Epidemiological study of multiple sclerosis in Israel¹

Part III Multiple sclerosis and socio-economic status

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The frequency of multiple sclerosis increases with latitude both in the northern and southern hemisphere (Dean, 1949; Kurland, Mulder, and Westlund, 1955; Acheson, Bachrach, and Wright, 1960; Sutherland, Tyrer, and Eadie, 1962). This peculiar distribution suggests that an environmental factor (or factors) whose distribution is also correlated with latitude plays a role in the aetiology of the disease. The nature of the environmental factor remains obscure, although a wide variety of factors, including climatic variables, *e.g.*, sunlight, temperature, and cultural factors, *e.g.*, diet, have been considered over the years. In view of the apparent difficulty in determining the nature of the aetiological agent in multiple sclerosis, attempts to narrow the range of possibilities have merit. In this regard, the observations of Miller, Ridley, and Schapira (1960) that multiple sclerosis is more common among individuals in the higher socio-economic classes deserves attention. It is generally true that the socio-economic level of populations in temperate zones where multiple sclerosis is common tends to be higher than in tropical regions where the disease is rare. Therefore, a relation between socio-economic level and the distribution of multiple sclerosis seems feasible and the aetiological agent could conceivably be some condition related to socio-economic status.

Data collected in Israel afforded an opportunity to evaluate the suggestion of Miller *et al.* (1960) that there was a relation between socio-economic status and risk of multiple sclerosis, and Israel offers a number of advantages for studies of socio-economic factors in relation to chronic illnesses like multiple sclerosis. The country is small and its population is of a size permitting collection of data from the nation as a whole. Bias introduced by studying one region or another may thus be avoided in Israel. Moreover,

medical facilities are of excellent quality and a nationwide health insurance scheme makes medical care readily available to all the inhabitants regardless of their ability to pay for it.

In the present study, socio-economic status was measured in patients with multiple sclerosis and in controls.

SUBJECTS AND METHOD

A nation-wide survey of multiple sclerosis was completed in Israel in 1961 (Alter, Halpern, Kurland, Bornstein, Leibowitz, and Silberstein, 1962). Of 282 patients identified in the survey, 241 were successfully contacted again in 1963 and comprised the patient population of the present study.

The control population consisted of 917 individuals selected by a cluster random sampling procedure from the three major population centres of Israel. Controls were individually matched with patients on the basis of age and sex. In addition, the patients and controls were matched for region of origin as more than four-fifths of Israel's adult population is not native born. For statistical purposes, it was decided to have four control responses for each patient response, as described in an earlier report (Antonovsky, Leibowitz, Smith, Medalie, Balogh, Kats, Halpern, and Alter, 1965). The analyses were carried out between 241 patient responses and 964 control responses.

A questionnaire was formulated to elicit epidemiological information and was administered to the patients and controls by a team of trained field interviewers. A summary of the methods and results of that study has already been published (Antonovsky *et al.*, 1965).

Items in the questionnaire relevant to socio-economic status included questions about the type of occupation and amount of education. In addition, respondents were asked to estimate the socio-economic status of their family on a self-estimate scale. Information about size of population in the community of residence was also elicited. Information was requested about the head of the respondent's household in the latter's childhood as well as about the respondent. In order to compare the same time periods for patients and controls an 'age at onset' was assigned to each control which corresponded to the age at onset of multiple sclerosis in the patient with whom

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the control was matched. Questions pertained only to the period of onset or before the onset of illness because only information of possible relevance to the aetiology of multiple sclerosis was desired. The mean age at onset of multiple sclerosis for patients in Israel was 32.6 years (Leibowitz, Halpern, and Alter, 1964; Leibowitz, Alter, and Halpern, 1964).

RESULTS

OCCUPATION The occupations were classified according to a graded scheme and the percentage in each category was compared. Table I shows comparisons between patients and controls at the age at onset of illness and between their respective heads of households both at age at onset and at age 10 years. It would appear that in so far as occupation reflects socio-economic status, patients did not differ from controls in the Israeli population.

EDUCATION Another method of assessing socio-economic status is educational level. Comparisons were made regarding education achieved by the head of the parental family of the respondent and also the education the respondents had achieved in the period before the onset of multiple sclerosis. The data are shown in Table II. On the education items, as with occupation, patients did not differ significantly from controls and no difference in socio-economic status can be inferred.

SELF-ESTIMATE OF SOCIO-ECONOMIC STATUS The percentage distribution of patients and controls on a scale representing graded steps of socio-economic level is shown in Table III. The validity of self estimates may, of course, be open to question. In any

TABLE II
LEVEL OF EDUCATION OF RESPONDENTS AND HEADS OF HOUSEHOLDS

Education Completed	Respondents (%)		Heads of Parental Household (%)	
	Patients	Controls	Patient's Family	Control's Family
Eight years or less	45	51	61	59
More than eight years,				
academic	48	43	33	35
Vocational	7	6	2	3
No answer	—	—	4	3
Total number	100	100	100	100
	241	964	241	964

TABLE III
SELF-ESTIMATE OF SOCIO-ECONOMIC STATUS OF FAMILY OF ORIGIN OF RESPONDENT AT AGE 10 YEARS

Self-estimate	Patients (%)	Controls (%)
Well-to-do	14	11
Comfortable	53	50
Not so comfortable	24	32
Poor	6	4
Very poor	3	3
	100	100
Total number of cases	241	964

event, the differences between patients and controls were small and not statistically significant.

Having failed to demonstrate any significant differences on these three indices of socio-economic status for the groups as a whole, we turned our attention to comparisons between various sub-groups of patients and controls. The indices were arranged to represent a higher and a lower socio-economic grouping. Data are here presented only in

TABLE I
OCCUPATION OF RESPONDENTS AND HEADS OF HOUSEHOLDS

Occupation	Occupation at Onset (%)				Occupation at Age 10 Years (%)	
	Respondent		Head of Household		Head of Household	
	Patients	Controls	Patient's Family	Control's Family	Patient's Family	Control's Family
Unskilled	17	9	14	11	10	7
Skilled	13	18	18	24	13	12
Lower white collar	15	11	15	14	8	9
Retail business	5	4	11	13	30	30
Artisan	1	2	6	7	8	9
Official (medium level)	1	2	4	2	2	2
Official (large business, property)	3	2	6	6	20	17
Professional	6	7	9	11	2	5
Religious	0	1	2	3	3	5
Farmer, fisherman	2	0	5	1	2	2
Not in labour force	31	38	—	—	—	—
Unclassified	6	6	10	8	2	2
	100	100	100	100	100	100
Number of cases	241	964	241	964	241	964

terms of lower status; other cutting points revealed the same picture. In the occupation category, the lower socio-economic group included individuals employed as manual workers, pedlars, or home-workers. On the education item, lower status included those who had completed less than eight years of education.

REGION OF ORIGIN The percentage of patients and controls in the lower socio-economic occupation and education category was then determined for respondents from different regions of origin. Comparisons were made for respondents from eastern Europe, central Europe, and Afro-Asian countries. The numbers of respondents from southern and western Europe and native-born Israelis were so small that they were excluded from this analysis. Comparisons are shown in Table IV. The percentage of Afro-Asians, both patients and controls, which was classified as of low socio-economic status, was considerably higher than the percentage of Europeans so classified. It may be recalled that in previous publications (Alter *et al.*, 1962; Alter, Leibowitz, and Halpern, 1964), it was shown that multiple

sclerosis was at least six times higher in European than in Afro-Asian immigrants to Israel. This subgroup analysis provided evidence that socio-economic level was, indeed, higher in the population which had a higher frequency of multiple sclerosis. On the other hand, comparison of Afro-Asian patients and controls showed a lower status in the patient group, while no significant difference was revealed between patients and controls in the European groups.

AGE IN 1962 A second subgroup analysis was carried out for those who were of different ages in 1962. Since socio-economic status is not necessarily constant, it was of interest to determine whether groups of different ages would report differences in socio-economic status before the onset of illness. Three age groups were compared and the percentage in each age group having a low socio-economic status at onset is shown in Table V. Among respondents 55 years of age or older in 1962, the percentage of patients classified as having a lower socio-economic status was, in general, lower than controls, *i.e.*, patients had a relatively higher socio-economic

TABLE IV

SOCIO-ECONOMIC STATUS OF PATIENTS WITH MULTIPLE SCLEROSIS AND CONTROLS BY REGION OF BIRTH¹

Socio-economic Indices	Percentage in Lower Socio-economic Category					
	Eastern Europeans		Central Europeans		Afro-Asians	
	Patients	Controls	Patients	Controls	Patients	Controls
Head of household's occupation at onset	31	33	24	27	52	43
At age 10	15	15	14	10	51	29
Education completed						
By respondent	26	29	12	19	81	57
By respondent's father	41	41	26	30	82	73
Number of cases	125	500	50	200	32	128

¹Patients born in Israel (18), in southern Europe (11), or in western Europe (5) and their respective controls are excluded from these tabulations. Lower socio-economic category is defined as: occupation, manual worker, pedlar, home worker; education, less than eight years of education completed.

TABLE V

SOCIO-ECONOMIC STATUS OF PATIENTS WITH MULTIPLE SCLEROSIS AND CONTROLS BY AGE IN 1962

Socio-economic Indices	Percentage in Lower Socio-economic Category of Age Groups					
	39 Years or Less		40 to 54 Years		55 Years or Above	
	Patients	Controls	Patients	Controls	Patients	Controls
Head of household's occupation at onset	39	44	31	30	28	30
At age 10	36	31	16	13	18	17
Education completed						
By respondent	42	28	26	23	24	40
By respondent's father	47	39	47	38	35	53
Number of cases	66	271	104	400	71	293

Lower socio-economic category defined as: occupation, manual worker, pedlar, home worker; education, less than eight years of education completed.

status. However, among younger respondents the converse was true and relatively more of the patients were classified as having a lower socio-economic status. The results based on comparisons of different age groups appear contradictory unless it is assumed that the environmental factors correlated with higher socio-economic status and related to risk of multiple sclerosis when the older individuals acquired the disease was less important for younger patients.

DURATION OF ILLNESS Another subgroup analysis was carried out for those with different durations of illness in 1962. In a sense, this analysis served as a check of the previous analysis in that individuals who were ill longer were likely to be older. Three subgroups with different durations of illness were compared and the data are shown in Table VI. In the group ill longest, patients had a higher socio-economic status than controls whereas in the group ill for a shorter period of time the patients tended to have a lower socio-economic status. The comparisons of groups of different ages and of groups having different durations of illness gave similar results and increased the confidence in their validity.

If the risk of multiple sclerosis is actually different for groups of different socio-economic status depending on their age and origin, it might be helpful to ascertain what factor might account for the difference. One factor which might be considered is the degree of urbanization. A general trend toward urbanization has certainly affected many populations and therefore younger and older people may have been influenced by different environments during early life. As urbanization also bears a relation to socio-economic factors, it seemed worthwhile to assess the type of community in which patients and controls resided for the major part of their lives before the onset of illness.

The percentage of patients and controls who reported living in a metropolitan centre of over half

TABLE VII

PERCENTAGE OF RESPONDENTS RESIDING IN A METROPOLITAN COMMUNITY BY REGION OF BIRTH, DURATION OF ILLNESS, AND AGE IN 1962

	<i>Percentage of Respondents in the Metropolitan Community</i>	
	<i>Patients</i>	<i>Controls</i>
<i>Region of Birth</i>		
Eastern Europe	30	17
Central Europe	26	18
Afro-Asia	9	25
<i>Duration of Illness (years)</i>		
< 9	24	14
10 to 19	23	19
20 +	31	20
<i>Age in 1962 (years)</i>		
< 39	11	13
40 to 54	32	20
55 +	28	18

a million inhabitants was compared for groups of different origin, different ages in 1962, and different durations of illness in 1962. The data are presented in Table VII. Subgroups in which patients had a relatively lower socio-economic status than controls, *i.e.*, Afro-Asians, individuals who were youngest in 1962, and individuals who were ill for a shorter period, contained a lower percentage who reported living in a large metropolitan centre. On the other hand, groups in which patients reported a relatively higher socio-economic status than controls, in general also included a high percentage of individuals from metropolitan centres.

These results suggest that an association between risk of multiple sclerosis and socio-economic status may exist but it is conditioned by the degree of urbanization of a region. Where a region is predominantly rural, the risk of multiple sclerosis may be greater in individuals from low socio-economic classes. In an urban setting, risk may be higher for individuals from higher socio-economic groups. If

TABLE VI

SOCIO-ECONOMIC STATUS OF PATIENTS WITH MULTIPLE SCLEROSIS AND CONTROLS BY DURATION OF ILLNESS

Socio-economic Indices

Percentage in Lower Socio-economic Status of Duration of Illness Groups

	<i>Under 10 Years</i>		<i>10 to 19 Years</i>		<i>20 or More Years</i>	
	<i>Patients</i>	<i>Controls</i>	<i>Patients</i>	<i>Controls</i>	<i>Patients</i>	<i>Controls</i>
Head of household's occupation at onset	46	39	30	36	16	25
At age 10	31	22	19	17	14	19
Education completed						
By respondent	30	27	34	31	23	33
By respondent's father	43	41	45	44	44	45
Number of cases	93	372	93	372	55	220

Lower socio-economic category defined as: occupation, manual worker, pedlar, home worker; education, less than eight years of education completed.

this interpretation is valid, it would indicate that the relation between risk of acquiring multiple sclerosis and socio-economic factors is not a simple one.

DISCUSSION

Miller *et al.* (1960), who reported an association between high socio-economic status and frequency of multiple sclerosis, studied an English population and used only one index of socio-economic status, namely, the Registrar-General's five-class system based solely on occupation at the onset of multiple sclerosis. Moreover, they had no matched controls for comparison. On the other hand, Westlund and Kurland (1953b) used both occupation and education to measure socio-economic status and compared patients with a control group. The design of the latter and of the present investigation was similar. They found no differences in socio-economic status between patients and controls. The present investigation also failed to demonstrate statistically significant differences in socio-economic status between patients and controls when groups as a whole were compared. However, subgroup analyses suggested that some association between socio-economic status and risk of multiple sclerosis may exist but the kind of environment in which an individual lived before the onset may determine whether a higher or a lower socio-economic status confers greater risk. It may be that in the European environment of the early twentieth century the childhood environment of many of the older patients identified in the Israeli survey a higher socio-economic status conferred a greater risk of acquiring multiple sclerosis. In the Afro-Asian environment of more recent decades, the environment of many of the younger patients with multiple sclerosis identified in Israel a lower socio-economic status conferred a greater risk.

On considering the differences in the environment of the European group and the Afro-Asian group, one may speculate that before the time a region reaches a certain 'threshold' of socio-economic development, the poorer classes are the most susceptible to multiple sclerosis. Beyond this 'threshold', the better off socio-economic classes are somewhat more susceptible to multiple sclerosis. The threshold may depend on the degree of urbanization or industrialization or some other factor.

It may also be postulated that the general level of socio-economic development in a region is related to the frequency of multiple sclerosis in the region. In regions below a given threshold, the rate of multiple sclerosis may be low and individuals in the lower socio-economic strata are most susceptible. Above a certain level the rate would increase rapidly with changes in socio-economic level. Beyond an upper

limit, further economic development in a region would not be expected to cause an increase in the frequency of multiple sclerosis. This scheme would be compatible with the S-shaped curves of the prevalence of multiple sclerosis plotted for north America, Europe, Afro-Asia, and Australia (Westlund and Kurland 1953a; Alter *et al.*, 1962; Sutherland *et al.*, 1962). It might also account for our failure to find appreciable differences in socio-economic level between patients and controls in the same region. It would also account for the apparent failure of multiple sclerosis to increase in frequency toward northern regions of Scandinavia and Canada (Alter, Allison, Talbert, and Kurland, 1960; Kurtzke, 1965a). The notion seems, at first glance, to be incompatible with the reported low frequency of multiple sclerosis in Japan and South Africa, both of which are highly industrialized countries with many urban centres. However, in these countries, large segments of the population have very marginal socio-economic status and thus these regions are not comparable in overall standard of living with the industrialized regions of Britain and northern United States. The fact that multiple sclerosis has not been recognized among the poorer classes in these regions may reflect the lack of adequate medical care for these groups rather than a true absence of the disease.

A test of the notions presented here would derive from observations on the frequency of multiple sclerosis in a region in which the standard of living is improving. The Afro-Asian group in Israel constitutes an appropriate population for such a study as this group has immigrated from a region with a low standard of living to one in which the general standards approach those of the socio-economic advanced regions of Europe and America. Unfortunately, the 'incubation' period of multiple sclerosis may be long (Poskanzer, Schapira, and Miller, 1963; Kurtzke, 1965b) and it may take a generation before it is possible to detect an increased frequency of multiple sclerosis in the Afro-Asian group in Israel.

SUMMARY

Although the pattern of geographic distribution of multiple sclerosis, which follows a gradient of decreasing prevalence toward the equator, seems well established, the reason for this distribution continues to elude discovery. A report that frequency of multiple sclerosis was higher for groups with a higher socio-economic level suggested a possible explanation for the distribution of the disease, as socio-economic level, in general, tends to be high in temperate regions where the disease is also common.

Socio-economic level was estimated in 241 patients and 917 matched controls in an Israeli population. Advantages offered by Israel for such a study are described. Socio-economic indices included occupation and education both of the respondents and the head of a respondent's household. In addition, a self-rating scale of socio-economic status was included. The estimates were made for age at onset of illness and age 10 years. The assigned 'age at onset' for controls was the same as that of patients with whom the controls were matched.

Comparison of patients and controls on the various socio-economic indices showed no significant differences. However, analysis of subgroups suggested that the European immigrants to Israel had a higher socio-economic status than Afro-Asian immigrants. As multiple sclerosis has been shown to be five to 10 times more prevalent in Europeans than in Afro-Asians in Israel, the subgroup analysis suggested that a relation between socio-economic status and frequency of multiple sclerosis may exist. Further analysis suggested that the degree of urbanization of a region might influence the susceptibility of different socio-economic groups to multiple sclerosis. It was speculated that in rural regions, those individuals with lower socio-economic status might be more susceptible, whereas in urbanized regions those from higher socio-economic strata may be more susceptible.

If a relationship between socio-economic status and the risk of multiple sclerosis exists, the present study suggests that the relation is not a simple one.

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