Mortality of Pesticide Applicators

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Information has been obtained on a cohort of professional pesticide applicators which will be followed *prospectively*. The cohort consists of *16,126* males employed for three months *or* more between *1967* and *1976* by any of three nationwide pest control companies. Deaths which occurred between *1967* and *1976* were reported by the *Social* Security Administration as a result of a search of its records. Overall, 311 deaths were ascertained, giving a standardized mortality ratio *(SMR)* of 84. SMRs were over *100* for three causes of death — cancer of the lung *(115)*, cancer of the skin *(173)* and cancer of the bladder *(277)*. *The* confidence intervals of two of these ratios include 700, and the observed numbers therefore do *not* differ significantly from those expected. For bladder cancer the excess is on the border of statistical significance *($p < 0.05$)*. The excess of deaths from lung cancer was not seen for *applicators* classified as termite control operators, a group more likely to be exposed to chlordane and heptachlor. There were significantly low *SMRs* for cancer of the digestive organs *(46)* and for other diseases of the digestive *(55)* and respiratory *(29)* systems. Deaths from cerebrovascular disease were *also* less than expected, though not significantly so.

Chemical control of insect pests essentially began in the middle of the nineteenth century with the introduction of arsenical pesticides. However, pesticide use was confined to fruit and high value crops, or to instances of severe infestation, until the development of the chlorinated hydrocarbons a little over 30 years ago. The high potency and residual action of these compounds reduced the cost of pest control and led to a rapid increase in the levels of chemical pesticides in the environment generally.

Acute health effects of heavy exposure to chemical pesticides are reasonably well known. They can be serious and sometimes fatal. Whether there are long-term health effects of chronic exposure of humans to levels that do not produce acute symptoms is still not known. In particular, there is concern, deriving from experimental work on laboratory animals, that chronic exposure may be associated with increased risk of malignancy. There has been little published epidemiologic work addressing this problem in humans.

The cancer experience of professional pesticide applicators would seem to be relevant. Although, from any presently available information, it is not possible to assess the doses to which professional applicators are, or in the past have been, exposed, it is unquestionable that as a group their exposures exceed many-fold those of the general population. It is reasonable, therefore, to look among this group for the first signs of a carcinogenic effect of pesticides in man.

This paper reports on the establishment of a cohort of professional pesticide applicators which will be followed prospectively. It also reports the results of such observations as can be made retrospectively on the same cohort.

Materials and Methods

Employees of three nationwide pest control companies form the study cohort. The three companies have headquarters in Atlanta, Ca., Memphis, Tenn., and Tucson, Ariz., respectively, but their branch offices cover more than 40 states. At the time this study was begun, centralized personnel records had been maintained only for approximately 10 years in all three companies because of the record storage problems associated with rapid turnover and a large number of employees. In two companies January 1, 1967, was identified as the earliest date for which a roster of all personnel — those inactive as well as those still active in 1976 — could be assembled, and in the third, and largest, company this date was January 1, 1968. Personnel records of all persons in job categories potentially involving exposure to pesticides and employed on those dates or hired between those dates and June 30, 1976, were reviewed. From a total of 44,083 records, 16,126 subjects were identified who satisfied the criteria of (1) being male, (2) being employed for three months or more, and (3) having name, Social Security number, date of birth and dates of employment recorded. The assembly of the cohort involved a combination of computer and manual procedures and, without considerable clerical labor, it is not possible to say precisely

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Supported by grants from the Velsicol Chemical Corporation and the National Cancer Institute, U.S. Public Health Service (5-P01-CA08373).

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Table t. — Distribution of Study Population by General Level of Exposure to Pesticides and by Whether or Not Employed in Termite *Control.*

Exposure Level	Termite Control Yes	No	Total
Minimal	2713 (40 3)	1426 (15 2)	4139 (25 7)
Moderate	664 (9 9)	4320 (46 0)	4984 (30 9)
Heavy	3357 (49 9)	3642 (38 8)	6999 (43 4)
Total	6734 (100 1)	9392' (100 0)	16126' (100 0)

Figures in parentheses are percentages
•Includes tour subjects with unknown level of general exposure

on what grounds each of the 27,957 excluded subjects was declared ineligible. However, a sample of 4,000 of these was examined and in this sample 11% had been excluded because they were female, 71% because they were employed for less than three months and 18% because of missing information.

Information on race was not available on personnel records and could not be used as an eligibility criterion. However, ihe majority of the workers were white. In the course of the study death certificates — which did specify race — were obtained for 269 of the subjects; 253 of these subjects were white, 15 were black and the race ot one was unrecorded

Individual follow-up was not attempted. Identifying information on the 16.126 eligible subjects was submitted to the Social Security Administration which provided, for those known to be dead, information on date of death and the state in which the death certificate might be found. In another set of records submitted together with those from this study, the SSA search identified 104 of 109 deaths which had been ascertained through individual follow-up.' Among the 16,126 subjects in this cohort, SSA identified 311 deaths, for 269 of which death certificates from the states or registration areas were obtained. There was no reason to believe that the deaths for which death certificates could not be obtained are distributed by cause differently from those for which certificates were obtained. For some estimates, therefore, as the total number of "observed" deaths by cause, the actual number observed, plus the 42 deaths with missing certificates distributed by cause according to the distribution of causes noted in the death certificates obtained, were used.

Expected numbers of deaths by cause have been estimated by means of a computer program described by Monson.[2] The program applied national mortality rates of white males specific for five-year categories of age and for calendar year to the person-years accumulated during the period of observation. The beginning of this period was January 1, 1967, or January 1, 1968 (as described earlier). For employees entering after these beginning dates the beginning date was taken to be the end of the third month of employment. There were also two termination dates since records were submitted to SSA in two batches. For individuals whose record was submitted in the first batch the termination date was June30, 1976. For the second group it was December 31, 1976. In the computations, persons who were known to have died did not contribute person-years after the year of death but, otherwise, subjects were assumed to be alive until the end of the follow-up period. Standardized mortality ratios (SMR) were estimated by dividing the numbers of observed deaths (with the 42 of unknown cause distributed as previously described) by the expected values and multiplying by 100. An extension of the Cornfield method' was used to compute 95% asymptotic confidence intervals of the SMRs.

The applicators had been exposed to a broad spectrum of pesticides including fumigants, botanicals, carbamates, chlorinated hydrocarbons and organophosphates. Particular interest was focused on applicators exposed to chlordane and heptachlor. In addition, some measure of

Table 2. — Observed and Expected Deaths from Selected Causes.

Cause of Death	Observed A'	Observed B†	Expected	SMR‡	C.I. of SMR§
All causes	311	311.0	370 9	84	75- 94
Infective and parasitic diseases	2	2.3	2 8	83	25-281
Malignant neoplasms	47	54 3	65 2	83	64-109
Digestive organs and peritoneum	6	6 9	15 1	46	22- 95
Lung	21	24.3	21.2	115	77-170
Skin	3	3 5	2 0	173	63-473
Bladder	3	3 5	1 3	277	101-761
Lymphatic and hematopoietic	5	5 8	8 8	66	30-146
Other	9	10 4	16 9	61	34-112
Diseases of circulatory system	111	128 3	139 9	92	77-109
Ischemic heart disease	86	99 4	104 4	95	78-116
Cerebrovascular disease	7	8 1	15 3	53	27-104
Other	18	20 8	20 2	103	67-158
Diseases of respiratory system	4	4 6	16 0	29	12- 70
Diseases of digestive system	10	11 6	20 9	55	3T- 98
External causes	82	94 a	98 7	96	79-117
All other causes	55¶	15 0	27 4	55	33- 90

'Actual numbers lor which causes of death known
†With 42 deaths with missing certificates distributed according to the distribution in Column A
‡SMR = Observed (B)/Expected x 100 (computed from values expressed to two decimal places)
§95% asymptotic contidence intervals'
(Including 42 with missing death certificates

Table 3. — Observed and Expected Deaths from Selected Causes in Termite Control Operators and Other Applicators.

Cause of Death	Termite Control Operators Observed*	Expected	SMR	Others Observed'	Expected	SMR
All causes	138	150 1	92	173	220 9	78
Malignant neoplasms	21 6	25 9	a3	32 6	39 3	83
Cancer of digestive organs and peritoneum	1 2	5 9	20	5 6	9 1	62
Cancer of lung	7 2	8 3	a7	16 9	12 9	131
Cancer of skin	1 2	0 8	148	2 2	1 2	187
Cancer of bladder	1 2	0 5	245	2 2	0 8	296
Ischemic heart disease	37 2	41 2	90	61 8	63 2	98
Cerebrovascular disease	2 4	6 1	39	5 6	9 2	61
External causes	50 4	41 a	120	44 9	56 9	79

'Deaths with missing certificates distributed according to the distribution of actual observed numbers for each cause TCOs . 23 others - 19

intensity of exposure was desired Each company was supplied with a list of all the job titles found among the cohort members and a knowledgeable person or persons was asked to classify each title into one of three groups according to relative intensity of exposure In an attempt to evaluate the effect of exposure to chlordane and heptachlor, separate analyses have been conducted for persons ever holding jobs as "termite control operators" (TCOs) Chlordane and heptachlor are particularly effective in the control of termites and, since 1975, their use has been legally restricted to the subterranean control of them and to a very few other applications It is recognized that TCOs are also exposed to a variety of other pesticides and that general pest control operators may well have had exposure to chlordane and heptachlor, particularly prior to 1975 Nevertheless, it is almost certainly true that, as a group, TCOs have heavier exposure to chlordane and heptachlor than those in other job categories The distribution of the study population as to TCO or non-TCO status and by estimated relative intensity of exposure is shown in Table 1 The 243 applicators who had held job titles under more than one level of intensity of exposure are classified according to the one held for the longest period of time

Results

Observed and expected deaths by cause are shown in Table 2. The overall SMR has a point estimate of 84 and a 95% confidence interval of 75-94 Underascertainment of deaths, as well as the selective factors involved in the "healthy worker effect," no doubt contributes to the fact that the SMR is less than 100, although the value of 84 is not atypical for an occupational cohort. SMRs are over 100 for only three causes of death — cancer of the lung (115), cancer of the skin (173) and cancer of the bladder (277). The confidence intervals of two of these ratios (for lung and for skin) include 100 and so the excess is not formally significant ($p > 0.05$). For bladder cancer the excess is on the borderline of statistical significance. The very low SMRs for cancers of the digestive organs and for other diseases of the digestive and respiratory systems are notable. The extent to which occupational selection is responsible for these low ratios can only be conjectured, but it is probably considerable. There was one death from cancer of the common bile duct but none attributed to cancer of the liver.

Table 3 gives observed and expected deaths separately for the TCOs and for other applicators. The only significant differences between expected and observed values ($p < 0.05$) are those for cancer of digestive organs and for cerebrovascular disease, both in TCOs and both in the direction of lower observed values than expected. None of the differences between SMRs in TCOs and non-TCOs is significant but the slight excess of lung cancer is restricted to the non-TCO group.

Table 4 shows observed and expected deaths by estimated relative intensity of exposure. For lung cancer there is no evidence that risk increased with intensity of exposure as judged from job title; in fact, there is a slight, though not significant, trend in the opposite direction.

Further analysis of the lung cancer data showed only one curious feature. The lung cancer deaths were

Table 4. — Observed and Expected Deaths from Selected Causes According to Intensity of Exposure.

Cause of Death	Intensity of Exposure: Minimal Observed*	Expected	SMR	Intermediate Observed*	Expected	SMR	Highest Observed*	Expected	SMR
All causes	91	111.9	81	64	102.0	63	156	157.2	99
Malignant neoplasms	19.8	20.6	97	12.8	18.4	69	21.4	26.3	82
Cancer of digestive organs & peritoneum	2.3	4.9	48	3.2	4.2	76	1.2	5.9	20
Cancer of lung	9.3	6.8	138	7 5	6 2	120	7 1	8 2	87
Cancer of skin	1 2	0.6	198	1 1	0 6	187	1 2	0 9	138
Cancer of bladder	2.3	0 4	530	0	0 3	0	1 2	0 5	243
Ischemic heart disease	31 5	344	92	23 5	294	80	44 1	40 7	108
Cerebrovascular disease	1.2	5.3	22	2.1	3.8	56	4.8	6.2	77
External causes	23.3	24.5	95	22.4	26.3	85	48.8	47.9	102

*Deaths with missing certificates distributed according to the distribution of actual observed numbers for each cause: minimal exposure - 13, moderate - 4, heavy - 25

Table 5. — Observed*/Expected Deaths from Lung Cancer According to Age at Entry into Occupation and Age at Death.

Age at Observation	Age at Entry into Occupation <45	45-49	60 +	Total
<50	12/5.4	0/0.8	—	12/ 6.2
50-64	0/2 6	5/84	1/0.4	6/11.5
65 +	*010* 1	*010* 6	312 8	3/ 35
Total	12/8 1	5/9.8	4/3 2	21121.2

*Observed numbers not adjusted for deaths of unknown cause

Table 6. — Observed*/Expected Deaths from Lung Cancer According to Duration of Employment and Years Since Employment Began.

Duration of Employment	Years Since Employment Began 0-4	5-9	10 +	Total
0-4	13/11.1	6/4.4	0/0.0	19/15.6
5 +	—	2/2.3	0/3.3	2/ 5.6
Total	13/11.1	8/6.7	0/3.3	21/21.1

*Observed deaths not adjusted for deaths of unknown cause

clustered among workers who were first employed prior to age 45 and who died before age 50 (Table 5). In fact. in this sub-group the excess is formally significant ($p < 0.05$), if one disregards the facts that this was not an a priori hypothesis and that manv comparisons have been made in the data No explanation for this observation has been found yet

Table 6 examines the question of "latency" — the interval between the time the individual's employment began and the years during which he was observed in the study The table shows that relatively few of the study subjects so far were followed for 10 years or more after first employment None of those with lung cancer fell into this category If the excess of lung cancers had been of occupational origin, one would have expected to see most of the excess in this category

Discussion

Although there have been several clinical studies of workers occupationally exposed to pesticides, these generally have been based on small numbers and have involved clinical and laboratory examination at a single point in time.[4-12] Essentially no data could be found on the long-term mortality of occupationally exposed workers other than a study of workers employed in the manufacture of chlordane and heptachlor.[1]

There is no consistent pattern of excess mortality seen in either of these two studies. The overall SMRs were 72 in the manufacturing workers and 84 in the applicators — both figures expressing the reduced mortality generally found in occupational cohorts. SMRs for deaths from cancer were 82 and 83, respectively. In both groups there was a slight excess of deaths from lung cancer but in neither is it significant, and even if the two series are combined, there are 36 3 observed and 30.2 expected — a difference that is neither significant nor remarkable in the absence of data on cigarette smoking in the two cohorts. Moreover, the manufacturing workers were exposed predominantly to chlordane and heptachlor. Among the applicators, the excess lung cancer mortality occurred not among the group most likely to be exposed to chlordane and heptachlor — the termite control operators — but among the general pesticide applicators. Nevertheless, special attention should be paid to this cause of death in the future follow-up of these cohorts.

The excesses of cancer of the skin and of the bladder seen in the applicators were not reflected in the manufacturing workers Similarly the unexpected excess of deaths from cerebrovascular disease seen in the manufacturing workers is not seen in the applicators, either in the group as a whole or in the termite control applicators

The principal limitation of the present study, particularly as it relates to cancer experience, is that there were relatively few workers who had substantial work experience and who were followed for long periods after first employment Thus, only about 15% of the person-years were contributed by workers who had more than five years of employment and who were observed more than 10 years after first employment It is hoped that the establishment of the cohort at this point in time will permit more decisive analyses in the future

The authors are indebted to Mr John D Conner Jr of Sellers Conner and Cuneo Washington DC for suggesting this study and for making arrangements with the companies for provision of data Management and staff of Rollins, Inc , Terminex International. Inc , and Truly Nolen International were helpful in supervising data abstraction and in providing other information The Social Security Administration arranged for the data processing in that agency

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