Article abstract—Prevalence studies and investigations based on death certificates and disability assistance have shown that western Norway has been a medium-frequency area for MS. The prevalence of definite/probable MS on January 1, 1963 was 20.1/100,000. Based on the same diagnostic criteria, the prevalence of definite/probable MS had increased to 59.8/100,000 on January 1, 1983 in the county of Hordaland. We consider this increase of MS cases in the population to be due to real biologic changes, although factors affecting the figures were found. Most important was a reduction in the interval from onset to diagnosis. The rise in prevalence was also supported by an increase in the annual incidence of the disease. The incidence rate averaging 2 per 100,000 in the period 1953 to 1962 rose to 3.5 for 1968 to 1977. This marked rise in prevalence/incidence supports the concept that an exogenous factor is important in the pathogenesis of MS.

NEUROLOGY (Cleveland) 1984;34:1202-7

Western Norway, a high-risk area for multiple sclerosis:

A prevalence/incidence study in the county of Hordaland

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The prevalence of MS is related to latitude.[1,2] The geographic distribution plus the migrant data[3,4] indicate that MS is an acquired, exogenous (environmental) disease whose acquisition under ordinary circumstances may take place years before clinical onset. The concept of MS as an exogenous disease is also corroborated by recent reports by Kurtzke and collaborators, who described two probable epidemics of MS on the Faroe Islands[5] and in Iceland.[6]

Western Norway[7] and the northern part of Norway[8] are generally regarded as medium-high prevalence zones of MS. This is in contrast to the rest of the country,[9] which constitutes a high-prevalence area. Hordaland county in western Norway had an MS prevalence of approximately 20/100,000 in 1963.[7]

The aim of the present study was to examine whether this low MS prevalence in the county of Hordaland was still low or had changed since 1963. We have therefore reassayed retrospectively the prevalence on January 1, 1963 and on January 1, 1983, using the same diagnostic criteria. We have also calculated the annual incidence from 1953 through 1982.

Materials and methods. *Characteristics of the area.* The county of Hordaland (figure 1) is located in the western part of Norway between latitudes 59°30′ and 61° N. The coastline is marked by numerous deep fjords. Much of the inland consists of rocky slopes with mountains and deep valleys. The total area is 15,634 km^2, and 80% of the area is more than 150 meters above sea level.

The climate in the western part of Hordaland county is coastal with a high annual rainfall. The winters are mild, and the summers are not hot. Inland, the rainfall is less, and the differences in temperature are greater. The climate has been stable over the past 30 years.

The major economic activities are industry, commerce, shipping, agriculture, fishing, and services. Fishing has declined over the past decades.

The population on January 1, 1963 was 347,464 and on January 1, 1983 was 394,568. In 1970, 57% of the inhabitants lived in densely populated areas. The coastline is 10 times as densely populated as is the inland area. The main city is Bergen, where just above one-half of the population in the county live. The population is stable, and the Public Health Service System has been well developed for many decades.

Case selection and data collection. The primary source for MS patients was the patient files at the Department of Neurology at the University Hospital of Bergen. The department was opened in 1952 and has accurate files of every in- and outpatient referred. The clinical data on all patients with a diagnosis of MS, encephalomyelopathy, myelopathy of unknown cause, and spastic paraparesis were reassessed. The files of the Department of Ophthalmology were also scrutinized for patients with a diagnosis of MS.

For the 1983 prevalence study, we also asked the two neurologists in private practice, the regional health officers, the three local hospitals, and the nursing homes in Hordaland for information on patients who might have had MS without being

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Accepted for publication February 2, 1984.

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Fig. 1

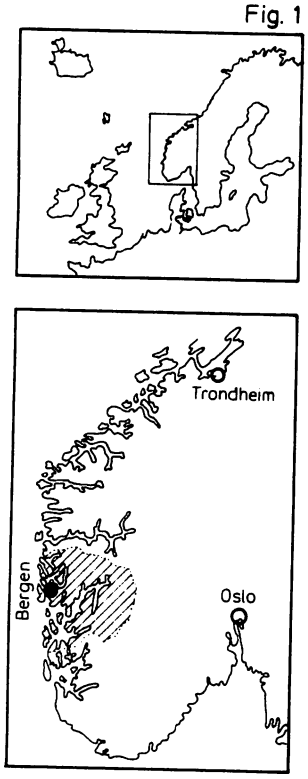

Figure 1. Area of investigation. The small map shows northern Europe, and the detail map shows a part of Norway. The county of Hordaland is hatched.

referred to the Department of Neurology in Bergen. Only one patient had not been examined by doctors at our or other neurologic departments.

For the 1963 prevalence study, we used the hospital material and the files of patients not in contact with the Department in the study by Presthus in 1960.[7] His sources were mainly the same as those indicated for the 1983 prevalence study.

The intention of this study was to trace all patients with onset of MS from 1953 through 1982, and every patient living in Hordaland with the disease from January 1, 1963.

In both prevalence studies, only patients diagnosed before prevalence day were included. Onset of disease was defined as year of onset of symptoms. Year of diagnosis of disease was defined as the year when the diagnosis of MS based on clinical criteria was made by a neurologist.

The Central Bureau of Statistics provided information on the patients' places of residence on the actual days of prevalence and on their possible dates of death. All patients were examined during the course of their illness by a clinical neurologist.

For each patient, the case history and the clinical findings were analyzed retrospectively. The patients were then grouped according to special diagnostic criteria.

Diagnostic criteria. The diagnosis of MS was based on the criteria presented by MacAlpine.[10] The same criteria were applied for the 1963 and 1983 studies. The patients were classified in definite, probable, and possible groups. We also scored the patients according to the six criteria set down by the Schumacher Committee[11] for definite MS, and concluded with "accepted" or "not accepted."

For a closer characterization, we also subclassed patients in three groups according to the clinical course: (1) remittent type, with a stable phase between relapses throughout the duration of the illness, (2) remittent-progressive type, with an initial remittent phase followed by the progressive phase, and (3) progressive type, with no stable phase, but with the illness commencing with the progressive phase.[12]

Prevalence calculation. The prevalence ratio was calculated as the number of MS cases per 100,000 inhabitants on a given date. We calculated the prevalence of MS on January 1, 1963 (study I) and on January 1, 1983 (study II). For each study, the prevalence of definite and probable MS (group A) and definite, probable, and possible MS (group B) were calculated.

We also calculated age-specific prevalence ratios. The MS patients were divided into 10-year age groups according to the age of the patients in 1963 and 1983. We then found the prevalence for each group both in 1963 and 1983 based on the total population in the same age groups.

Incidence calculation. When calculating the inci-

Table 1. Diagnostic classification of the total MS patient material and of MS patients on January 1, 1963 (study I) and on January 1, 1983 (study II)

	Total material			Study I			Study II		
	No. of pts	%	Schumacher*	No. of pts	%	Schumacher*	No. of pts	%	Schumacher*
Definite	320	75.1	317	68	78.2	68	216	72.5	214
Probable	27	6.3	17	2	2.3	2	20	6.7	12
Possible	79	18.6	0	17	19.5	0	62	20.8	0
Total	426	100.0	334	87	100.0	70	298	100.0	226

* Number of patients with a diagnosis of definite MS according to the criteria given by the Schumacher Committee.[11]

dence of MS, we excluded patients with onset of the disease outside the county. Three hundred ninety-six patients had onset of the disease when living in Hordaland. The incidence was defined as number of patients with onset of the disease in 1 year per 100,000 inhabitants.

Age-adjusted incidence rates were calculated for 5-year periods. We used the direct standardization method with the European Standard as the reference population.

Results. *Total patient material.* The total initial clinical material comprised 1,018 patients referred between 1952 and January 1, 1983. Of these, 471 were presumed to have a diagnosis of MS and had been living in Hordaland after onset of disease. Using the criteria of MacAlpine,[10] 45 of these 471 were excluded.

Of the remaining 426 patients with a diagnosis of MS, 79 were defined as possible MS, 27 as probable MS, and 320 as definite MS. Three hundred thirty-four patients fulfilled the criteria of the Schumacher Committee.[11] Table 1 presents details on the diagnostic classification in the total MS population, the prevalence group on January 1, 1963 (study I), and the prevalence group on January 1, 1983 (study II).

The 70 patients with a diagnosis of definite or probable MS in 1963 all fulfilled the criteria of the Schumacher Committee.[11] In study II, 10 patients with the diagnosis of definite or probable MS did not fulfill the Schumacher[11] criteria. (Two patients in the group of definite MS who were age 52 and 54 years, respectively, at the onset of disease, were excluded. Eight patients had only one attack of optic neuritis together with signs of long tract involvement and were classified as probable according to MacAlpine.[10])

Study I: Prevalence day January 1, 1963. Up to this date, the material comprised 84 patients with definite and probable MS (group A). When possible MS was included, the group (group B) consisted of 103 patients. Fourteen patients of group A and 16 patients of group B had died or had moved out of the county. In groups A and B, 70 and 87 patients, respectively, were living in Hordaland on the prevalence day. The calculated prevalence in group A on January 1, 1963 was 20.1/100,000 and in group B 25.0/100,000. Clinical data from study I are given in tables 2, 3, 4, and 5.

Study II: Prevalence day January 1, 1983. Up to this date, the material comprised 347 patients in group A (definite/probable) and 426 patients in group B (definite/probable/possible).

Eighty-eight patients of group A and 102 of group B had died. Twenty-three patients in group A and 26 in group B had moved out of the county.

On January 1, 1983, group A consisted of 236 patients and group B of 298 patients. The prevalence on January 1, 1983 was calculated as 59.8/100,000 for group A and as 75.5/100,000 for group B. The clinical

Table 2. Sex distribution for patients in groups A and B in study I and study II

	Study I				Study II			
	Group A		Group B		Group A		Group B	
	No.	%	No.	%	No.	%	No.	%
Females	44	62.9	51	58.6	145	61.4	185	62.1
Males	26	37.1	36	41.4	91	38.6	113	37.9
Total	70	100.0	87	100.0	236	100.0	298	100.0

Table 3. Mean age (in years) at onset of disease of patients in groups A and B in study I and study II

	Study I			Study II		
	Total	Female	Male	Total	Female	Male
Group A	29.5	29.4	29.8	30.3	30.4	30.2
Group B	31.8	31.0	32.8	31.3	31.4	31.1

Table 4. First symptom at onset of disease for patients in study I and II

	Study I				Study II			
	Group A		Group B		Group A		Group B	
	No.	%	No.	%	No.	%	No.	%
Optic neuritis	14	20.0	14	16.1	43	18.2	45	15.1
Diplopia	10	14.3	10	11.5	28	11.8	35	11.7
Other eye symptoms	4	5.7	4	4.6	19	8.0	21	7.1
Vertigo	6	8.6	6	6.9	30	12.6	38	12.6
Motor weakness	35	49.9	51	57.4	88	37.3	127	42.6
Paresthesia	14	20.0	15	17.2	72	30.5	91	30.6
Other symptoms	7	10.0	11	12.5	28	11.9	40	13.4
Total	90	128.5*	111	126.2*	308	130.3*	397	133.1*

* More than 100%, since some patients had more than one presenting symptom.

Table 5. Clinical course: Distribution and relation to age at onset for patients in study I and study II

	Study I						Study II					
	Distribution				Mean age at onset		Distribution				Mean age at onset	
	Group A		Group B		A	B	Group A		Group B		A	B
	No.	%	No.	%	Years	Years	No.	%	No.	%	Years	Years
R	20	28.6	23	26.4	27.3	28.1	128	54.2	168	56.4	28.8	29.4
R/P	40	57.1	41	47.2	28.3	28.8	80	33.9	81	27.2	29.8	30.0
P	10	14.3	23	26.4	39.1	40.9	28	11.9	49	16.4	39.1	39.7
Total	70	100.0	87	100.0	29.5	31.8	236	100.0	298	100.0	30.3	31.3

R Remittent.
R/P Remittent/progressive.
P Progressive.

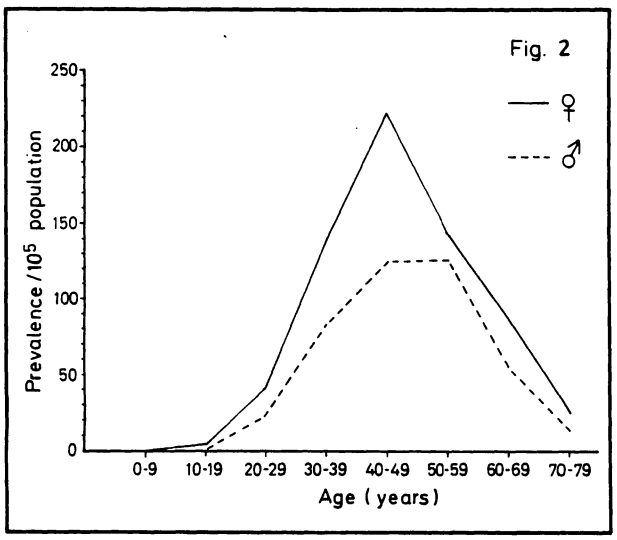

Figure 2. Age-specific prevalence ratios by sex of definite/probable MS in study II (January 1, 1983).

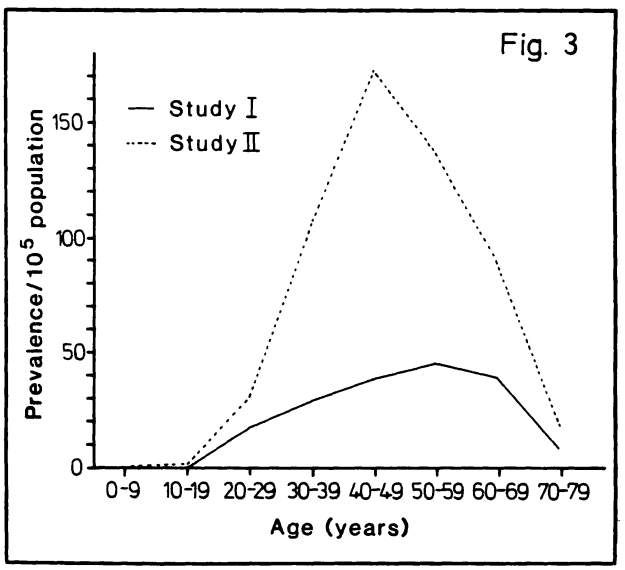

Figure 3. Age-specific prevalence ratios of definite/probable MS in Hordaland county, Norway, in study I (January 1, 1963) and in study II (January 1, 1983).

details in study II are given in tables 2, 3, 4, and 5.

The age-specific prevalence ratios by sex for definite/probable MS in study II are shown in figure 2. The patterns are similar for both sexes.

Prevalence adjustment. The mean interval of time from onset to diagnosis for group A in 1963 was 9.9 years. The corresponding mean interval in 1983 was 5.6 years. For patients diagnosed in the years 1973 to 1982, this interval was calculated as approximately 2 years. The reduction of the interval from onset to diagnosis in 1983 clearly influenced the prevalence figures. The 1963 prevalence was therefore adjusted by giving patients with an onset before this date a mean interval of 2 years. The adjusted prevalence on January 1, 1963 for group A was then 29.0/100,000.

The number of patients who had been born outside Hordaland had increased only slightly (table 6). Therefore, alterations in migration to the county cannot explain the increase in the prevalence rate.

To determine whether the rise in prevalence could be explained by a longer survival of MS patients in 1983 as compared with 1963, the age-specific prevalence ratios were calculated. Figure 3 shows that there are in fact more young patients in the 1983 cohort than there were in 1963. Accordingly, the increased prevalence in 1983 cannot be explained by MS patients living to an older age with their disease in 1983 than was the case in 1963.

The average duration of illness for group A (definite/probable) was 26.4 years in study I (1963). The figures for males and females were 26.6 and 26.0 years, respectively. In study II (1983), the average duration for definite/probable MS was 15.7 years. The average duration was 15.9 years for males and 15.6 years for females.

Table 6. Place of birth for patients in study I and study II

	Study I				Study II			
	Group A		Group B		Group A		Group B	
	No.	%	No.	%	No.	%	No.	%
Born in Hordaland	61	87.1	78	89.7	190	80.5	239	80.2
Born in western Norway (Hordaland exclusive)	5	7.1	5	5.7	26	11.0	32	10.7
Born outside western Norway	4	5.7	4	4.6	20	8.5	27	9.1
Total	70	100.0	87	100.0	236	100.0	298	100.0

Table 7. The crude incidence rates (given in parentheses) and the age-adjusted incidence of MS patients with onset from 1953 through 1982 in 5-year periods*

	Average annual incidence per 100,000 population age-adjusted† and crude incidence rates (in parentheses)				Number of patients		Mean population in the 5-year periods
	Group A		Group B		Group A	Group B	
1953-57	1.12	(1.10)	1.76	(1.71)	18	28	326,752
1958-62	2.15	(1.99)	2.34	(2.17)	34	37	340,986
1963-67	2.80	(2.47)	2.99	(2.63)	44	47	356,983
1968-72	3.49	(3.00)	4.14	(3.53)	56	66	373,844
1973-77	3.50	(3.15)	4.09	(3.66)	61	71	387,619
1978-82	1.71	(1.69)	3.21	(3.17)	33	62	391,463

* The observed number of cases and the mean population of Hordaland in these 5-year periods are also shown. The results are given for group A (definite/probable MS) and for group B (definite/probable/possible MS).
† Age adjusted by the direct standardization method with the European Standard as the reference population.

Incidence. The average age-adjusted incidence and the number of MS patients with onset from 1953 through 1982 are shown in 5-year periods in table 7. The average incidence for definite/probable MS increased from 1.12/100,000 in 1953 to 1957 to 3.50/100,000 in 1973 to 1977. In the 5-year period 1978 to 1982, the incidence was lower. The data for this period must be evaluated with some caution because of the long interval from onset to diagnosis. This may also bear some relevance for the period of 1973 to 1977.

Discussion. The prevalence of MS in the county of Hordaland in western Norway on January 1, 1963 was 20.1/100,000. This observation confirms earlier data and demonstrates that the prevalence of MS at that time was low in this county compared with the prevalence in most other parts of northern Europe.

The nonuniform distribution of MS in Norway has been the object of several investigations. Swank et al[13] carried out an incidence study for the whole of Norway between 1935 and 1948. They found a clear difference in the incidence of MS between the various parts of the country, with low figures in western and northern Norway and high figures in the rest of the country. This pattern was later supported by several prevalence studies.[7-9,14] These studies were mainly based on data obtained from hospital files. Also, in a study based on death certificates and cases of disability assistance, Westlund[15,16] discovered the same pattern.

The prevalence of MS in western Norway was assessed by Presthus.[7,14] He found that the prevalence of MS in 1960 in the county of Hordaland was 22/100,000 in the city of Bergen and 17/100,000 in the rest of the county. All published studies thus agree that the prevalence of MS in the county of Hordaland was low around 1960.

On January 1, 1983, the prevalence of MS in Hordaland was 59.8/100,000. This is a threefold rise in prevalence over a 20-year period. This increase is seen in both sexes and is mainly found in young age groups with a remittent course of disease.

In nearly all known geographic areas throughout the world that are being surveyed at repeated intervals, the prevalence has been stable or has shown a

moderate increase. This increase has been explained as a result of better case ascertainment, improved survival, and different diagnostic methods.[17-19] The exceptions are two probable epidemics on the Faroe Islands[5] and in Iceland,[6] described by Kurtzke and collaborators.

Retrospective prevalence studies are bound to contain sources of error. The case collection and the diagnostic classification are of crucial importance. In the present investigation, the diagnosis of MS in the 1963 study and in the 1983 study were built on the same clinical criteria. The methods and procedures adapted for the definition of the material for both prevalence groups are therefore identical. Better diagnostic possibilities resulting from modern supportive laboratory data should not then influence our results. The Public Health Service System, although now improved, was well developed in 1963. The clinical data for both study I and study II are well in agreement with each other and with earlier investigations.

It could be argued that a greater prevalence of MS in 1983 is an effect of a longer patient survival because of better care for chronically ill and disabled patients. If this was an important factor, the mean age would be higher in 1983 than in 1963. However, the age-specific prevalence ratios show an opposite trend. The shift to a younger dominance in the 1983 group than in the 1963 group demonstrates that a longer survival cannot contribute essentially to the rise in prevalence. This is also reflected in the findings of a decrease in the average duration of illness for definite\probable MS from 1963 to 1983.

The mean interval from onset to diagnosis has been reduced considerably during the past 20 years. The net effect of an earlier diagnosis is in itself a rise in prevalence. Our data are therefore adjusted to a corresponding interval in the 1963 material also. The adjusted 1963 prevalence of 29\100,000 is still considerably lower than the 1983 prevalence.

There were more MS patients born outside Hordaland in study II (1983) than in study I (1963). There were also relatively larger groups at risk judged by age and sex in 1983 than in 1963. These factors may also reduce the difference in prevalence, but cannot explain more than a minor correction.

The average annual incidence of the disease shows an increase that corresponds to the rise in prevalence. Therefore, the increase of MS prevalence in Hordaland from 1963 to 1983 cannot be due to variations in the clinical material, but rather seems to reflect a biologic change. A more detailed study of the increasing incidence in different subgroups is to be published in a subsequent paper.

Prevalence\incidence data show a marked increase that corroborates the idea that exogenous factors that vary over time are important in the pathogenesis of MS. Apparently these factors have shown an increasing activity in the county of Hordaland since World War II.

Acknowledgments

The authors are grateful to G. Kvåle, MD, Institute of Hygiene and Social Medicine, University of Bergen, for valuable help and advice, and to the regional health officers for assistance in tracing new patients.

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