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Multiple sclerosis distribution in England and Wales and parts of Europe

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SUMMARY

Scotland and Ireland have the highest death rates from multiple sclerosis and high rates are recorded in an area extending south-eastward from Britain through central Europe. The rates tend to diminish with rising latitude and longitude. In England and Wales the county boroughs with notably high rates during 1958–67 were mostly textile towns with cotton and wool mills, situated in the area recording the lowest average levels of sunshine. In the London area mortality from multiple sclerosis was high in those western boroughs and adjacent counties most exposed to the noise of aircraft using the airports of London. The geographical pattern in England suggests that noise and vibration of particular kinds may be a factor in causation along with a climatic factor, but this hypothesis is speculative until further evidence is found to support it.

INTRODUCTION

The causes of multiple sclerosis are shrouded in mystery notwithstanding considerable studies of the geographical incidence of the disease in North America and Australia. Limburg (1950), Kurland (1952) and Westlund & Kurland (1953*a*, *b*) revealed a variation with latitude by surveys of mortality and morbidity rates in Canadian cities of Manitoba and Winnipeg and in New Orleans in the United States. Hypotheses that relations with climate arise from differing intensities of solar radiation or cosmic rays were later discussed by Barlow (1960) and by Acheson, Bachrach & Wright (1960). A similar association with latitude in Australia was found by Sutherland, Tyrer & Eadie (1962) and a hypothesis that poliomyelitis or related virus disease might be connected with appearance of multiple sclerosis in later life was investigated by the same authors (Eadie, Sutherland & Tyrer, 1965).

Kurland & Reed (1964) made a useful summary of the consensus of views regarding the possible causation factors, as did also Miller (1968). A local survey of prevalence has been made in north-east England based on some 50 cases (Poskanzer, Shapira & Miller, 1963), but it is not practicable to make a nation-wide survey of over 1000 cases per annum in order to establish the geographical distribution. For such a purpose statistics provide the only measure of incidence despite their deficiencies for such a chronic disease.

Not much attention has been paid to distribution of death-rates in the British Isles, although, as will be seen, Scotland and Ireland have the highest rates of any

country. In the present paper death-rates from multiple sclerosis in parts of Europe and some other countries during the decade 1951–60 have been calculated from the data published by the World Health Organization, and a detailed study of the deaths during 1958–67 in the towns and counties of England and Wales has been made in the hope of throwing some light on the aetiological factors.

TREND OF MORTALITY IN ENGLAND AND WALES SINCE 1921

It was apparent from the surveys in North America that assessment of rates of prevalence of multiple sclerosis is so difficult that rates of mortality probably provide as good a measure of frequency of the disease. The official records of deaths have been used exclusively in this paper as measures of relative incidence in different places, though a considerable proportion of those affected are recorded as dying of other associated causes. Crude death-rates of males and females have been recorded by the Registrar General of England and Wales for each year since 1921 and the mean annual rates per million living in 5-year periods (or shorter periods when necessary) and in 1966–7 are shown in Table 1, with the ratios between female and male rates.

Table 1. *Mean annual death rates by sex at all ages from multiple sclerosis in England and Wales*, 1921–67

Period	Rates per million		Ratio
	Males	Females	F/M (%)
1921–25	18·6	17·6	95
1926–30	20·2	20·6	112
1931–35	20·0	23·0	115
1936–39	20·0	21·7	108
1940–43	24·7	23·7	91
1944–45	22·5	22·5	100
1946–50	16·2	19·8	122
1951–55	15·2	22·0	145
1956–60	15·2	22·4	147
1961–65	14·4	21·2	147
1966–67	13·5	19·5	144

From 1946 to 1967 the female rate at all ages varied little from about 22 per million. The male rate, after remaining at 20 during 1926–39, rose to 24·7 during the four years 1940–3 owing to the rates being based on the civilian population, only 7 deaths of non-civilians from multiple sclerosis being registered in those years. From the end of the war the rate, based again on the whole population, declined rapidly to 13·5 in 1966–7. The reason for this pronounced fall in male mortality after 1945 must be important from the point of view of aetiology since it had no parallel in the female rate. There was no sex difference of importance before 1946, but since 1950 the crude male mortality level has become established at only two-thirds of that of females.

The improvement shown by males must have been due to removal, or great

diminution, of some factors affecting them such as large changes which took place in industry and conditions of life in factories. For example, heavy work on munitions was replaced by a growth in lighter industries. This will be referred to in the examination of death-rates in large towns.

In order to eliminate the effects on crude rates of the increasing average age of the population and discover at what ages the change in death-rate of males since 1925 has occurred, Table 2 compares the rates per million of each sex at different ages in the recent years 1963–7 with those in 1926–30.

Table 2. *Mean annual death-rates per million by sex and age from multiple sclerosis in* 1963–67 *compared with* 1926–30

Age group	Males		Females		Change of rate % of that in 1926–30		Comparison of sex change
	1926–30	1963–7	1926–30	1963–7	Male	Female	
0–14	0	0·4	0	0·6	—	—	
15–24	2	0·8	3	1·4	−60	−47	Both sexes affected
25–34	10	5·8	12	7·6	−42	−63	Both sexes affected
35–44	24	18·2	29	27·0	−24	−5	Males only affected by change
45–54	36	29·8	44	44·6	−17	+1	Males only affected by change
55–64	61	35·6	49	47·8	−42	−2	Males only affected by change
65–74	91	30·0	61	33·8	−67	−45	Both sexes affected
75+	54	16	44	13·8	−70	−69	Both sexes affected

The people who died in 1963–7 at ages under 35 were children during the war or had been born after it, and both sexes showed a drop of about 50% in death-rate compared with the pre-war level. One or more of the causes of multiple sclerosis productive of death in early life must have been reduced in both sexes after the war. Males dying at ages between 35 and 65 also showed falls in death-rate in 1963–7 by 17–42% whereas females dying at those ages showed no appreciable change in the rate compared with that in 1926–30. This means that some change in the mode of life or environment peculiar to males in middle life and resulting from or following the war caused a diminution of incidence of the disease to lower levels than hitherto. At ages over 65 a considerable fall in death-rates since the war has occurred for each sex, rather greater for males than females.

MULTIPLE SCLEROSIS IN COUNTY BOROUGHS AND COUNTIES OF ENGLAND AND WALES IN 1958–67

From 1958 multiple sclerosis was distinguished as a subdivision of the Registrar General's Supplementary Abridged List, no. 32 (2), and table 21 in the Statistical Reviews recorded the numbers of deaths by sex at all ages in each county borough, Metropolitan borough and administrative county. This has made it possible to aggregate the deaths during the 10 years 1958–67 and obtain sufficient frequencies in the larger towns and counties to reveal differences which are of statistical significance. No details of age at death are available.

Table 3 shows the actual numbers of deaths of males (D_1) and of females (D_2)

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Table 3. *Multiple sclerosis mortality in county boroughs in* 1958–67

(Grouped according to industry divisions in table A of Census of 1951 giving proportions per 10,000 persons in textiles (Order X, subdivided into cotton and wool, 110–12, rayon, hosiery, etc., 113, 114, 118, 134, others in X); metals, engineering, shipbuilding, electrical (Orders V, VI, VIII).

Group A: towns with 10 % or more in textiles (cotton, wool). B: towns with 5–9 % in textiles (cotton, wool) and over 10 % in metals and machinery, etc. C: towns with 10 % or more in textiles (rayon and other). D: towns with 25 % or more in metals, etc. (textiles less than 5 %). E: towns with 15–24 % in metals, etc. (textiles less than 5 %). F: towns with 10–14 % in metals, etc. (textiles less than 5 %). G: inland towns with less than 10 % in metals, etc. (textiles under 5 %). H: seaside resorts with industry as in G.)

	Males			Females				Both sexes, significant excess areas
	No. of deaths (D_1)	Expected (E_1)	Ratio $100D_1/E_1$	No. of deaths (D_2)	Expected (E_2)	Ratio $100D_2/E_2$	d^2/E	P
Group A. Textile towns with 10 % or more in cotton or wool manufacture								
Blackburn	12	7·5	160	14	11·5	122	—	*
Bolton	16	11·1	144	22	17·5	126	4·8	0·03
Bradford	22	20·0	110	39	32·5	120	—	—
Burnley	13	5·6	232	21	8·5	247	15·7	< 0·001
Bury	4	4·3	93	11	6·7	164	—	*
Dewsbury	7	3·7	189	2	5·8	34	—	*
Halifax	9	6·7	134	17	10·4	163	4·8	0·03
Huddersfield	16	9·7	170	17	14·4	118	3·8	0·05
Oldham	12	7·7	156	14	12·0	117	—	—
Preston	11	7·8	141	7	11·2	63	—	—
Rochdale	9	6·0	150	12	9·4	120	—	—
Stockport	13	9·9	131	33	13·6	200	16·5	< 0·001
Wakefield	2	4·2	48	10	6·6	152	—	—
Group B. Textile towns with 5–9 % in cotton or wool and over 10 % metals, etc.								
Coventry	15	21·5	70	14	34·2	41	—	—
Darlington	6	6·0	100	12	9·5	129	—	—
Doncaster	6	6·1	98	8	9·6	83	—	—
Manchester	67	45·6	147	83	21·7	116	6·2	0·01
Salford	26	10·8	241	18	17·0	106	9·4	0·007
Totals of A and B	266	194·2	137	354	252·1	139	—	—
Group C. Textile towns with 10 % or more in rayon, etc., factories								
Derby	12	9·1	132	11	14·2	77	—	—
Leicester	16	18·9	85	24	29·9	80	—	—
Nottingham	11	21·9	51	22	34·7	63	—	—
Totals of C	39	49·9	78	57	78·8	72	—	—
Group D. Towns with 25 % or more working in metals, machinery, etc.								
Barrow-in-Furness	4	4·5	89	7	7·1	99	—	—
Birmingham	71	76·9	92	116	122·0	95	—	—
Gateshead	2	7·4	27	11	11·4	96	—	—
Lincoln	7	5·3	130	7	8·3	84	—	—
Newport (Mon.)	7	7·4	95	6	11·7	51	—	—
Rotherham	6	6·0	100	9	9·4	96	—	—
Sheffield	51	32·7	153	59	54·3	109	6·1	0·015
Smethwick	6	4·8	125	4	7·7	52	—	—
Sunderland	10	13·2	76	6	20·7	29	—	—
Warrington	8	5·6	155	7	8·7	80	—	*

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Table 3. (*cont.*)

	Males			Females			Both sexes, significant excess areas	
	No. of deaths (D_1)	Expected (E_1)	Ratio $100D_1/E_1$	No. of deaths (D_2)	Expected (E_2)	Ratio $100D_2/E_2$	d^2/E	P
Walsall	6	8·3	72	11	13·1	84	—	—
West Bromwich	1	6·7	15	11	10·7	103	—	—
West Hartlepool	5	5·4	92	11	8·5	118	—	—
Wolverhampton	2	10·3	19	18	16·4	110	—	—
Totals of D	186	194·5	96	283	310·0	91	—	—
Group E. Towns with 15–24% working in metals, machinery, etc.								
Birkenhead	7	10·1	69	16	15·8	101	—	—
Cardiff	12	18·0	67	20	29·6	70	—	—
Dudley	8	4·5	178	7	7·1	79	—	*
Ipswich	5	8·3	60	17	11·1	151	—	*
Middlesborough	11	10·8	102	18	17·1	105	—	—
Newcastle-on-Tyne	25	18·5	135	39	29·0	134	5·5	0·02
Plymouth	16	15·0	94	11	23·6	46	—	—
Portsmouth	12	15·2	79	24	23·9	100	—	—
Southampton	15	14·1	104	13	22·6	58	—	—
South Shields	4	6·9	58	7	6·2	113	—	—
Swansea	13	11·8	110	15	18·7	80	—	—
Worcester	7	4·6	152	3	7·4	41	—	*
Totals of E	135	137·8	98	190	212·1	89	—	—
Group F. Towns with 10–14% working in metals, machinery, etc.								
Bootle	3	5·8	52	3	9·8	31	—	—
Chester	3	4·2	71	8	6·5	123	—	—
Croydon	16	19·1	84	39	30·1	129	—	*
Kingston-on-Hull	23	21·1	109	31	33·1	94	—	—
Leeds	37	35·8	103	45	56·3	80	—	—
Liverpool	47	51·7	91	57	81·2	70	—	—
Merthyr Tydfil	3	4·1	73	4	6·5	62	—	—
Tynemouth	2	5·0	40	5	7·9	63	—	—
Totals of F	134	146·8	91	192	231·4	83	—	—
Group G. Towns (inland) with less than 10% working in metals, etc.								
Barnsley	9	5·3	170	3	8·3	36	—	*
Bath	5	5·8	86	11	9·1	121	—	—
Burton-on-Trent	4	1·7	135	5	2·8	179	6·5	0·03
Bristol	18	30·3	32	46	47·6	98	—	—
Canterbury	3	2·2	136	4	3·5	114	—	—
Carlisle	2	4·9	41	12	7·8	154	—	—
East Ham	2	5·3	38	6	8·4	71	—	—
Exeter	9	5·7	158	15	8·9	169	6·1	0·015
Gloucester	4	4·9	82	8	7·7	104	—	—
Great Yarmouth	14	2·6	389	9	5·8	155	19·1	< 0·001
Grimsby	7	6·7	104	7	10·7	55	—	—
Northampton	7	7·6	92	6	12·0	50	—	—
Norwich	4	8·3	48	14	13·1	107	—	—
Oxford	5	7·5	67	12	11·9	101	—	—
Reading	8	8·4	95	9	13·3	88	—	—
Stoke-on-Trent	12	19·0	63	16	30·2	53	—	—
St Helens	7	7·5	93	12	11·7	103	—	—
West Ham	2	7·0	86	5	12·6	40	—	—
York	9	7·3	123	17	11·5	148	—	*
Totals of G	131	148·0	89	217	236·9	91	—	—

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Table 3 (*cont.*)

	Males			Females			Both sexes, significant excess areas	
	No. of deaths (D_1)	Expected (E_1)	Ratio $100D_1/E_1$	No. of deaths (D_2)	Expected (E_2)	Ratio $100D_2/E_2$	d^2/E	P
Group H. Seaside resorts with less than 10% working in metals, etc.								
Blackpool	9	10·4	87	16	16·2	99	—	—
Bournemouth	19	10·4	183	8	16·4	49	—	*
Brighton	18	11·3	159	26	18·0	144	7·4	< 0·01
Eastbourne	7	4·3	163	16	6·8	235	12·8	< 0·001
Hastings	6	4·6	130	10	7·3	137	—	—
Southend-on-Sea	15	11·4	132	22	17·4	126	—	—
Southport	8	5·7	140	13	8·9	146	—	—
Wallasey	1	7·2	14	15	11·4	132	—	—
Totals of H	83	65·3	127	126	102·4	122	—	—

* $P < 0{\cdot}10$ for one sex.

in each town compared with the numbers expected by applying the national death-rates to the estimated populations in each year (E_1 and E_2). Comparative mortality ratios not standardized by age (CMR = $100D/E$) are given for each sex, and as a measure of statistical significance of the combined rate the value of

$$d^2/E = (D_1+D_2-E_1-E_2)^2/(E_1+E_2)$$

has been shown wherever the excess of actual over expected deaths is significant at the 5% level ($P < 0{\cdot}05$ for $d^2/E > 3{\cdot}8$).

The towns have been classified into a few industrial groups based on the Census of Industries 1951 (table A of the Report), using the orders and subdivisions of the official list used by the Registrar General. Since it appeared that multiple sclerosis mortality in 1958–67 was notably higher in the textile towns where 10% or more of the working population was engaged in cotton or wool manufacture (Order X, 110–112), those towns were first identified as group A. The next group, B, consists of towns with 5–9% of the population in cotton or wool processing combined with at least 10% in occupations with other heavy machinery such as metal manufacture, ship-building and engineering, including electrical goods (Orders V, VI, VIII).

After the war there was a rapid growth in the manufacture of man-made fibres in the textile industry, and this occurred particularly in Leicester, Nottingham and Derby, which have been identified as group C since the machinery in these factories was different from that employed in the cotton and wool mills (Order X, 113, 114, 118, 123).

The remaining groups, D–G and H, were based on the percentage of the population engaged in industry orders V, VI, VIII, as defined above, these towns having less than 5% in textile work and proportions in the other heavy industries diminishing from over 25% to under 10%. The classification and definition of the eight groups is shown at the head of Table 3. Examination of the other industries in the residue of the seven groups (e.g. chemicals, transport) failed to show any association with multiple sclerosis mortality, but it was found that group H, consisting

of seaside resorts, has such an association for reasons which probably have nothing to do with industry.

In Table 3 the deaths from multiple sclerosis in 1958–67 for each sex are compared with the calculated numbers obtained by applying the national rates to the estimated populations in each of the 82 county boroughs, and within each industrial group the towns are arranged alphabetically. The old textile towns in group A employed in 1951 large proportions of their workers, both men and women, in cotton and wool mills, 7 being in Lancashire, 5 in Yorkshire and 1 in Cheshire. In 11 of the 13 the deaths in the 10 years exceeded the number expected amongst males (with comparative mortality ratios (CMR) ranging from 110 to 232 per 100) and in 11 of the towns this was true also of females (CMR's 117–247). In 5 towns the excess

Table 4. *Frequency of actual/expected (A/E) values above and below* 100 *for multiple sclerosis mortality in county boroughs*, 1958–67

Group by industry†	No. in group	Males: No. with 100A/E		Males: Significance		Females: No. with 100A/E		Females: Significance	
		< 100	⩾ 100	χ^2	P	< 100	⩾ 100	χ^2	P
A	13	2	11	5·56(+)	0·02	2	11	4·61(+)	0·025
B	5	2	3			2	3		
C	3	2	1			3	0		
D	14	9	5	1·14(−)	0·29	10	4	1·51(−)	0·22
E	12	6	6	0		6	6	0	
F	8	6	2	2·0(−)	0·17	6	2	2·53(−)	0·12
G	19	12	7	1·32(−)	0·26	8	11	1·90(−)	0·23
H	8	2	6	2·0(+)	0·17	2	6	2·53(+)	0·11

† For explanation of groups see Table 3.

in the two sexes together was significant ($P < 0·05$), Burnley and Stockport showing the most notable excess. Every town registered an excess over expectation either in males or females (see also footnote to Table).

Group B consisted of five towns having at least 5 % but less than 10 % of their populations working in textiles but 10 % or more in metals or other heavy industry, and of these three show an excess over expected mortality, statistically significant in Manchester and Salford. Combining groups A and B, there were 266 deaths of males from multiple sclerosis compared with 194 expected (CMR 137) and in females there were 354 compared with 254 (CMR 139).

Contrasting with the above, the three towns in group C with 10 % or more engaged in manufacture of the newer fabrics from man-made fibres had 96 deaths compared with 129 expected, a large deficiency being apparent for both males and females.

The next groups, D–F, consisting of towns with less than 5 % working in textiles and 10 % or more in the other heavy industries, have total deaths of males 106, 135, 134, all below expectation (CMR's 96, 98, 91) and of females 283, 190, 192, also below the expected numbers (CMR's 91, 89, 83), with only two towns, Sheffield and Newcastle-on-Tyne, showing a significant excess. Sheffield has a high proportion

of people engaged in manufacture of miscellaneous metal goods such as cutlery (in Order VIII), matched only by Warrington, Smethwick and West Bromwich.

Group G consists of 19 inland towns with less than 10 % in the heavy industries, registering 131 deaths of males (CMR 89) and 217 of females (CMR 91), and three of them show significant excess over expectation, namely Burton-on-Trent, Exeter and Great Yarmouth. The first of these is remarkable in that 23 % of its working population are engaged in brewing and manufacture of drinks (Order XII, 163–8), a proportion some ten times as great as in any other county borough. Great Yarmouth has 6½ % engaged in making wireless apparatus (Order VI, part), the largest proportion in any county borough, Southend-on-Sea in group H ranking next with 5½ % so occupied.

Table 5. *Increase or decrease in multiple sclerosis mortality from* 1958–62 *to* 1963–7 *in the county boroughs*

		Males				Females			
		No. of deaths				No. of deaths			
Groups of towns		1958–62	1963–7	Rise or fall	%	1958–62	1963–7	Rise or fall	%
Textiles									
Cotton, wool	A	77	69	−8	−12·4	132	87	−45	−23.7
	B	57	63	+6		69	66	−3	
Rayon, etc.	C	15	24	+9	+60	23	34	+11	+48
Other towns	D–H	371	314	−57	−15	541	467	−74	−14

Group H comprises eight seaside resorts and is the only group other than the cotton and wool textile towns (A, B) to show an average excess of deaths over the numbers expected (CMR's 127 for males and 122 for females). The reason for this is probably the choice by some chronic invalids with multiple sclerosis to move to these resorts, where they die of the disease. Two of the towns show a large excess of mortality in each sex, namely Brighton and Eastbourne.

Table 4 shows clearly the contrast between the cotton and wool towns (A, B) and other groups in their association with multiple sclerosis. Out of 18 towns only 4 for each sex had mortality ratios below 100, and the χ^2 test for such a distribution produced probabilities of 0·02 for males and 0·025 for females, both significant. All of the other groups produced negative or zero associations with mortality, except the seaside resorts (H), for which the relation was insignificantly positive, with $P > 0{\cdot}1$ for each sex.

The contrast in Table 4 between groups A–B and C–G could result if work over long periods in cotton and wool mills, with their peculiar noise and vibration, was a factor in initiating multiple sclerosis in some of the people of both sexes who were exposed to those conditions of work. The absence of any suggestion of such an effect arising in more than an occasional town with heavy metal and machinery production suggests that there is a special kind of noise and vibration in the cotton and wool factories which affects the central nervous system, but that this is not present in the factories producing rayon fabrics. This hypothesis is not yet supported by other evidence but the indications are strong enough to suggest that workers in

textile mills who show early symptoms of multiple sclerosis should be moved as a precaution to other kinds of work.

In view of the progressive changes which have taken place in the textile industry since the war, the deaths in 1958–62 have been compared with those in the next 5 years, 1963–7, in Table 5.

In the cotton and wool towns (A, B) deaths of males scarcely changed, but those of females fell from 201 to 153, a reduction for females of about 24 %. In the towns with rayon factories (C) the deaths of males rose from 15 to 24 and of females from 23 to 34, so the mortality of females in the textile towns seems to have followed the shift in numbers working from the old to the new processes, and seems to support the supposition that there was a smaller risk in the new than in the old. In all the other groups there was a total fall of deaths in males by 15 % and in females by 14 %.

Table 6. *Multiple sclerosis in Metropolitan boroughs in* 1958–64

Metropolitan boroughs	Males			Females			Both sexes areas with significant excess,	
	No. of deaths (D_1)	Expected (E_1)	Ratio $100D_1/E_1$	No. of deaths (D_2)	Expected (E_2)	Ratio $100D_2/E_2$	d^2/E	P
Battersea	2	5·1	39	13	8·1	160	—	**
Bermondsey	2	2·5	80	5	4·0	125	—	—
Bethnal Green	1	2·3	43	5	4·6	109	—	—
Camberwell	7	8·6	81	13	13·4	97	—	—
Chelsea	3	2·4	125	4	3·7	108	—	—
Deptford	2	3·4	59	—	5·3	0	—	—
Finsbury	2	1·6	125	2	2·5	80	—	—
Fulham	3	5·4	56	11	8·6	128	—	—
Greenwich	4	4·2	95	5	6·6	79	—	—
Hackney	8	8·0	100	11	12·6	79	—	—
Hammersmith	2	5·3	38	3	8·3	36	—	—
Hampstead	2	4·8	42	7	7·5	93	—	—
Holborn	1	1·0	100	2	1·6	125	—	—
Islington	9	11·0	82	8	17·3	46	—	—
Kensington	1	8·3	12	16	13·1	122	—	—
Lambeth	17	11·7	143	23	18·3	126	(3·3)	0·06
Lewisham	12	10·9	110	11	17·1	64	—	—
Paddington	4	5·5	73	7	8·6	81	—	—
Poplar	2	5·6	36	3	8·7	34	—	—
St Marylebone	3	3·4	88	8	5·4	88	—	—
St Pancras	7	6·2	113	8	5·7	140	—	—
Shoreditch	1	2·8	36	2	3·1	65	—	—
Southwark	1	4·5	11	6	6·7	89	—	—
Stepney	2	4·5	44	4	7·1	56	—	—
Stoke Newington	3	2·5	120	5	4·0	125	—	—
Wandsworth	29	16·8	163	82	26·4	311	10·6	0·001
Westminster	4	4·2	95	7	6·6	106	—	—
Woolwich	2	7·1	28	6	11·2	54	—	—
City of London	—	—	—	—	—	—	—	—
London Administrative County	137	156·3	88	280	248·7	113	—	—
Total A.C. without Wandsworth	108	139·5	72	198	222·3	89	—	—

** For females, $d^2/E = 3·0$, $P = 0·09$.

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Table 7. *Multiple sclerosis in administrative counties in* 1958–67

Administrative county outside county boroughs	Males			Females			Both sexes, areas with significant excess	
	No. of deaths (D_1)	Expected (E_1)	Ratio $100D_1/E_1$	No. of deaths (D_2)	Expected (E_2)	Ratio $100D_2/E_2$	d^2/E	P
Bedfordshire	30	23·3	129	41	36·6	112	—	—
Berkshire	23	37·7	61	45	43·6	103	—	—
Buckinghamshire	22	34·2	70	32	53·7	60	—	—
Cambridge and Ely	10	19·6	51	26	30·0	87	—	—
Cheshire	82	65·2	120	122	102·4	119	7·3	< 0·01
Cornwall	29	23·7	122	60	36·7	163	13·5	< 0·001
Cumberland	11	15·5	73	21	24·3	87	—	—
Derby	41	52·7	78	78	82·7	73	—	—
Devon	45	36·8	122	63	58·2	108	—	—
Dorset	22	22·2	99	30	34·9	87	—	—
Durham	64	67·1	75	71	105·4	86	—	—
Essex	125	112·5	111	110	76·7	143	11·6	< 0·001
Gloucester	30	38·9	77	60	61·1	98	—	—
Hampshire	54	65·8	82	113	103·3	109	—	—
Hereford	5	9·3	54	12	14·5	83	—	—
Hertford	48	57·9	83	85	91·0	93	—	—
Huntingdon and Peterborough	7	11·2	62	15	17·6	85	—	—
Kent	108	107·6	101	215	169·1	126	7·7	< 0·01
Lancashire	181	155·5	116	293	244·4	120	13·7	< 0·001
Leicester	29	29·5	98	9	11·4	79	—	—
Lincoln (Holland)	6	7·3	82	20	15·2	132	—	—
Lincoln (Kesteven)	14	9·7	144	31	35·9	86	—	—
Lincoln (Lindsey)	27	22·9	118	53	46·3	114	—	—
Middlesex	113	110·4	108	196	173·4	113	†	—
Norfolk	37	27·8	133	47	43·7	108	—	—
Northampton	15	20·8	72	30	32·6	92	—	—
Northumberland	45	34·1	132	54	53·6	101	—	—
Nottingham	33	41·9	78	66	65·7	100	—	—
Oxford	7	12·7	55	29	23·1	126	—	—
Rutland	3	1·8	166	0	2·8	0	—	—
Shropshire	15	21·5	70	47	43·7	108	—	—
Somerset	46	40·4	114	57	63·6	91	—	—
Stafford	49	70·1	70	58	110·1	53	—	—
Suffolk East	17	11·2	152	38	25·5	149	9·1	0·003
Suffolk West	7	9·4	74	20	14·8	135	—	—
Surrey	109	91·9	119	158	144·4	130	3·9	0·05
Sussex East	28	70·4	40	51	63·5	80	—	—
Sussex West	34	28·8	118	57	45·2	126	3·9	0·05
Warwick	58	40·6	143	72	63·8	113	6·3	0·01
Westmorland	5	5·6	89	7	8·7	79	—	—
Isle of Wight	4	6·6	61	17	10·3	165	‡	—
Wiltshire	24	30·2	80	44	47·5	93	—	—
Worcester	25	31·3	80	48	49·2	98	—	—
Yorkshire, E. Riding	18	16·1	112	37	25·3	145	4·5	0·04
Yorkshire, N. Riding	17	28·5	60	41	44·8	91	—	—
Yorkshire, W. Riding	123	113·8	108	175	178·8	98	—	—

† For females $d^2/E = 2·9$. ‡ For females $d^2/E = 10·4$.

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Table 7 (*cont.*)

Administrative county outside county boroughs	Males			Females			Both sexes, areas with significant excess	
	No. of deaths (D_1)	Expected (E_1)	Ratio $100D_1/E_1$	No. of deaths (D_2)	Expected (E_2)	Ratio $100D_2/E_2$	d^2/E	P
Anglesey	6	3·7	162	6	5·5	91	—	—
Brecknock	2	3·7	51	5	16·1	31	—	—
Caernarvon	13	8·5	153	103	13·3	75	—	—
Cardigan	6	3·7	162	7	5·9	119	—	—
Carmarthen	11	11·7	94	7	16·4	43	—	—
Denbighshire	10	12·1	83	15	19·0	79	—	—
Flintshire	28	10·6	264	17	16·6	102	11·6	< 0·001
Glamorgan	38	52·6	72	63	83·7	75	—	—
Merioneth	2	2·7	74	2	4·3	47	—	—
Monmouth	13	23·6	55	23	37·1	62	—	—
Montgomery	3	3·0	100	0	4·8	0	—	—
Pembroke	9	6·2	142	7	9·8	72	—	—
Radnorshire	1	1·3	77	2	2·1	95	—	—

MULTIPLE SCLEROSIS IN ADMINISTRATIVE COUNTIES AND METROPOLITAN BOROUGHS

Until 1964 London County comprised 29 metropolitan boroughs and the city, so Table 6 shows the distribution of deaths in the various divisions from 1958, when multiple sclerosis was first identified in the Registrar General's Abbreviated List of causes of death, to 1964, when the parts of Greater London were redefined. The format of the Table is the same as in Table 3. In the whole area during the 7 years there were 137 deaths of males compared with 156 expected from national rates, giving a CMR of 88 (not standardized for age variations in the populations), and there were 280 deaths of females compared with 249 (CMR 113). The crude ratio of female to male deaths was 2·04, compared with 1·41 in the county boroughs.

In the borough of Wandsworth 111 deaths were recorded by the Registrar General compared with only 43 expected, a highly significant excess ($P < 0·001$). In Lambeth, with 40 deaths compared with 30 expected, the excess was just below the conventional level of significance, and in Battersea this was true for females. No other borough showed any remarkable excess over expectation. The very high rate in Wandsworth seems to be partly accounted for by the presence in the borough of the Royal Hospital and Home for Incurables, which takes patients resident in other districts with chronic disease such as multiple sclerosis, who may then die at the institution after a long stay and be counted in the statistics as residents of Wandsworth. This may be the main factor increasing the death-rates in that borough, but it is curious that the three boroughs with high rates contiguous with Middlesex, Croydon and Surrey are also exposed to the maximum continuous noise of aircraft arriving at and leaving the London airports. Excluding Wandsworth, because of its special hospital, the numbers of deaths in the area defined above, with Lambeth and Battersea, were 257 of males and 429 of females, giving CMR's 108 and 115, compared with only 72 and 89 in London County except

Wandsworth. If Wandsworth is included these become 88 and 112. As will be seen in considering Table 7, however, the four counties of West Sussex, Kent, Essex and East Suffolk, which are affected, though in lesser degree, by aeroplane noise from military training activities, have just as high mortality rates, and this lends doubtful support to the hypothesis that noise is the important factor.

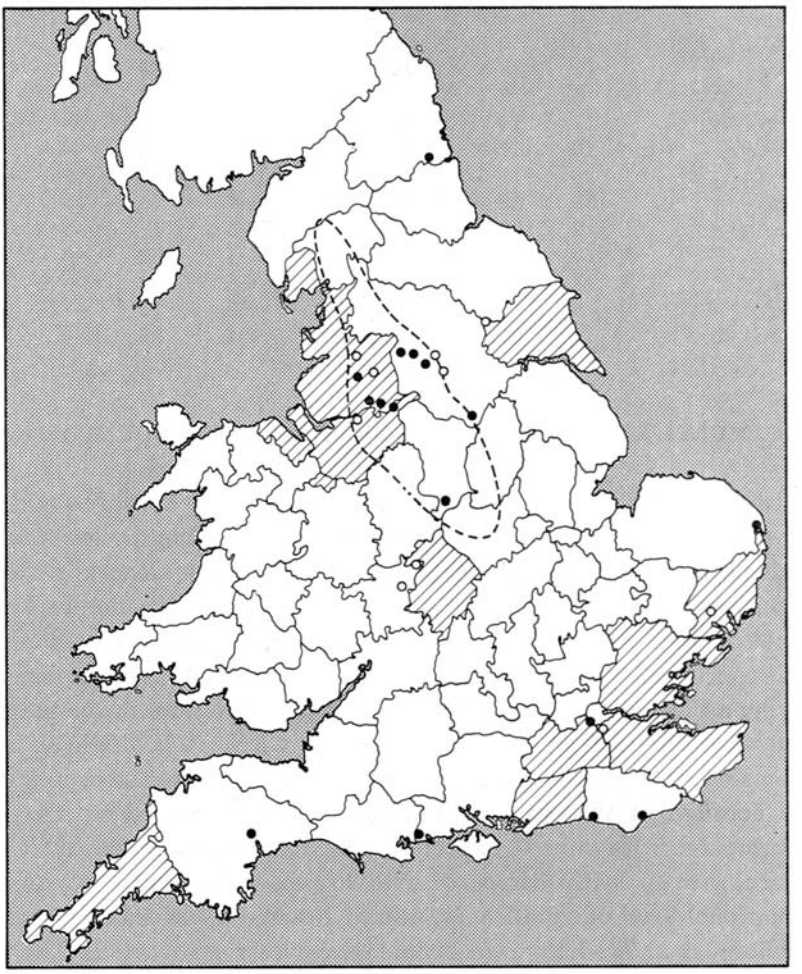

Fig. 1. Multiple sclerosis in 1958–67. ●, County boroughs with significant excess ($P < 0{\cdot}05$). ▨, Administrative counties with significant excess. ○, County boroughs with excess for one sex ($P < 0{\cdot}10$). – – –, Boundary of area with daily sunshine below $3\frac{1}{2}$ hr.

Table 7 shows the deaths in 1958–67 in the other 59 administrative counties excluding county boroughs. Those with significant excess over expectation at the conventional level ($P < 0{\cdot}05$) in the sexes together were Lancashire, East Riding and Cheshire in the north with Flintshire in North Wales; Surrey, West Sussex, Cornwall and Kent in the south; and Essex, East Suffolk and Warwick elsewhere. Middlesex gave a rate just below the significance limit for females and the Isle of

Wight gave a highly significant excess for females. Fig. 1 depicts the county boroughs and counties with high mortality.

In view of the statistical relationship with latitude in North America and Australia and presumed relation with amount of solar radiation, the distribution of the mean annual hours of bright sunshine during years 1931–60 as recorded by the Meteorological Office (1963) has been examined. In Fig. 1 the area enclosed by the broken line represents approximately the part of England where less than $3\frac{1}{2}$ hr. per day of bright sunshine was registered as the 30-year average. Out of the 20 county boroughs located in this area with lowest sunshine 14 have notably high mortality from multiple sclerosis. The area with over $3\frac{1}{2}$ hr. but less than 4 hr.

Table 8. *Multiple sclerosis in hospital regions*, 1963–7

	Males			Females		
Hospital region	No. of deaths	Mean annual rate	Ratio to national	No. of deaths	Mean annual rate	Ratio to national
Manchester	212	19·5	140	299	23·8	119
Metropolitan S.W.	123	15·6	112	217	25·4	127
South Western	107	16·0	115	169	22·0	110
Leeds	113	15·0	108	179	21·9	109
Wessex	70	15·2	109	106	21·8	109
Sheffield	161	14·3	103	213	18·6	93
East Anglia	48	12·4	89	95	23·4	117
Metropolitan S.E.	106	13·0	93	193	21·7	108
Metropolitan N.E.	104	13·3	96	178	20·9	104
Metropolitan N.W.	138	13·5	97	211	19·0	95
Liverpool	67	12·6	90	102	17·5	87
Newcastle-on-Tyne	95	12·4	89	128	16·4	82
Birmingham	147	12·1	88	206	16·4	82
Welsh	76	12·6	90	102	14·9	75
Oxford	85	8·0	57	74	16·2	81
England and Wales	1,614	13·93	100	2,452	20·00	100

average covered most of the north-east of England, including the high-mortality localities of East Riding and Newcastle-on-Tyne. In contrast, most of the south-east of England and south coast recorded averages over $4\frac{1}{2}$ hr. per day but nevertheless included some counties with high mortality, as already noted. Table 8 shows the distribution in 1963–7 of mortality according to sex in the Hospital Regions which incorporate all classes of area, urban and rural.

Supposing that noise and vibration of particular kinds such as textile machinery and aircraft is one factor in the aetiology of multiple sclerosis and lack of solar radiation and warmth is another, the workers in the northern textile towns would have been exposed to both factors, whilst the south-eastern area exposed to the excessive air-traffic noise would suffer from the noise factor with the effects offset by about 1 hr. per day more sunshine than in the north. This would be consistent with the high death-rates in Manchester and Leeds Hospital regions and in the

South-West Metropolitan region (shown in Table 8), but it would leave unexplained the high rate in Cornwall.

It must be emphasized that the hypothesis that vibratory noise is a factor in causation is purely speculative and is not supported at present by any other evidence.

MULTIPLE SCLEROSIS DEATH-RATES IN 30 COUNTRIES IN 1951–60

The World Health Organization (1966) published details by sex and age in years from 1951 for 30 countries where the information was available, and in Table 9 mean annual death-rates have been calculated at ages 25–44, 45–64, 65–74 for each sex. There are 20 countries in Europe with age distinction and 2 without, and 8

Table 9. *Mean annual death-rates from multiple sclerosis per million living in* 1951–60 *or years specified in* 22 *countries of Europe and* 8 *other countries*

Countries (Europe, ranked in order of mean annual rate)†	Males				Females				Both sexes	
	All ages	25–44	45–64	65–74	All ages	25–44	45–64	65–74	Mean rate, all ages	Ratio *F/M* rates
Europe										
Scotland	27·0	25	66	65	35·0	36	80	59	31·0	1·33
Northern Ireland	23·5	26	66	52	35·0	41	87	59	29·3	1·49
Ireland	26·5	—	—	—	27·5	—	—	—	27·0	1·04
Belgium (1)	27·0	18	42	57	22·0	18	39	49	24·5	0·81
Switzerland	17·0	15	39	38	30·5	29	69	51	23·8	1·79
German F.R. (2)	19·0	16	40	38	25·0	25	47	40	22·0	1·32
Austria (1)	16·0	6	29	38	29·0	20	58	43	21·5	1·83
Denmark	20·5	21	49	45	22·0	25	52	32	21·3	1·07
Czechoslovakia (3)	17·7	14	44	43	23·3	25	53	39	20·5	1·31
England and Wales	15·0	15	33	29	22·0	22	48	32	18·5	1·47
Netherlands	15·5	18	39	41	21·0	23	55	39	18·3	1·35
Norway	16·0	16	36	41	16·5	17	34	36	16·3	1·03
Hungary (3)	13·7	12	34	39	14·7	13	27	31	14·2	1·07
Sweden	11·0	12	6	16	13·0	14	27	16	12·0	1·18
Portugal	14·0	—	—	—	10·0	—	—	—	12·0	0·70
Poland (3)	10·7	11	42	66	11·7	12	19	59	11·2	1·07
France (4)	8·0	7	17	21	12·0	12	25	22	10·0	1·50
Finland	10·0	10	22	43	9·0	8	16	33	9·5	0·90
Italy	6·5	5	13	26	7·0	6	14	16	6·8	1·08
Roumania (3)	5·3	6	33	10	6·7	8	11	15	6·0	1·26
Greece (3)	2·7	4	4	9	2·7	2	7	5	2·7	1·00
Bulgaria (3)	2·7	3	7	4	2·3	3	5	2	2·5	0·85
Other countries										
U.S.A.	9·0	7	19	27	9·0	10	21	21	8·5	1·12
Canada	10·0	10	23	34	11·0	15	27	25	10·5	1·10
Iceland	3·0	—	—	—	10·0	—	—	—	6·5	3·33
Israel	5·0	6	14	11	4·0	4	14	4	4·5	0·80
Japan	1·0	0	2	5	0·5	1	1	3	0·7	0·50
Australia	5·5	4	15	15	8·0	6	19	22	6·8	1·45
New Zealand	7·5	6	22	27	12·0	11	34	31	9·8	1·60
Venezuela	0·5	0	3	11	1·0	2	2	1	0·75	2·00

† (1) 1956–60, (2) 1952–60, (3) 1961–3, (4) 1956–63.

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other countries, giving 30 in all with crude rates at all ages for each sex. In the last columns are given the mean crude rates without age distinction and the ratio of female to male rate. The European countries are ranked in order of the rates per million persons, which range from 31·0 in Scotland to 2·5 in Bulgaria.

Table 10. *Countries of Europe, and others, ranked according to latitude, with longitude, population density and (where data were available) mean annual consumption of total fuel, tea and coffee*

Countries (Europe ranked in order of latitude of capital	Capital city		Population density	Annual consumption per capita			Multiple sclerosis death-rate (Table 9)
	Lat.	Long.		Total fuel, 1955–8	Coffee, 1965–6	Tea, 1965–6	
Europe, Iceland, Israel							
Iceland	65	22° W.	3	—	—	—	6·5
Finland	61	25° E.	34	1147	10·2	0·40	9·5
Norway	60	11° E.	1	1504	9·6	0·29	16·3
Sweden	59	15° E.	46	2709	12·9	0·46	12·0
Scotland	56	3° W.	171	—	—	—	31·0
Denmark	55	13° E.	257	2478	11·5	0·70	21·3
Northern Ireland	54	6° W.	261	—	—	—	29·3
Ireland	53	6° W.	49	—	0·2	9·37	27·0
Netherlands	52	5° E.	796	2451	7·1	1·85	18·3
Poland	52	21° E.	206	—	—	—	11·2
England and Wales	51	0	860	—	—	—	18·5
United Kingdom				4872	1·6	9·66	(20·0)
Belgium	51	4° E.	724	3528	—	—	24·5
German F.R.	51	12° E.	502	3265	4·9	0·33	22·0
Czechoslovakia	50	15° E.	246	—	—	—	20·5
Austria	49	16° E.	214	1637	2·8	0·24	21·5
France	49	2° E.	190	1288	4·9	1·19	10·0
Switzerland	47	7° E.	291	1296	7·1	0·51	23·8
Hungary	45	19° E.	107	—	—	—	14·2
Roumania	44	16° E.	191	—	—	—	6·0
Italy	42	12° E.	406	615	2·4	0·10	6·8
Bulgaria	42	15° E.	164	—	—	—	2·5
Greece	38	23° E.	148	—	—	—	2·7
Israel	32	35° E.	196	—	2·5	1·40	4·5
North America and Japan							
U.S.A.	41	(73° W.)	550	5428	7·0	0·73	8·5
Canada	50	(74° W.)	4	4298	3·9	2·44	10·5
Japan	35	(140° E.)	605	770	0·5	—	0·7
Mean	49	10° E.	259	2990	5·33	1·36	14·05
No. of countries	26	23	26	15	16	15	26

(Figures in parentheses are not included in the means.)

The male rates for early death at 25–44 rank rather differently from the order in the table; thus Belgium moves down from 3rd to 4th place and Austria from 6th to 18th, whilst Denmark moves up from 7th to 3rd, Netherlands from 10th to 4th and Norway from 11th to 5th. In Denmark, Norway and Holland deaths of males evidently tend to occur at an earlier age, but this does not apply to females.

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Scotland and Northern Ireland rank first or second in each sex–age group, whilst Canada and U.S.A. rank about 15th at all ages and also at early ages.

For the sex ratio of female to male rates at all ages, values over 1·5 appear in Iceland, Austria, Switzerland and New Zealand, and the lowest values, below 1·0, in Finland, Belgium, Portugal, Bulgaria, Israel and Japan.

In Table 10 the European countries and Israel are ranked according to the geographical latitude of their capital cities, ranging from Iceland (65°) to Israel (32°), and it is apparent that the multiple sclerosis death-rate (repeated in the final column) tends to fall on moving farther south. The correlation with latitude is + 0·43 for males and + 0·50 for females. There is also a relation with longitude of the capital cities, the death-rates tending to fall as the degrees East of Greenwich increase, giving correlations of − 0·29 for males and − 0·34 for females, as shown in Table 11.

Table 11. *Correlation between multiple sclerosis death-rates in countries and climatological and environmental factors*

Factors in Table 10	No. of countries	Correlation with death-rate in Table 7	
		Males	Females
Latitude of capital city	26	+ 0·430	+ 0·500
Longitude of capital city	23	− 0·294	− 0·337
Population density	26	+ 0·374	+ 0·351
Fuel consumption	15	+ 0·144	—
Tea consumption	15	+ 0·340	+ 0·360
Coffee consumption	16	—	+ 0·126

Death-rates exceeding 18 per million occur in a region extending from the United Kingdom, Ireland, the Netherlands, Denmark and West Germany (lat. 51–56°, long. 6° W.–14° E.), to Switzerland, Austria and Czechoslovakia (lat. 46–50°, long. 7–16° E.). Rates below 18 occur in countries to the north of this area – Norway, Sweden, Finland and Iceland (lat. 56–65°, long. 22° W.–15° E.) – and to the south and south-east of it, namely France (lat. 46–50°, long. 2° E.), Italy, Bulgaria, Roumania, Hungary, Poland (lat. 41–45°, long. 12–21° E.) and Portugal, Greece and Israel (lat. 31–40°, long. 9° W.–35° E.). Though sunshine records are lacking for these countries, the average length of daylight certainly increases down the table from Britain and Scandinavia to Greece, consonant with the hypothesis that lack of solar radiation is a factor in causation.

The correlation with longitude indicates, however, that the climatic connexion with multiple sclerosis is not a simple one. It appears that the mean annual air temperature, which depends on extent and altitude of the land mass, distance from the ocean and prevailing winds, is also a factor of importance. The countries with death-rates exceeding 18 per million correspond approximately with an area bounded by the isotherms of 45° and 55° F. and the meridians of longitude between 10° W. and 16° E. This extends from Britain across western Europe in a south-easterly direction, and although it lies between the lines of latitude at 60° and 40° its axis is not parallel with those lines. North and south of the high mortality

wedge, and to the east of its termination, the death-rates become much lower. It is possible that the lower rates in the Balkan countries east of the 16th meridian may be due in part to less complete recognition of the disease on death certificates.

Table 10 gives data for most of the countries for population density per square mile and annual consumption per person of fuel (coal and oil), coffee and tea. Table 11 shows that population density correlates with multiple sclerosis mortality to the extent of +0·37 for males and +0·35 for females, and this might result from some effects of one or more urbanization factors such as noise. Fuel consumption per person has no appreciable relation with male mortality. Tea consumption correlations are +0·34 for males and +0·36 for females, but coffee consumption shows no association with the death-rate.

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