Risk of Multiple Sclerosis in Relation to Industrial Activities: An Ecological Study in Four European Countries[1]

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Abstract. The pattern of industries, in terms of workers in any individual industry in relation to total population, was compared with multiple sclerosis (MS) risk, as reported in previous communications in Norway, Denmark, Sweden and Switzerland. A great number of correlations with MS was found but, when intercorrelations were considered, paper manufacturing appeared to be the most closely associated with MS. The possible relevance of these findings in view of the methodological limitations is discussed.

Introduction

The problem of a possible influence of industrial factors on the risk of multiple sclerosis (MS) is still highly controversial. Various approaches have been used to settle this The investigation of urban or rural origin of patients revealed conflicting results [1–4]. Evaluation of the occupational pattern of patients in comparison with the general population [5–7] or with control groups [8] showed either no, or no consistent, deviation. When the time course of MS incidence was followed in defined regions over several years or decades during which industrialization took place, some authors found a fairly constant rate [9, 10] whereas a considerable increase was observed in other regions [11, 12]. Ecological correlation studies [13, 14] also revealed no consistent picture. The lack of association found in studies on occupation does not definitely argue against the role of an industrial factor which might affect the general population in a modified form, or in combination with cofactors which are absent in industrial workers themselves.

In a recent paper [14], an association between MS risk and industrial activity as a whole was described in 3 of 6 European countries, for which nationwide data on MS morbidity or mortality were available. In the present study, an attempt is made to correlate MS risk with individual industries as generally defined by the departments of statistics in 4 European countries. The main intention was to see if our previous finding

was caused by a high correlation to a specific industry or if it pointed more to industrialization (or related factors).

Methods

The source and type of MS rates were described previously [14]. Appropriate data on the industrial patterns within each subunit of the country (for example county, province, etc.) were available for Norway, Denmark, Switzerland and Sweden. For Finland, unfortunately, the published data were not grouped according to province (län), and Holland was omitted because no association with industry was found [14]. Generally each country was considered as a whole, with the exception of Denmark where the Copenhagen-Frederiksberg-Roskilde area was omitted. The following industries were evaluated: (a) mining, (b) quarrying, (c) food processing, (d) wood processing, (e) printing and publishing, (f) paper manufacturing, (g) metal processing and machine industry, (h) chemical industry, (i) textile and clothing industry, and (k) leather processing. The definitions of these groups varied between the countries; for example, the rubber industry was included in the chemical industry in Denmark, and in the leather industry in Norway. As a measure of activity within one subregion, the ratio:

$$\frac{\text{workers in the specific industry}}{\text{total population}}$$

was used.

No age or sex adjustment could be made. In order to estimate the rank of the specific industry in one country, the ratio:

$$\frac{\text{number of workers in the specific industry}}{\text{total number of workers}}$$

was calculated for each country.

Furthermore, intercorrelations were computed in each country for those branches, for which a significant association with MS was found. The industrial data originated from 1919 in Norway [15], from 1925 (based upon the population in 1930) in Denmark [16], from 1929 in Switzerland [17], and from 1915 in Sweden [18]. The rank order test according to Spearman (two-tailed) was used throughout. The level of significance was 0.05.

Results

The correlation coefficients between the MS rates and the size of each individual industry are given in table I. In Norway, the MS mortality 1951–1965 correlated significantly with paper and wood industries as well as with the leather industry in 1919. Wood processing and paper industry ($r_s = 0.7322$; $p < 0.005$) and leather and paper industry ($r_s = 0.7090$; $p < 0.005$) were highly correlated, whereas leather industry showed a weaker association with the wood processing industry ($r_s = 0.5862$; $p < 0.025$). Wood processing was the second important industry in Norway at that time (16% of all workers), whereas the paper industry ranged at the 4th place (10%) and leather industry in at the 8th place (1.7%). In Switzerland, prevalence was associated with leather, metal, paper manufacturing, printing, wood processing and textile industries (in this order). There was a high degree of intercorrelation between these industries: the leather industry correlated with all the remaining 5 branches, textile industry with 4 out of 5, paper and metal industry with 3 out of 5 each, and wood processing with 1 out of 5 remaining branches [detailed data not shown]. Metal industry took 2nd place (24%), wood processing 4th (10%), printing 6th (3.8%), paper manufacturing 8th (1.7%) and leather manufacturing 9th place in the rank order of Swiss industries at that time. In Denmark, paper manufacturing, printing, textile and chemical industries were associated with MS prevalence according to childhood residence (based upon the population aged 5–24 years in 1921), the first industry showing the highest correlation. Whereas paper manufacturing and printing ($r_s = 0.6248$; $p < 0.01$), and textile and chemical industry

Table I. Correlation coefficients r_s between different industries (worker/total population) and MS morbidity or mortality in 4 countries

Industry	Norway (n = 18)	Switzerland (n = 22)	Denmark (n = 20)	Sweden (n = 24)
Chemicals	+0.0702	−0.0503	+0.4725*	+0.0362
Metals	+0.4112	+0.7501***	+0.3105	+0.0636
Textile and clothing	+0.1140	+0.4650	+0.5064*	+0.0217
Food	+0.0439	+0.3492	+0.1214	−0.3979
Wood processing	+0.5939*	+0.5006*	+0.2910	+0.0420
Paper manufacturing	+0.8013***	+0.6917***	+0.5767**	+0.1179
Printing	+0.0439	+0.6544***	+0.5410*	−0.1333
Leather	+0.5521*	+0.8038***	−0.2162	+0.3883
Mining	−0.0404	−0.2403	–	−0.2071
Quarrying	+0.3298	−0.2403	+0.2771	–

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.002$. n = Number of subunits (counties, provinces).

($r_s = 0.6271$; $p < 0.01$) were closely associated, no correlation was found between these two complexes. In the rank order of industries textile ranged at 5th place (6.8%), chemical industry at 6th place (4.3%), paper manufacturing at 8th (0.7%) and printing at 9th place (0.3%). No association with any industry was found for MS prevalence in Sweden.

Discussion

The general reservations with respect to ecological studies in epidemiology which have been outlined before [19] apply to the present investigation. Thus, individual exposure to the factors under study is not measured, and even a slight surplus of respective factors in patients as compared to nonaffected in each geographical subunit results in a highly significant correlation. Furthermore, a high degree of intercorrelation between the factors tested, also with unknown variables, must be assumed. The method is, therefore, more suited to encourage considerations about further variables somehow associated with those pointed out by those who are more familiar with the local conditions than to elaborate substantial risk factors per se.

A further limitation of the present study is the use of crude rates instead of age- and sex-adjusted data for both MS risk and distribution of industries. Since marked differences in the sex ratio in the population of different administrative subunits of a country are not to be expected and, in addition, the risk to the total population given by the presence of an industry, rather than the occupational risk to the workers, was the subject of this study, sex adjustment seemed dispensable, whereas the lack of age adjustment

might, indeed, be a source of bias. Unfortunately, age adjustment was not feasible throughout, since appropriate data were lacking in the reports, on which the investigation was based. A cautious interpretation is, therefore, essential.

The present comparison revealed a highly significant association between the regional risk of MS and the extent of paper manufacturing in 3 of 4 European countries. Wood processing correlated in 2 countries with MS (Norway and Switzerland), but its weaker association with MS and its much higher correlation with paper manufacturing suggest that the association of this branch with the MS risk is confounded by the latter factor. The same is true for the association found between the leather industry and MS in Norway and Switzerland. The lack of any association in Sweden might be due to the lower reliability of the Swedish MS data which were based mainly on hospitalized patients.

The association between MS and paper manufacturing is all the more surprising, since this industry played only a minor role in the respective countries. It is in agreement with the high correlation of MS with the felling of coniferous wood described previously in Norway [14] and might point to one or several factors geographically related to the processing of coniferous wood. The finding is, furthermore, in agreement with earlier observations of a high MS rate [20] and of an additional relation to wood-processing occupations [5] in regions that are particularly rich in coniferous trees (e.g. southwest Germany). Whether the lack of a similar occupational risk in other regions [7] has to do with the type of processed wood remains obscure. The speculative character of all these considerations must be emphasized, since the ques-

tion of whether the association is reflecting directly a biological principle or is simply confounded is unsettled.

Finally, the present data suggest that the earlier observation of an association between MS and industrial activity as a whole in some countries is not explained by a consistent correlation with a particular industry. Thus, a possible influence of factor(s) related to industry and/or its social background must be discussed independently of the special type of industry pointed out in the present paper.

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