

# Multiple sclerosis in the Faroe Islands

## 7. Results of a case control questionnaire with multiple controls

Kurtzke JF, Hyllested K, Arbuckle JD, Brønnum-Hansen H, Wallin MT, Heltberg A, Jacobsen H, Olsen Á, Eriksen LS. Multiple sclerosis in the Faroe Islands. 7. Results of a case control questionnaire with multiple controls. *Acta Neurol Scand* 1997; 96: 149–157. © Munksgaard 1997.

Detailed questionnaires were completed in 1978–79 by 23 of the 28 then known resident Faroese multiple sclerosis (MS) patients and 127 controls. These controls were divided into 69 Group A (patient sibs and other relatives), 37 Group B (matched neighbor controls, their spouses and sibs, plus patient's spouse), and 21 Group C (distant matched controls, spouses, relatives living where MS patients never resided and British troops were not encamped during the war). No differences between cases and controls were found for education, occupation, types of residence, bathing, sanitary or drinking facilities, and nature of house construction or heating. Detailed dietary histories, available for half the subjects, revealed no difference, cases versus controls, for four age periods between age 0 and 30 years, and for 16 specified foodstuffs. Animal exposures showed overall no consistent differences by location or type of animal. There was a tendency to greater exposure to British troops during the war for cases versus Groups A and B, but this did not attain statistical significance. Vaccinations for smallpox, tetanus and diphtheria were less common in the MS; no difference was found for other vaccinations. Except for a relative deficit in the cases for rubella and (insignificantly) for measles, mumps and chicken pox, reported illnesses were equally common among all groups. Operations, hospitalizations and injuries did not differentiate the groups, nor did age at menarche for women. Neurologic symptoms were significantly more common in the cases than in the controls.

**J. F. Kurtzke<sup>1</sup>, K. Hyllested<sup>2</sup>,  
J. D. Arbuckle<sup>3</sup>, H. Brønnum-  
Hansen<sup>4</sup>, M. T. Wallin<sup>1</sup>,  
A. Heltberg<sup>5</sup>, H. Jacobsen<sup>6</sup>,  
Á. Olsen<sup>7</sup>, L. S. Eriksen<sup>4</sup>**

<sup>1</sup>Veterans Affairs Medical Center and Georgetown University, Washington, DC, <sup>2</sup>Danish MS Registry, Copenhagen, Denmark, <sup>3</sup>Whitinsville, MA, <sup>4</sup>The Danish Institute for Clinical Epidemiology, Copenhagen, Denmark, <sup>5</sup>Roskilde Hospital, Roskilde, Denmark, <sup>6</sup>Faroese Nursing Association, Tórshavn, Faroe Islands, <sup>7</sup>The National Hospital, Tórshavn, Faroe Islands

Key words: multiple sclerosis; risk factors; case control questionnaires; Faroe Islands

John F. Kurtzke, MD, Neurology Service, Route #127, VA Medical Center, Washington, DC, 20422, USA

Accepted for publication April 20, 1997

The occurrence of multiple sclerosis (MS) in the Faroe Islands as successive epidemics beginning in 1943 has been described elsewhere (1–4). We attributed the introduction of the disorder to occupation of the Faroes by British troops for 5 years during World War II. In our view, the British introduced an unknown infection, which we have called the primary MS affection (PMSA), to the susceptible part of the exposed Faroese population cohort, those aged 11–45 years in 1941. Part of this affected cohort transmitted PMSA to the next cohort of Faroese formed by those attaining age 11 during the interval when the first cohort was transmissible. The second cohort in like manner transmitted PMSA to a third, and the third cohort to a fourth. Clinical neurologic MS (CNMS) is considered the late rare result of infection with PMSA. PMSA is transmissible; CNMS is not.

In order to define characteristics of the patient with CNMS, an extensive questionnaire was administered and blood drawn for serologic tests and HLA typing in 1978–1979. This paper reports the results of analyses of the questionnaire.

### Methods

Table 1 displays the subject groups who had questionnaires administered (Q), blood drawn for HLA and other blood group typing (B), and serum therefrom processed for antibody testing (S). Blood grouping data have been presented (5). Serologic results will follow separately. Questionnaires were completed by 15 of the 17 living MS patients then known to us and by knowledgeable relatives of 8 of the 11 patients then dead; 2 of these 3 latter deceased had had questionnaires too incomplete to

Table 1. Faroese case-control series 1978–1979. Subject groups and data resources (number of subjects)

Group number	Subject group <sup>a</sup>	Data resources <sup>b</sup>					Total			
		QSB	Q	QB	SB	B	Q	S	B	All
1	Patients	12	8	3	–	–	23	12	15	23
2	Patient spouses	8	4	–	3	–	12	11	11	15
3	Patient sibs	24	39	2	2	3	65	26	31	70
4	Patient children	19	20	–	3	–	39	22	22	42
5	Neighbor controls	10	3	2	1	1	15	11	14	17
6	Neighbor spouses	4	2	2	3	–	8	7	9	11
7	Neighbor sibs	1	1	–	–	–	2	1	1	2
8	Neighbor children	6	2	5	1	–	13	7	12	14
9	Distant controls	6	1	4	1	1	11	7	12	13
10	Distant spouses	6	–	–	–	–	6	6	6	6
12	Distant children	5	3	4	2	2	12	7	13	16
13	Other pt relatives	1	3	–	3	–	4	4	4	7
15	Other distant relatives	3	1	–	–	–	4	3	3	4
	Total controls	93	79	19	19	7	191	112	138	217
	Total subjects	105	87	22	19	7	214	124	153	240

<sup>a</sup> No subjects were distant controls sibs (group 11) or other neighbor relatives (group 14).

<sup>b</sup> Resources: Questionnaire (Q), Serum (S), Blood (B).

be assessed, and they were discarded. About two thirds of the patients (and their controls) were members of the first epidemic (1) and the rest of later ones (2, 3). Proportions within each control group were quite similar for each epidemic subdivision. Accordingly, in the analysis of the questionnaires, all subjects were combined, regardless of epidemic.

Type of control is largely self-apparent. A “neighbor control” was the nearest neighbor of the same sex and approximate age as the matched MS patient. “Distant controls” were subjects of the same sex and age as their MS match, but who lived in villages where there were never residents with MS and where British troops were not stationed during the war. Except for the patients, siblings and other relatives were limited to those living in the same house as the index control. Data for children of cases and controls have not been analyzed.

Comparisons between MS subjects (group 1) and controls were made after combining the latter groups into 3 categories. Group A ( $n=69$ ) consists of patients’ siblings (group 3,  $n=65$ ) plus other patient relatives (group 13,  $n=4$ ). Group B ( $n=37$ ) comprises neighbor controls, and their spouse and siblings (groups 5, 6, 7,  $n=25$ ) plus patient’s spouse (group 2,  $n=12$ ). Group C contains the distant controls, their spouses, and other relatives (groups 9, 10, 15,  $n=21$ ).

Questionnaires were constructed in English (JFK) and translated into Faroese (JA). They were mailed in advance to all subjects in order to permit collection of the required information, and were completed with the personal or telephone assistance

of Helena Jacobsen of the Faroese Nursing Association, supervised on site for much of the period by John Arbuckle (American anthropologist working on the Faroes). Each questionnaire was some 30 pages in length and required about 3 h to complete. Revised forms excluding diet were used for the last half of the study because of subject objections and very uniform responses across all groups to the diet questions. The questionnaires were available for 127 of the controls (59 male, 68 female), and for 23 of the MS cases (14 male, 9 female). Differences by sex were not significant.

Statistical testing was carried out by standard methods and by exact inference including Fishers’ exact test, Zelen exact test, homogeneity of odds ratios, and exact estimation and testing of common odds ratios (Applied software: StatXact, Version 2.02. Cytel Software Corporation, 137 Erie Street, Cambridge, MA 02139, USA). All analyses were performed by the Danish Institute for Clinical Epidemiology (HBH, LSE). Except where inappropriate (e.g., pregnancy and menarche in males, childhood ages for occupations, educational level), all blank items on the questionnaires were taken as negative responses.

## Results

*Education* – Patients vs Groups A, B, and C, alone or combined did not differ significantly in completed years of education. Excluding unknowns, about four-fifths of all subjects had 7 years of schooling. There was some tendency for MS

patients to have had more overseas schooling: 5/23 vs 12/123 (22% vs 10%), including unknowns – but see below.

**Occupation** – The major occupational groups are summarized by age-group and order in Tables 2A, 2B and 2C. Most of those with second or third occupations had fishing as the primary vocation. There is no significant difference between the MS group and any or all control groups for occupational status at any age. Only the first occupations had sufficient numbers for comparisons among the groups, but the later occupations did not appreciably alter the findings. The higher status classes of executive, services and skilled workers (O+2+3) were apparently less common among the MS group than among groups A or B: at ages 16–20 they included 23% MS vs 36% (A) and 32% (B); at ages 21–30, the respective percentages were 24, 31, and 46. Only for ages 31–40 were they equivalent at 36, 35 and 43%. But unskilled laborers (class 4) also were low among MS patients at ages 16–20: 23% vs 41% (A) and 38% (B), while the seafaring trades (class 431, 609, 407) were higher at 55% (MS) vs 34% (A) and 31% (B). At ages 21–30, unskilled workers now were higher (41%) than the sailing crafts (35%) among the MS patients. After age 20, the numbers in group C were too small for comparison.

**Residence** – Foreign residence was artifactually low for MS vs A+B, with odds ratio of 0.30. However, when the 4 Faroese with prolonged foreign residence (who had been excluded for that reason from the resident MS series (1, 2)) who were then living in the Faroes were added, the odds ratio was 1.83 (not significant). All groups showed a significant excess vs Group C.

Subjects had not considered overseas schooling (see above) as “foreign residence”. When such periods were added, the revised odds ratio for MS vs A+B was 2.55 (3.04 (significant) for group A and 1.91 (not significant) for group B). Group C still showed the significant deficit vs all others.

On the Faroes, type of residence for each of 7 life periods, birth onward, did not differ for cases vs controls. Almost all residences were single family homes. More than 4 residences were rare for any subject; about one-quarter lived in only 1 or 2 houses. The number of subjects with 3 and 4 residences per subject was roughly equal in number among all groups.

About one third of cases and controls had no bath or shower in any of their homes, and another third had such in 1 house only. Somewhat lower but similar proportions had no hot water, or hot water in only 1 house. About one quarter had no water closet (indoor sanitary plumbing) in any house. Water closets shared with other families were available for at least 1 residence for over 80% of respondents. Again, there were no apparent differences, cases vs controls.

For each residence, the type of sewage/drainage was defined as: none, pit, into the sea, septic tank, and public sewer. None or pit drainage in some houses was recorded for one-fifth, but most also recorded other modes for other houses. Into the sea, septic tank, and public sewer were similar in frequency, but as time progressed, the latter 2 systems were more frequently used by all subjects.

Public water supply was listed for some 85% of all respondents. Drinking water was almost always obtained from a spring or piped from a stream or lake. Only 2 control persons recorded a septic tank near the drinking water.

Table 2A. Occupational classes by age, order, and subject group. Ages 16–20 years (number of subjects)

Occupation Class <sup>b</sup>	1st Occupation <sup>a</sup>				2nd Occupation				3rd Occupation				4th Occupation	
	A	B	C	1	A	B	C	1	A	B	C	1	A	C
O+2	8	6	1	3	3	2	–	1	1	–	–	–	–	–
3	7	4	–	2	1	1	–	1	–	–	–	–	–	–
4\$	24	12	9	5	10	4	2	4	3	–	1	2	1	–
431	–	–	–	1	–	–	–	–	–	1	–	–	–	–
609	18	8	5	9	1	–	–	–	–	–	1	–	–	1
407	2	2	1	2	1	–	1	–	–	1	–	–	–	–
Total	59	32	16	22	16	7	3	6	4	2	2	2	1	1
N/A#	10	5	5	1	53	30	18	17	65	35	19	21	68	20
Totals	69	37	21	23	69	37	21	23	69	37	21	23	69	21

<sup>a</sup> Occupation; See text for definition of control groups A, B, C; MS Group 1.

<sup>b</sup> Occupational class: 0: Executive; 2: Services, including professional and government; 3: Skilled workers; 4: Unskilled workers; \$ excludes 431 and 407; 431: Seaman; 609: Fisherman; 407: Fishing assistant.

# Not applicable.

Table 2B. Occupational classes by age, order, and subject group. Ages 21–30 years (number of subjects)

Occupation Class <sup>b</sup>	1st Occupation <sup>a</sup>				2nd Occupation				Others	
	A	B	C	1	A	B	C	1	3 <sup>rd</sup> A	4 <sup>th</sup> A
0+2	11	9	1	1	3	2	–	–	–	–
3	5	2	–	3	2	–	–	–	1	–
4\$	16	4	3	7	5	3	2	–	–	–
431	1	–	–	1	–	–	–	–	–	1
609	18	8	4	5	2	–	–	1	1	–
407	1	1	1	–	2	–	–	–	–	1
Total	52	24	9	17	14	5	2	1	2	2
N/A#	17	13	12	6	55	32	19	22	67	67
Totals	69	37	21	23	69	37	21	23	69	69

Footnotes as in Table 2A.

Table 2C. Occupational classes by age, order, and subject group. Ages 31–40 years (number of subjects)

Occupation Class <sup>b</sup>	1st Occupation <sup>a</sup>				2nd Occupation				3rd Occupation
	A	B	C	1	A	B	C	1	A
0+2	11	8	3	2	1	–	–	–	–
3	5	1	–	2	3	–	–	–	–
4\$	13	5	2	–	1	–	1	1	1
431	1	–	–	1	–	–	–	–	–
609	13	7	2	6	–	–	–	–	–
407	2	–	–	–	–	–	–	–	–
Total	45	21	7	11	5	–	1	1	1
N/A#	24	16	14	12	64	37	20	22	68
Totals	69	37	21	23	69	37	21	23	69

Footnotes as in Table 2A.

Building material was stone (74%), old wood (73%), new wood (41%), wood siding with tar (53%), wood siding with paint (38%), corrugated iron (34%), and plastic siding (8%) with no differences by group. Roofing was most often corrugated iron, especially in newer homes, although a small proportion used asbestos and an even smaller number had grass roofs. Only some 10% had a stable/barn attached to the house. Approximately 80% had a cellar in at least 1 house.

Heating in at least 1 house was with peat for 80%, coal for 70%, kerosene for 30%, and central heating for 70% of respondents. Again, there were no differences in any of these factors for cases vs controls.

*Diet* – Detailed dietary histories were taken for 73 subjects: 62 controls and 11 MS patients. Sixteen types of food and whether diet changed were recorded and analyzed by frequency for ages 0–6, 7–15, 16–20 and 21–30. Foodstuffs included sheep

head, two types of wind-dried meat, rare meat, raw fish, two types of wind-dried fish, raw eggs, cooked eggs, unpasteurized/pasteurized (cow) milk, goat milk, sea bird eggs, potatoes, and vegetables. Wind-dried meat, age 21–30, was eaten less often regularly by the MS patients, but seasonally more so. Otherwise there was no evidence of any difference, patients vs controls. Data for 3 age groups (31–40, 41–50, 51+ years) were not analyzed.

*Animal exposure* – Although recorded for each of the separate age groups as well, animal exposure was analyzed as to presence of specified animals at any period of life in the house, in the infield (på marken), in the outfield (í haganum), at other places, or at any other location. Dog exposure in the MS group was somewhat less common (52%) than for Group A (79%), Group B (68%) or Group C (82%) in the house, and less than Group C in the infield (43% vs 76%) and outfield (30% vs 53%). There was no appreciable variation for MS patients vs Group A+B for exposure to cats, chickens, ducks, geese, wild birds, pet birds, horses, cattle, pigs, goats, sheep, rabbits, hares, mice, hamsters or others in either the house or infield. There were somewhat more MS patients with exposure to cattle (74% vs 58% for A+B) and sheep (78% vs 59% for A+B) in the outfield. Group C tended throughout to have fewer contacts with cats and more with ducks, horses, sheep, and hares than any other group. Their outfield values for cattle were 65% and for sheep 76%, thus more closely approximating the MS in the locale. Few animals were cited for any group in “other places”. For exposure at any location, the MS patients were not in excess for any animal.

*Dog exposure* – Canine distemper (CD), dogs, and sick animal exposure had previously been analyzed from this questionnaire, together with measles and CD antibody levels. As reported, the MS patients did not differ from controls in any aspect (6). Reanalysis of the supplementary questionnaire on dogs was also done here. Sleeping with a dog was rare. Sick dogs were uncommon, but equal in frequency between cases and controls (A+B+C). CD was even more rare: 1/23 MS vs 3/123 controls, and none of these were diagnosed by a veterinarian. Fourteen percent of controls and 17% of cases reported distemper in the village; 2 controls and no patients had contact with the suspect dogs. Contact with other sick animals was recorded for one-sixth of respondents, with no difference for cases vs controls.

*British troop exposure* – There were 22 patients and 115 controls born before 1945. Residence

location vs troop encampments for each year 1940–1945 did not differ for the MS cases vs controls (A+B), but (by design) did differ for MS cases vs Group C. There was no overlap in residence between these latter 2 groups. No significant difference was found for working with the British. Numbers with British quartered in the village were insignificantly in excess at 71% MS cases vs 58% for all controls (group A+B=69%; group C=0%), and with British in the subjects' home (28% MS cases, 20% all controls; A+B=22%). No difference was noted for British eating in the house. Social contact with the British was frequent (43% MS cases, 23% controls), seldom (29% MS cases, 39% controls), or never (29% MS cases, 43% controls), but this apparent difference did not attain statistical significance. Limiting comparison to the MS group vs Group A+B, frequent contact was 43% vs 28%, seldom was 29% vs 34%, and never was 29% vs 38%. However, there was no statistically significant difference in overall contact with troops for MS patients vs Group A or Group B. For MS patients vs Group C, the exact estimation of common odds ratio for any troop contact stratified by sex was 9.88 (95% CI: 1.91–72.62,  $P=0.003$ ). This result is largely due to the definition of Group C.

Receiving food, clothes or pets from the British was common in 9% of MS cases and 15% of controls, seldom in 38% of MS cases and 19% of controls, and never in 52% of MS cases and 66% of controls. Group A+B percentages were 18%, common; 19%, seldom; and 63%, never. None of these differed significantly.

Contact with the British away from the home was common for 18% of MS cases and 10% of controls, seldom for 12% of MS cases and 17% of controls, and never for 65% of MS cases and 71% of controls; Group A+B percentages were 15%, common; 17%, seldom; and 68%, never. Twenty-two percent of MS patients and 54% of controls noted that women of their village married British troops and moved away. For Group A+B, this percentage was 63%, and for Group C it was 7%. Only the Group C comparison, vs all other groups was significant. Women in the family married British troops for 41% of MS cases and 28% of controls (Group A+B=30%, and Group C=18%), none of which were significantly different.

*Age at menarche* – This ranged from 11 to 17 years, and did not differ significantly between the groups. Mean age at menarche was 13.6 years for the MS group ( $n$  known=7/9) and 14.0 for the controls ( $n$  known=60/68).

*Vaccinations* – MS cases tended to be under-vaccinated compared with controls (Table 3).

Table 3. Vaccinations reported as percentage positive (blank responses included as negatives)

Type	MS	A+B+C	A+B	C	Significance vs MS
Smallpox	78	94	94	95	+
Tetanus	35	54	55	52	±
Diphtheria	35	55	54	62	+(Group C)
Pertussis	9	19	17	29	–
Measles	4	9	8	14	–
Mumps	0	2	1	5	–
Polio	61	66	66	67	–
Typhoid	13	18	22	0	–
Yellow fever	0	5	6	0	–
Other	39	35	38	19	–
(No. subjects)	(23)	(127)	(106)	(21)	

Specifically, smallpox vaccinations were significantly higher in all control groups (A, B, and C) vs cases. Diphtheria vaccinations were significantly higher in control group C vs other groups. There was a trend of borderline significance towards higher rates of tetanus vaccinations in Groups A, B, and C vs cases. Other vaccinations were not significantly different between cases and controls.

*Illnesses* – Reported illnesses are shown in Tables 4 and 5. Reported rubella cases were significantly less common in MS cases vs Groups A and B. Rubella cases also occurred much earlier compared with all other control groups. There were fewer reported measles cases among MS patients vs all other control groups, but this did not reach statistical significance. In regards to the other listed illnesses, there was no significant differences between cases and controls.

*Operations* – Operations were equally prevalent: 61% of MS cases and 57% of controls had one operation with no obvious difference by type or age. Most were performed in Tórshavn and only a few overseas in Denmark or (rarely) elsewhere. Only 12 controls and no MS patients reported more than 1 operation, and only 1 control had 3.

*Hospitalizations* – Hospital stays for other than an operation were also equal at 80% of MS patients and 71% of controls, again with no major difference by age or diagnosis. These hospitalizations were similar to the surgical ones as to location. Some 30% of MS patients and 10% of controls had a second hospitalization, and only 2 MS cases and 1 control had a third.

*Injuries* – Injuries with either fracture or loss of consciousness were reported by 20% of cases and 11% of controls. No patients and only 1 control reported a second injury.

Table 4. Illnesses reported as percentage positive (blank responses included as negatives)

Type	MS	A+B+C	A+B	C	Significant vs MS
Scarlet fever	9	4	4	5	—
Pertussis	83	80	81	76	—
Measles	83	93	92	95	±(all)
Rubella	61	79	82	62	+(A+B)
Mumps	70	84	84	86	—
Typhoid	4	4	4	5	—
Chicken pox	52	68	69	62	?
Small pox	0	0	0	0	—
Diphtheria	0	2	2	0	—
Polio	0	0	0	0	—
Hepatitis	0	6	7	0	—
Meningitis	0	0	0	0	—
Encephalitis	4	1	1	0	—
Pulmonary TB	17	9	8	19	—
Other TB	0	2	2	0	—
Asthma	0	5	5	5	—
Hay fever	0	7	8	5	—
Urticaria	4	6	7	0	—
Hypertension	4	11	12	5	—
Diabetes	4	3	4	0	—
Arthritis	0	6	6	10	—
Allergies <sup>a</sup>	17	20	21	14	—
Take medicines	57	40	42	33	—
(No. subjects)	(23)	(127)	(106)	(21)	

<sup>a</sup> Allergies, not otherwise specified.

*Neurologic symptoms* – Neurologic symptoms, as expected, were significantly more common in the MS patients (Table 6) and rather unusual in the controls, supporting the utility of these complaints as a screening device for patients requiring evaluation as possible MS. Convulsions or seizures were reported by an unrealistically high proportion of MS patients, as we know from our own review of these patients. A positive answer here may well have included syncope or other states of altered consciousness.

## Discussion

The Faroe Islands are a group of 18 volcanic islands between Iceland and Norway in the North Atlantic Ocean. Their population is roughly 48,000 (7). British troops had both a temporal and a spatial relationship to the development of the MS epidemics in the Faroe Islands. Their occupation in the Faroes in the early 1940s was the major environmental event preceding the first point source epidemic. Moreover, all patients who developed clinical MS came from regions occupied by British troops or those that were cases in the epidemics. There have been 4 epidemics of MS since the arrival of British troops in the Faroes with 13 years separating the peak of each epidemic. The only possible

Table 5. Age at selected infections for those reporting age

Index group	No. reporting	% Affected	Age (mean)	SEM <sup>a</sup>
<b>Pertussis</b>				
MS	6	32	6.0	2.08
A+B+C	30	29	7.3	0.99
A+B	23	27	7.2	1.24
C	7	44	7.9	1.42
<b>Measles</b>				
MS	8	42	13.4	3.47
A+B+C	49	42	15.7	1.55
A+B	37	38	14.1	1.46
C	12	60	20.4	4.31
<b>Rubella</b>				
MS	4	29	6.5	1.85
A+B+C	18	18	12.8	1.40
A+B	15	17	12.5	1.63
C	3	23	14.0	2.52
<b>Mumps</b>				
MS	4	25	11.0	4.44
A+B+C	27	25	14.1	1.69
A+B	18	20	12.6	1.68
C	9	50	7.2	3.75

<sup>a</sup> Standard error of the mean.

Table excludes scarlet fever (0 MS, 1 control); typhoid fever (0 MS, 2 control); chicken pox (0 MS, 8 control; 6A+B, 2C); pulmonary TB (1 MS, 7 control; 5A+B, 2C).

explanations are that the British brought a transmissible infection or a persistent toxin. The weight of evidence favors a transmissible infection (PMSA) as a toxin cannot explain successive epidemics (3, 8).

The Faroe Islands are isolated with little immigration and out-migration and are an ideal location to study a disease like MS. Cases were identified in the various epidemics and worked-up as described previously (3) with a majority analyzed here belonging to the first MS epidemic. Control Group A was genetically related to the MS cases. Control Group B was spatially related to the cases and, therefore, at higher risk to be exposed to the PMSA. Control Group C were individuals separated from the British troops and cases and, therefore, at lower risk to contract the PMSA. The 3 control groups gave the study a more sensitive means to identify possible modes of transmission of the PMSA and an opportunity to understand genetic factors in developing MS.

Evidence from migration studies (9–11), the unique worldwide prevalence of MS (12), and the relatively low concordance rate of MS in monozygotic twins (31%) (13) are some factors giving evidence for an environmental etiology in MS. The variables examined in the questionnaire have been proposed as potential risk factors for MS (14, 15). Stepwise multiple regression analysis on

United States data have found latitude, dairy food, low temperature, and meat to be independent variables (15).

Despite MS patients having more overseas schooling, there were no differences in the amount of education between cases and controls. However, 4/5 of this largely pre-war population had only 7 years of education, a sign of the times. These data would reflect reports in Russia, where in the majority of regions, the education among MS patients was equal to the population as a whole (16). A predominance of MS patients with high education were located in the larger cities, however. Significant relations with higher education and socioeconomic status were found for MS in 2 separate US military-veteran case-control series (17, 18).

By age 31, occupational class was not significantly different between MS cases and controls for any age groups. Younger age groups showed MS patients to be well represented in seafaring trades and nonprofessional occupations. Occupational exposures and hazards have been proposed as risk factors for MS, particularly interesting is the association with physical strain to the cervical spine by lifting and twisting (19, 20).

There were no differences between MS cases and controls in regard to residence and water or sewer supply, with the exception of lower foreign residence for Group C. Both high dwelling density (21, 22) and sanitation levels (21, 23) have had mixed results as risk factors for MS. A recent Canadian study found 8 MS cases in a population of less than 75 with high soil concentrations of chromium and low concentrations of aluminium, borium, cobalt, manganese, molybdenium, and others (24). In addition, the lead concentration was fairly high in the soil, but low in the water.

In regards to diet, wind dried meat was used less regularly, but more seasonally, by the MS in the 21–30 year age group. Animal fat was initially reported by Swank et al. as a risk factor for MS (25). Peat-smoking of meat and importing of pork to the Faroe Islands has been correlated temporally to MS epidemics by Lauer (26), but our dietary and heating results do not confirm any of these findings.

There was not a statistically significant increased animal exposure in MS cases compared with controls in any location. Exposure to ducks, horses, sheep, and hares was more common in Group C. Several animal viruses can produce CNS demyelination including: coronavirus, mouse hepatitis, Theilers virus, visna virus, and CD virus. CD virus, a measles-like morbillivirus, has received the most attention as a candidate in the causation of MS (27–29). Cook et al. (30) had proposed relating CD

and MS in the Faroes based on veterinarian reports of its being brought in by British troops. Reanalysis of the supplementary questionnaire on dogs, along with checking for antibody titers to CD and measles, showed no significant correlation between villages with CD and MS residents (6).

British troops tended to have a greater, but not statistically significant, exposure to the MS cases versus controls during their WWII occupation of the islands, even after excluding the Group C subjects. Compared with Group C, MS cases were found to have significantly more contact with British troops. Previous reports have correlated troop encampment with place of residence of MS patients on the Faroes (2, 4, 31). These associations give further weight to the thesis that the PMSA was introduced to the Faroe Islands by British troops.

MS cases tended to be under-vaccinated compared with controls and had fewer reported rubella cases. While no common reportable infectious illness was found to be more common in the MS cases, a number of studies have associated common childhood infections with high MS prevalence (32–36). Increased titers of viral antibody in the serum and cerebrospinal fluid of MS patients (vs controls) have also been found particularly for measles, but also for rubella and other viruses (37).

Health care, injuries, and hormonal influences have all been proposed as potential MS risk factors (16). These variables were not significantly different here between cases and controls. Not surprisingly, neurologic complaints were more common in MS cases versus controls. While part of the disparity may have resulted from recall bias in cases, it seems much more likely that the neurologic questions serve as an adequate screening device for population-based surveys of MS. This has been demonstrated elsewhere with this same questionnaire (38).

The questionnaire method in this study allowed for a large number of variables to be evaluated in the selected sample. Because of the size and isolation of the Faroe Islands and our continued and intensive efforts at case ascertainment and definition, we believe that all cases of possible MS that came to medical attention have been identified. Virtually all of the identified cases participated in the survey. Neighborhood and family controls provided an efficient source for information. The number of cases and controls gave sufficient power to avoid a major Type II error. Two-tailed tests were expected to (and did) show significant differences with odds ratios of about 2. Such a ratio would be found if patients differed from control percentages by only some 17% or less, depending on the proportions positive. Lesser discrepancies would not seem likely to have much biologic meaning. Furthermore, the fact that most study

Table 6. Neurologic symptoms by subject group (percentage positive)

Type	MS	A+B+C	A+B	C	Significance vs MS
Limb weak/stiff	44	13	14	10	+
Incoordination	48	14	15	10	+
Gait difficulty	39	14	15	10	+
Sensory disturbance	52	13	14	10	+
Diplopia	66	13	13	10	+
Decreased vision	39	6	7	10	+
Urinary difficulty	52	6	7	10	+
Speech disturbance	21	5	6	0	+
"Seizures"	26	8	8	10	+
(No. subjects)	(23)	(127)	(106)	(21)	

characteristics were similar in each control group (A, B, C) compared with cases makes selection bias an unlikely explanation for the observed differences.

Overall, the Faroe Islands provide an ideal setting to study not only occurrence but also risk factors for a relatively uncommon disease like MS. Exposure to British troops is significantly associated with developing MS through what we believe to be an as yet unidentified infection we call PMSA. An update of the cases and a more extensive evaluation of infections using serum and further surveys may better clarify the nature of PMSA.

#### Acknowledgements

This work has been supported by the National Multiple Sclerosis Society, New York; the Department of Veterans Affairs (Neuroepidemiology Research Program, VAMC, Washington, DC); and the Danish Multiple Sclerosis Society.

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