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Report/Article Title   Memorandum: To Acting Director, Agent Orange
Projects Office (10A7), Veterans Administration, from
Han K. Kang, Chief, Research Section Agent Orange
Projects Office (10A7B), regarding Malignant Neoplasm
Cases in the Agent Orange Registry with attachments,
dated April 14, 1983

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Veterans Administration

Memorandum

Date:

April 14, 1983

To:

Acting Director, Agent Orange
Projects Office (10A7)

From: Chief, Research Section
Agent Orange Projects Office
(10A7B)

Subj: Malignant Neoplasm Cases in the
Agent Orange Registry

1. Attached please find a table comparing distribution of malignant neoplasm cases in the Agent Orange Registry and in a reference population. Subjects in the SEER (Surveillance Epidemiology End Results) program were selected for the reference population. The Biometry Branch of the National Cancer Institute collected 'cancer incidence and mortality in the U.S. for a five year period (1973-77) through 11 SEER program centers. The total number of subjects in the SEER program represents about 10% of the U.S. population and is fairly representative with respect to age.

2. A total of 75,741 veterans were registered in the Agent Orange Registry as of December 25, 1982 computer print out. Among these veterans, 768 were diagnosed as having malignant neoplasm (ICD 140-208); 283 had previous personal history of malignant neoplasm (ICD V 10.0- V 10.9); 2 had carcinoma in situ of the skin; and 19 had neoplasms of uncertain behavior or unspecific nature (ICD 236-239). For the purpose of comparison, 139 cases of non-melanoma cancer of the skin (ICD 173) reported in the Agent Orange Registry were excluded from the analysis.

3. Although non-melanoma cancer of the skin is the most common malignant neoplasm in the white population of the U.S., statistics on skin cancer are usually incomplete and not comparable with other forms of cancer. This is due mostly to the fact that most skin cancer patients are seen and treated in physicians' offices and are not hospitalized, whereas the primary source of data for cancer registries including the SEER program is the hospital patient file.

4. Distribution of malignant neoplasm cases in the SEER program was calculated using the number of malignant cases diagnosed in 1973-77 among U.S. males aged 25 to 39. This age group should include most of the Vietnam era veterans and, therefore, would serve as a reasonable comparison group.

5. In general, no significant disparity in the proportion of cancer of various sites was noted between the two groups. Proportions of soft tissue sarcoma and skin cancer in the Registry were similar to the SEER population: 2.2% vs. 2.6%; 10% vs. 11.7%.

2.

Acting Director,
Agent Orange Projects Office (10A7)

6. Some differences, however, were found for cancer of the buccal cavity and pharynx, and lymphomas. The 95% confidence limits for differences in proportions for these two sites were 0.9-5.1% and 1.7-8.8%, respectively. In other words, proportions for these sites in the Registry were higher than expected from the reference population. Whether these marginal but statistical differences are artifacts or something of importance is not clear at this time. It should be noted, however, that an association between exposure to chlorinated phenoxy acids or chlorophenols and lymphoma has previously been reported in three different papers (Hardell, 1979; Hardell, 1981; Hardell et al., 1981). A recent study by Hardell et al. (1982) also implicated an association of phenoxy acid or chlorophenol exposure and nasal and nasopharyngeal cancer.

7. Given the limitations of the Agent Orange Registry data, namely, the selective and voluntary nature of the response, higher proportions observed in veteran patients are likely to be artifacts. Nonetheless, in light of the possible association suggested by the above studies, continual monitoring of the Registry data is warranted.

HAN K. KANG, Dr.P.H.

Attachments

References

Hardell, L (1979) Malignant lymphoma of histiocytic type and exposure to phenoxyacetic acids or chlorophenols. Lancet, i, 55.

Hardell, L., Eriksson, M., Lenner, P. and Lundgren, E. (1981) Malignant lymphomma and exposure to chemicals, especially organic solvents, chlorophenols and phenoxy acids: A case-control study. Br. J. Cancer 43:169-176.

Hardell, L (1981) Relation of soft tissue sarcoma, malignant lymphoma and colon cancer to phenoxy acids, chlorophenols and other agents. Scand. J. Work Environ. Health 7:119-13.

Hardell, L., Johansson, B., and Axelson, O. (1982) Epidemiological study of nasal and nasopharyngeal cancer and their relation to phenoxy acid or chlorophenol exposure. Am. J. Ind. Med. 3:247-257

Number and Percent Distribution of Malignant Neoplasm Cases Among 75,741 Veterans Recorded in the Agent Orange Registry and Comparison to a Reference Population

Primary Site (ICD)	Number of Cases	Percent Distribution Registry	SEER*
Buccal Cavity and Pharynx (140-149)	47	7.5[a]	4.5
Digestive System (150-159)	69	11	12.2
Respiratory System (160-169)	62	9.9	8.5
Bones and Joints (170)	9	1.4	1.1
Soft Tissue (171)	14	2.2	2.6
Skin (172)**	63	10	11.7
Breast (174, 175)	3	0.5	0.06
Male Genital System (185, 186, 187)	87	13.8	16
Urinary System (188, 189)	39	6.2	6.1
Eye (190)	4	0.6	0.5
Brain and Other Nervous System (191, 192)	32	5.1	6.0
Endocrine System (193, 194)	20	3.2	6.5
Lymphomas (200, 201, 202)	126	20[a]	15
Multiple Myeloma (203)	7	1.1	0.4
Leukemia (204-208)	31	4.9	6.0
Others and ill-defined sites (195-199)	16	2.5	3.0
TOTAL	629	99.9	100.2

* SEER (Surveillance Epidemiology End Resutls): Percent distribution of malignant neoplasm cases diagnosed in 1973-77 by primary site, aged 25-39, all races, males, and all areas excluding Puerto Rico.

** Excluding basal and squamous carcinoma

[a] The 95% confidence limits for differences in proportions do not include zero

Agent Orange Registry   SEER

Total cancer (N_1) = 629 N_2 = 5358

Baccal cavity $(X_{1 \cdot 1})$ = 67 $X_{2 \cdot 1}$ = 240

Lymphoma $(X_{1 \cdot 2})$ = 126 $X_{2 \cdot 2}$ = 805

Observed proportion

$\overline{X}_{1 \cdot 1}$ = 0.075 $\overline{X}_{2 \cdot 1}$ = 0.045

$\overline{X}_{1 \cdot 2}$ = 0.20 $\overline{X}_{2 \cdot 2 \cdot}$ = 0.15

The 95% confidence limits for $P_1 - P_2$ are:

$$X_1 - X_2 + z_{\frac{1}{2}\alpha} \sqrt{\frac{\overline{X}_1(1-\overline{X}_1)}{N_1} + \frac{\overline{X}_2(1-\overline{X}_2)}{N_2}} < P_1 - P_2$$

$$< X_1 - X_2 + z_{1-\frac{1}{2}\alpha} \sqrt{\frac{\overline{X}_1(1-\overline{X}_1)}{N_1} + \frac{\overline{X}_2(1-\overline{X}_2)}{N_2}}$$

Buccal cavity and pharynx: $0.9 < P_1 - P_2 < 5.1\%$

Lymphoma: $1.7 < P_1 - P_2 < 8.8\%$