 1959, but the period of interest is the 1940s and 1950s when all eight women in the longer exposure/longer latency group started employment (and during which they spent many years) in CWD. In another company "the drums on which the coils with the mandrels are wound *are immersed in a solvent* to remove any oil or grease" [Hall, 1941, emphasis added] in the 1940s, but the specific solvent was not mentioned and we do not know if the same process was used at the site of this study. Trichloroethylene was used to degrease the coils in 1955, but there are no data on the concentrations to which workers were exposed.

Finally, the etiology of most cancers is multifactorial. Kelsey and Hildreth [1983] summarized the known risk factors for breast cancer in females. Some are common to the other reproductive cancers and we tried to obtain information on them in the 36 women with one of these cancers. We wrote to physicians or hospitals named in OCFRF records but many did not reply or did not have the data we sought. For most risk factors we have no reason to believe that women in CWD differ from the general population or other women in the plant. However, Threlfall et al. [1985] found significantly increased Proportional Mortality Ratios among certain occupations, which disappeared when comparisons were made among "working women" only, perhaps due to differences in reproductive and marital status. However, the magnitude of the increase was small and the difference when working women only were included was roughly 20% for breast cancer and 30–40% for ovarian cancer. If these values are typical of working women compared with all women, they are too small to account for the increases found in our study or the differences with non-CWD workers. Women who have never married are at slightly increased risk but for

TABLE V. Observed (Obs) and Expected (Exp) Breast and Gynecological Cancers Among Women in Coiling and Wire Drawing Area, 1964-82, and Standardized Morbidity Ratios (SMbRs) with 95% Confidence Limits (C.L.), by Length of Exposure and Time Since First Exposure

Time since first experience in coiling/wire drawing (yrs)	Length of exposure in coiling/wire drawing (yrs)											
	<5					≥5						
	Obs	Exp	SMbR	95% CL	Obs	Exp	SMbR	95% CL	Obs	Exp	SMbR	95% CL
<15	2	2.52	79	10,287	1	0.95	106	3,586				
≥15	1	0.54	186	5,1031	8	2.67	300	129,590				

TABLE VI. Details on Cases of Cancers at Sites of Interest Among Women in Coiling and Wire Drawing (CWD) Area

Site of Cancer	Age first worked in CWD	Date first worked in CWD	Years worked in CWD	Date of diagnosis
Breast	32	1969	<1	1980
	36	1970	<1	1970
	31	1959	4	1974
	32	1944	16	1982
	30	1954	24	1980
	28	1943	29	1972
	29	1944	31	1976
	17	1940	35	1976
Ovary	30	1969	9	1978
Body of Uterus	27	1948	11	1971
	30	1950	14	1982
Cervix	28	1957	10	1973

TABLE VII. Methylene Chloride Consumption in CWD*

Prior to 1959	No records available of its use
1959 to 1975	Methylene chloride was used routinely but no estimate of amount available
1976	50 gallons
1977	40 gallons
1978	20 gallons
1979	40 gallons
1980	30 gallons
1981	90 gallons
1982	65 gallons
1983	90 gallons
1984	45 gallons
1985	90 gallons
1986	45 gallons

*Source: Company purchasing records.

TABLE VIII. Percentages Known to Have Been Ever Married Among CWD and non-CWD Women Workers by Birth Cohort

Exposure group	Percentage known ever married (Numbers of women in parentheses)			
	Birth Year			
	Before 1919	1920-	1930-	1940-
Ever CWD work	61 (36)	84 (58)	86 (49)	75 (60)
Never CWD work	62 (149)	84 (174)	87 (182)	62 (366)

women born before 1940 the proportions married in CWD and non-CWD were virtually identical (Table VIII).

Thus, in summary, we found an increase in the a priori cancers in CWD, which increased with duration of, and time since first, work in the operations. Studies of coiling workers elsewhere as well as of women exposed to methylene chloride (and perhaps other solvents) would be valuable, to see if the results can be confirmed and, if so, identify the likely cause.

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