Hodgkin's Disease in Workers in the Wood Industry

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WORKERS in the wood industry in upstate New York have been found to be at approximately double the normal risk of dying from Hodgkin's disease. However, subsequent examination of registered cases of the disease in an area of England failed to confirm this result. Milham and Hesser (*1*) analyzed data on death certificates in New York State to determine the workers' risk, while in England Acheson (*2*) examined registered cases of Hodgkin's disease among residents within the area of the Oxford Regional Hospital Board. Such disagreements, which may well persist through a number of studies, prevent the formulation of definite conclusions about the relative risk for workers in the wood industry of contracting the disease. The relative risk, of course, may actually vary from one area to another.

According to Jackson and Parker (*3*), Hodgkin's disease can be divided into three types, which, in increasing order of malignancy, are paragranuloma, granuloma, and sarcoma. Whether benign lymphogranulomatosis (sarcoidosis) might be included in this continuum seems never to have been discussed. Nevertheless, both the benign and malignant forms of lymphogranulomatosis are found similarly distributed throughout the body, and both conditions are generally associated with an insensitivity to tuberculin (*4*). The question, therefore, of whether the two diseases are etiologically related can perhaps be legitimately raised.

Much interest in recent years has centered around the hypothesis of Cummings and Hudgins (*5*) that sarcoidosis results from a hypersensitivity induced by pine pollen. While no condition actually resembling sarcoidosis has been observed following injection of pine pollen, in at least a few experiments, injection in normal animals has apparently produced epithelioid cell granulomata (*6*). Cummings suggests that some of the inconsistency in results might be attributed to the use of different varieties of pine pollen.

Thus far, then, Cummings' hypothesis has neither been confirmed nor disproved. In this paper I shall extend the original hypothesis and examine evidence for the postulate that the increased risk to Hodgkin's disease of workers in the wood industry arises from their occupational exposure to pine pollen.

Materials and Results

To test this postulate, data from secondary sources were used. It was predicted that a part of any variation observed among the 49 continental States, including the District of Columbia, in mortality of white persons from Hodgkin's disease would be accounted for by

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a combination of the size of the State's wood, lumber, and furniture industry and the degree of occupational exposure of the population to pine pollen.

The inclusion of only part of any interstate variation in mortality is due to recognition of the possibility that other agents or factors involved in the etiology of Hodgkin's disease could well determine an entirely different geographic pattern. Thus, use of crude death rates (age-adjusted rates are unobtainable) would not be appropriate. Also, if, as has been suggested, workers in the wood industry have only double the normal risk of Hodgkin's disease and comprise only a small percentage of the workers in any State (the average proportion in the United States being 1.5 percent), crude death rates would form an essentially insensitive index. Under these circumstances, some other appropriate index of mortality has to be found.

The format of the U.S. mortality statistics in the Public Health Service publications "Vital Statistics of the United States" is such that deaths from lymphoproliferative disorders, with all ages combined, are listed separately only for lymphosarcoma and reticulosarcoma (International Statistical Classification of Diseases, Injuries, and Causes of Death 200) and Hodgkin's disease (I.C.D. 201). Deaths from the remaining conditions that are usually subsumed under this category—namely, reticulosis (I.C.D. 202) and mycosis fungoides (I.C.D. 205)—are combined with those from multiple myeloma (I.C.D. 203).

Provided that certain assumptions are made, these figures afford two proportions (expressed as deaths from I.C.D. 201 over combined deaths from I.C.D.'s 200 and 201 and deaths from 201 over combined deaths from 201, 202, 203, and 205). These proportions can then be used as indices of mortality to measure the hypothesized variation in Hodgkin's disease mortality.

The assumptions involved in the two proportions are that the etiology of Hodgkin's disease, other than disease due to pine pollen, is similar to that of lymphosarcoma and reticulosarcoma (I.C.D. 200) and is similar also to the etiology of the three diseases reticulosis, multiple myeloma, and mycosis fungoides (I.C.D.'s 202, 203, and 205). Acceptance of the postulate, then, depends upon the degree of correctness of the assumption underlying the use of each of these indices. On the other hand, proof that the data examined are statistically significant would imply that the assumptions were, in fact, correct.

The postulate seemed to lend itself naturally to regression analysis. The proportions I.C.D. 201 over 200 and 201 and 201 over 201, 202, 203, and 205 were designated as Y_1 and Y_2, that is, the dependent variables. In the usual nomenclature, the percentage of all white employed persons in the State engaged in the wood, lumber, and furniture industries (*7*), or X_1, and the percentage of commercial forest land in the State covered by pine (*8*), or X_2, represented the independent variables. Since, however, X_1 and X_2 are in practice only rather rough estimates of the true independent variables, they will be referred to hereafter as predictor variables rather than independent variables. X_2 is perhaps a reasonable estimate of the relative volume of pine wood handled by workers in the wood industry of a State.

In a series of stepwise regression equations, the percent of commercial forest land in pine was always entered in second place, since occupational exposure to pine pollen was hypothesized as qualifying the effect of the relative size of the State's wood industry. The table shows the F values relating to the joint predictive significance of the two independent variables X_1 and X_2 operating together. The mortality data are for the period 1956–65. For white males, these values, 7.464 and 4.118, are significant for both dependent variables Y_1 and Y_2, being significant at the 0.01 level for Y_1 and at the 0.05 level for Y_2. On the other hand, the F values for white females, 0.678 and 0.218, clearly indicate nonsignificant prediction.

When the predictor variables are considered separately, only the X_2 variable (percentage of pine forest in the commercial forest area of the State) in the equations for males is associated with significant F values (10.535 and 7.220), both at the 0.01 level. Thus the lack of significance of the percentage of workers in the wood industry as a predictor in both equations related to males does not support the original postulate. However, the most reasonable interpretation of the observation that the percentage of pine forest in a State acts as a significant predictor of disease for males, but

Separate regressions of the percent of Hodgkin's disease deaths among white persons, 1956–65, on the percent of workers with wood and the percent of commercial pine forest

Area, sex, and dependent variable [1]	Multiple r	F values for independent variables [2] with degrees of freedom		
		X_1+X_2	[3](±) X_1	[3](±) X_2
Males in 49 States:				
Y_1	(.50)	[4] 7.464 (2, 46)	(+) 2.358 (1, 46)	(+) [4] 10.535 (1, 46)
Y_2	(.39)	[5] 4.118 (2, 46)	(−) 2.059 (1, 46)	(+) [4] 7.220 (1, 46)
Females in 49 States:				
Y_1	(.17)	.678 (2, 46)	(+) .688 (1, 46)	(−) .887 (1, 46)
Y_2	(.10)	.218 (2, 46)	(−) .235 (1, 46)	(+) .271 (1, 46)
Males in 37 Eastern States:				
Y_1	(.62)	[4] 10.365 (2, 34)	(+) [5] 5.377 (1, 34)	(+) [5] 7.291 (1, 34)
Y_2	(.32)	1.982 (2, 34)	(−) .071 (1, 34)	(+) 3.687 (1, 34)
Males in 12 Western States:				
Y_1	(.29)	.424 (2, 9)	(+) .019 (1, 9)	(+) .743 (1, 9)
Y_2	(.51)	1.617 (2, 9)	(−) 2.843 (1, 9)	(−) .079 (1, 9)

[1] Y_1=deaths from I.C.D. 201 over combined deaths from I.C.D.'s 200 and 201; Y_2=deaths from I.C.D. 201 over combined deaths from I.C.D.'s 201, 202, 203, and 205.

[2] X_1=percent of employed white population engaged in wood, lumber, and furniture industries; X_2=percent of area of commercial forest land covered by pine.

[3] The F values for X_1 and X_2 are preceded by the sign of the partial correlation coefficient.

[4] Significant at 1 percent level.

[5] Significant at 5 percent level.

NOTE: All variables=arc. sin. $\sqrt{P}$.

not for females, is that this variable operates through occupational response. An analysis of residuals (the differences between observed and predicted values) for both sets of data revealed an association between the larger residuals and the western States. This result may well reflect the fact that there are marked differences in the species of pine between the eastern and western parts of the United States, with the Rocky Mountains forming the natural dividing line (*8*). Accordingly, the data for males were divided between States east and west of this mountain range. The relevant F values for these four equations are given in the lower half of the table. In the West, these values indicate that prediction associated with both predictor variables is not significant. This result contrasts with the position in the East, where, for the dependent variable Y_1, both predictor variables make a significant prediction (F values of 5.377 for X_1 and 7.291 for X_2).

Discussion

For the 37 States east of the Rockies, the evidence associated with the dependent variable Y_1 supports the hypothesis that pine pollen accounts for the increased risk for workers in the wood industry of contracting Hodgkin's disease. This conclusion seems warranted in spite of the proportion X_2 that involves the grouping of all pine species in the East into one category. A more detailed and refined analysis may reveal a gradation in the strength of the roles played by the various types of pine pollen.

The fact that the predictor variables (X_1 and X_2) do not predict Y_2 significantly for eastern males seemingly indicates that the assumption that Hodgkin's disease (other than that caused by pine pollen) and the diseases identified by I.C.D. numbers 202, 203, and 205 have similar causes is basically incorrect. Such a conclusion would not be valid, of course, if the predictor variables had not predicted significantly for Y_1.

There are two ways in which the assumption could be incorrect. Either pine pollen also initiates the disease group I.C.D.'s 202, 203, and 205 or the etiology of these diseases and that of Hodgkin's disease not caused by pine pollen is not similar. The second explanation appears more likely to be correct, partly because there is no prima facie evidence for the first explanation and partly because, in numbers of deaths, the disease group I.C.D.'s 202, 203, and 205 is dominated by multiple myeloma, a disease which in many ways is dissimilar to those conditions which primarily affect the lymph nodes.

The absence of any confirmatory evidence for

the western States of a relationship between occupational exposure to pine pollen and Hodgkin's disease suggests that, in the main, pine species found in the West do not initiate the disease. It is conceivable that the results observed occurred because the parameters were too crude or were subjected to unknown forms of bias. They are consistent, however, with what appears to be a disproportionate number of cases of sarcoidosis among U.S. military veterans from the eastern States. For a map of the distribution of cases in the United States, see the report by Cummings and co-authors (*9*).

Confirmation of the postulate that exposure to pine pollen is related to Hodgkin's disease is based upon analysis of data from secondary sources. Ultimately the postulate can be adequately tested only by using data from primary sources and employing the individual as the unit of analysis rather than the State. The present results indicate, however, that only workers in the wood industry of the eastern States are at excessive risk of Hodgkin's disease. Conceivably the degree of risk will depend upon the extent of the person's exposure to pine pollen.

Summary

Certain evidence in the literature about Hodgkin's disease suggested the hypothesis that the excessive risk of workers in the wood industry of contracting it could be explained by their exposure to pine pollen. By regression analysis involving the use of mortality and commercial statistics, it was found that the variation between States in deaths from Hodgkin's disease (all ages combined) as a proportion of the sum of deaths from Hodgkin's disease and lymphosarcoma and reticulosarcoma could be predicted for white males in States east of, but not west of, the Rocky Mountains. As expected, no significant prediction of such deaths was obtained for white females. That a prediction of risk was possible for males implied that the built-in assumption, that the etiology of Hodgkin's disease (other than for the kind caused by pine pollen) and of lymphosarcoma and reticulosarcoma is similar, was correct. However, only data from secondary sources were examined. An adequate test of the hypothesis will require examination of data from primary sources.

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