Editorial

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Multiple Sclerosis in Latin America

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Key Words
Multiple sclerosis, geographic distribution · Latin America

Introduction

The epidemiology of multiple sclerosis (MS) has been thoroughly studied in developed countries, particularly in areas traditionally known for their high prevalence. However, there is a dearth of epidemiological information on MS from large areas of the world. It is generally accepted that MS incidence and prevalence are higher in latitudes north and south of the Equator with prevalences ranging from 80 to 300/100,000. In contrast, its prevalence in Africa, Asia and South America has been estimated around 5/100,000 [1, 2]. However, lack of adjustment of crude incidence and prevalence rates to a common standard population creates problems in the comparison and interpretation of geographic data [3]. Nonetheless, recent studies indicate an increasing risk of developing MS over time in areas such as Sardinia [4], Norway [5], and Sweden [6], as well as in countries previously considered to have low MS prevalence such as Mexico [7].

MS in Latin America

During the last decade, there has been a surge of research interest on the epidemiology of MS in Latin America. Despite some methodological shortcomings, recently published epidemiological studies begin to provide a reasonable estimate of the frequency and characteristics of MS in Latin America.

In Mexico, hospital-based and population-based studies indicate an increase in the incidence and prevalence of MS. In 1970, Alter and Olivares [8] reported a relatively low prevalence of 1.6/100,000. This study was not confirmed by community-based data. More recent studies based on referrals to a tertiary neurological center demonstrate an important increase in MS incidence [9–11]. A study in northern Mexico (25° north) found a prevalence of 13/100,000 inhabitants [9]. However, this study included only patients with social security benefits, representing 51% of the population. Other studies performed in central areas of the country have registered lower prevalences of about 5/100,000 at latitudes 16–20° north [10]. Clearly, MS has become one of the main causes of neurological consultation in Mexico. For instance, optic neuritis represents 12% of the patients referred to a specialized neuro-ophthalmology clinic [12]; about 40% of them are eventually diagnosed as having MS [12, 13]. Potential risk factors responsible for the increase in MS in Mexico include a decrease in breastfeeding for large segments of the society and an increased incidence of varicella and childhood eczema [14]. Research conducted at the National Institute of Neurology and Neurosurgery of Mexico has demonstrated activation of varicella-zoster virus during MS relapses [15], suggesting that this herpes virus could be an etiological agent of MS.

In 1999, the Latin American Committee for Treatment and Research in MS (LACTRIMS) was formally organized generating renewed interest in numerous coun-

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Multiple sclerosis in Oslo, Norway: prevalence on 1 January 1995 and incidence over a 25-year period

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The Oslo Multiple Sclerosis (MS) Registry was established in 1990, and this is the first report on the prevalence and incidence of MS in the city of Oslo, Norway. The prevalence rate of definite MS on 1 January 1995 was 120.4/105. Inclusion of patients of native Norwegian ancestry only and exclusion of non-Norwegian immigrants yielded a prevalence rate of 136.0/105. A similar prevalence rate (136.5/105) was found when patients and immigrants from the other Nordic countries (Finland, Sweden, Denmark) were included. Segregation of the native Norwegian patients according to the counties where they were born showed no significant differences except for a disproportionate increase of patients born in the inland county of Oppland. A total of 794 cases were resident in Oslo at the time of a diagnosis of definite MS in the period 1972-99. The crude average annual incidence rate for each 5-year period, between 1972 and 1996, increased significantly from 3.7/105 in the 1972-76 to 8.7/105 in the 1992-96 period. The increase was more marked in relapsing-remitting (RR) than in primary progressive disease and in female cases.

Introduction

A nation-wide survey of the prevalence of multiple sclerosis (MS) in Norway in 1948 (Swank et al., 1952) and a study based on mortality data from 1951 to 1965 (Westlund, 1970) suggested that the south-eastern part of Norway is the area with the highest MS prevalence in the country. Surveys of five out of a total of 19 counties (see Fig. 1) in Norway have since been reported. Studies of the county of Vestfold (on the west side of the Oslo Fjord) showed a prevalence rate of 61.6/105 in 1963 (Oftedal, 1965) and 86.4/105 in 1983 (Edland et al., 1996). In western Norway, the prevalence rate in Hordaland County was approximately 20/105 in 1960 (Presthus, 1960) and 59.8/105 in 1983 (Larsen et al., 1984a), and in Møre-Romsdal County it was 25.7/105 in 1961 (Presthus, 1966) and 75.4/105 in 1983 (Midgard et al., 1991). In northern Norway, the combined prevalence rate in Troms and Finmark counties was 20.6/105 in 1973 (DeGraaf, 1974), 31.5/105 in 1983 (Grønning and Mellgren, 1985) and 73.0/105 in 1993 (Grønlie et al., 2000). The prevalence rate in Gothenburg in Sweden (300 km south of Oslo, on the east coast of the Skagerrak) was 96/105 in 1988 (Svenningsson et al., 1990), and in Denmark 112/105 in 1990 (Koch-Henriksen, 1999).

In the Norwegian studies, an increase in incidence from 1953 to 1977 was concluded to have taken place in the county of Hordaland (Larsen et al., 1984b), whereas fluctuating incidence patterns were reported in Vestfold (Edland et al., 1996), Møre-Romsdal (Midgard et al., 1991) and Troms and Finmark (Grønning and Mellgren, 1985).

Oslo is at once both the capital and one of the 19 counties of Norway with 11.1% of the countrys population. The population of Oslo was 483 401 on January 1 1995 (Statistisk årbok, 1996). Since about 1970, the immigration of people of non-European (mainly African and Asian) ethnic origin

Progressive increase in incidence and prevalence of multiple sclerosis in Newcastle, Australia: a 35-year study

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J Neurol Sci. 2003 Sep 15;213(1-2):1-6
Barnett MH, Williams DB, Day S, Macaskill P, McLeod JG.
Institute of Clinical Neurosciences, Royal Prince Alfred Hospital, NSW 2006, Sydney, Australia

The prevalence of multiple sclerosis (MS) in Newcastle, Australia increased significantly between 1961 and 1981 and the incidence of the disease also increased between the decades 1950-1959 and 1971-1981.

The present study sought to determine whether there has been a further increase in the frequency of MS in the subsequent 15 years, and to examine the potential factors underlying this change.

The incidence, prevalence and clinical profile of multiple sclerosis were therefore re-examined in Newcastle, Australia in 1996 using comparable diagnostic criteria and methods to those employed in studies in the same region in 1961 and 1981.

There has been a significant progressive increase in prevalence from 19.6 to 59.1 per 100,000 population and a significant increase in incidence from 1.2 to 2.4 per 100,000 population from 1961 to 1996.

The most pronounced increase in prevalence was in females and in the age-group over 60 years, and there was also an increased incidence in females aged 20-29 years.

There was little change in the age of disease onset, but duration of disease in females had increased substantially.

The significant increase in prevalence is attributed to increased incidence, particularly in females; and to increased survival.

Although such trends in prevalence have been observed in the Northern Hemisphere, this is the first such study in the Southern Hemisphere to show a longitudinal increase in prevalence and incidence over a period of this duration.

1: J Neurol Sci. 2003 Sep 15;213(1-2):1-6. Related Articles, Links
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Progressive increase in incidence and prevalence of multiple sclerosis in Newcastle, Australia: a 35-year study.

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1: Acta Neurol Scand. 2001 Mar;103(3):153-8.

Increasing prevalence of multiple sclerosis in Finland.

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OBJECTIVES: To follow-up the prevalence trends of MS from 1983 to 1993 in western and southern Finland. MS epidemiology has been previously followed from 1964 to 1978 in these regions. The updated prevalences were correlated with incidence trends in the same period. METHODS: Age-adjusted and age-specific MS prevalence rates were calculated for cases classified by Poser's criteria. RESULTS: In the western health-care districts, Seinäjoki and Vaasa, prevalences in 1993 were 202/10(5) and 111/10(5). In the southern district Uusimaa the respective figure was 108/10(5). In Seinäjoki a significant 1.7-fold increase was found in 1993 as compared to 1983, mainly due to increased incidence. In Uusimaa a significant 1.2-fold increase in prevalence was found in the presence of stable incidence. In Vaasa prevalence was stable, although incidence was declining. CONCLUSION: The prevalence of MS is increasing in Seinäjoki and Uusimaa but not in Vaasa. Both the prevalence and incidence in Seinäjoki are now among the highest reported.

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Title Multiple sclerosis epidemiology in Sardinia: evidence for a true increasing risk.

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NLM Journal Name Acta neurologica Scandinavica.

Abstract **OBJECTIVES:** To update prevalence and incidence rates of MS among Sardinians. **MATERIALS AND METHODS:** The present work is a "spider" kind of population based survey, conducted over the interval 1968-97, on patients with MS (Poser criteria) living in the province of Sassari, Northern Sardinia (454,904 population). **RESULTS:** A crude total prevalence rate of 144.4 per 100,000, an onset-adjusted prevalence rate of 149.7 per 100,000 and an average annual incidence rate of 8.2 for the period 1993-7 were found. **CONCLUSION:** Repeated epidemiological assessments of MS in Sardinia over decades have shown that the island is at high risk for MS. The present work highlights that MS incidence in Sardinia has been increasing over time. Although a substantial and widely spread improvement in MS case ascertainment can be postulated as the reason for such observations, a comparison between our data and those recently reported from a more industrialized province in Northern Italy seems to prove an at least partially real increase in MS risk among Sardinians and favours the hypothesis of a MS "Sardinian focus" as related to its latitude.

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PAPER

Incidence (1988–97) and prevalence (1997) of multiple sclerosis in Västerbotten County in northern Sweden

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ABSTRACT

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Objective: To investigate the incidence and prevalence of multiple sclerosis in Västerbotten County in northern Sweden.

Methods: Multiple sources were used in the case identification process. Follow up interviews with clinical examinations were undertaken and, when indicated, additional paraclinical investigations were done. In this way case ascertainment was assured and supplemental clinical data were collected. The incidence rate was based on symptom onset. Onset adjusted prevalence was applied.

Results: The crude incidence rate of multiple sclerosis in 1988–97 in Västerbotten County was $5.2/10^5$ (95% confidence interval, 4.4 to 6.2): $6.7/10^5$ (6.0 to 8.3) in women and $3.7/10^5$ (2.7 to 4.9) in men. The

onset adjusted prevalence for 31 December 1997 was 154/10^5 (139 to 170): 202/10^5 (179 to 228) in women and 105/10^5 (89 to 125) in men. When compared with a previous estimate of prevalence, a yearly 2.6% increase in prevalence between 1990 and 1997 was found, mainly attributable to a higher incidence than mortality.

Conclusions: The present incidence rate and prevalence confirms earlier findings that Västerbotten is a high risk area for multiple sclerosis. The adjusted incidence was twice as high as the incidence from 1974–88 in the only previous Swedish population based study from Göteborg, but comparable with other recent Fennoscandian multiple sclerosis incidence rates.

Keywords: multiple sclerosis; incidence; Sweden

Geographical variation in multiple sclerosis occurrence has challenged researchers since the beginning of the 20th century.[1] Incidence data from different areas in Scandinavia are available and have been compared.[2] Population based studies of multiple sclerosis incidence in Sweden have previously only been done in Göteborg in south west Sweden.[3] Our aim in this study was to investigate multiple sclerosis incidence and prevalence in Västerbotten County in northern Sweden—using multiple sources for case identification and follow up interviews, together with medical records for data collection and case ascertainment—and to provide a base for further follow up studies.

METHODS

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Västerbotten County is located in northern Sweden at 64–65°N latitude. It is sparsely populated with 255 987 inhabitants at the midpoint of the incidence period 1988–97, and 259 163 on the prevalence day, 31 December 1997, in an area of 55 432 km^2.

The database used in a previous study, with the prevalence day 1 January 1990,[4] was extended using the same multiple sources. A computerised data register search from all three hospitals in Västerbotten County was extended through year 2000. Inpatients were selected from the neurology (also outpatients), neurosurgery, neurorehabilitation, internal medicine, ophthalmology, paediatric, and geriatric clinics with ICD codes corresponding to the following diagnoses: multiple sclerosis, demyelinating disorders in CNS, optic neuritis, spastic paraplegia, ataxia, myelopathy, spinocerebellar disease, and myelitis. In addition we used six other sources:

- Register for CSF electrophoresis analyses 1988–2000: analyses with presence of oligoclonal bands or signs of intrathecal IgG production were recorded.
- General practitioners, 1988–98: in April 1998 all general practitioners were contacted by letter; we asked for information on patients with multiple sclerosis or inflammatory disorder of the central nervous system for the past 10 year period.

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Original Paper

Increasing Incidence of Multiple Sclerosis in the Province of Sassari, Northern Sardinia

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Key Words

- Multiple sclerosis
- Epidemiology
- Sardinia

Abstract

Sardinia is a high-risk area for multiple sclerosis (MS), with prevalence rates of 150 per 100,000 population. The study included 689 MS patients (female-male ratio 2.6) with disease onset between 1965 and 1999 in the province of Sassari. The mean annual incidence rate increased significantly from 1.1 per 100,000 population in 1965-1969 to 5.8 in 1995-1999, with no significant difference for gender and province sub-areas. The mean age at onset increased significantly during the same period from 25.7 to 30.6 years, while the proportion of patients with progressive initial course declined over time. The marked increase of MS incidence and the change of MS clinical phenotype over time cannot be explained by ascertainment bias only, thus pointing to a corresponding change in the distribution of exogenous risk factors in this highly genetically stable population.

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Epidemiology and current treatment of multiple sclerosis in Europe today

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Abstract—Multiple sclerosis (MS) is a chronic disease affecting the central nervous system, usually leading to early disablement in young adults. At least 350,000 persons in Europe have the disease. Wide variations exist both between and within European countries in the incidence and prevalence of the disease as well as in the general standard of care for MS patients. The needs, well-being, and social participation of people with MS are systematically influenced by their physical and cultural environment and the nature of the community services. Moreover, the rate of introduction of the new disease-modifying therapy also widely differs from country to country. This article helps clinical researchers to understand better the differences in epidemiology and in the current treatment of MS in Europe.

Key words: *incidence, multiple sclerosis in Europe, prevalence, treatment.*

EPIDEMIOLOGY OF MS IN EUROPE

During the past 50 years, more than 150 descriptive studies on multiple sclerosis (MS) in Europe have been published. Despite considerable scientific effort, much of the variations of the distribution of MS found in different European countries may reflect, at least in part, methodological differences in surveys, especially in case ascertainment and selection.

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Most recent descriptive studies based on more appropriate methods contradicted the accepted belief that the distribution of MS in Europe is related to latitude (1). Until 1980, European countries from 36° to 46° north latitude were regarded as having a much lower prevalence rate of MS, about 5 to 25 cases per 100,000, compared to countries of central and northern Europe. This view was mainly based on old surveys done in Italy between 1959 and 1975. More recent studies performed in Italy and in other countries of southern Europe showed that MS prevalence is, in fact, much higher than had been previously believed (2). Therefore, the MS distribution in Europe appears to be more complex than supposed in the past, with great variations not only between areas at the same latitude but also within the countries. There are highly significant deviations from homogeneity, and the high-rate areas tend to be contiguous, forming clusters or foci. In Europe, MS is common in southern Scandinavian but not the north, in the Orkney and Shetland Islands but not the Faroes or Iceland, in Sardinia but not in Greece or Spain, and in Sicily but not in neighboring Malta.

Scandinavia

The distribution of MS in Scandinavia was studied over several years by Kurtzke (3–5). The high-frequency areas in the north appeared to describe a "Fennoscandian focus," in the southern inland lake region of Sweden. This probably is where MS originated in the early 18th century and diffused across the Baltic states, northern Europe, and other countries (4). Actually, the frequency of this disease is variable, and in some areas, incidences

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The worldwide prevalence of multiple sclerosis

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Keywords: Multiple sclerosis; Prevalence; World; Geography; Genetics; Environment

1. Introduction

Despite the wealth of epidemiological data deriving from the systematic studies of multiple sclerosis (MS) that have been carried out for over 70 years, any attempt at redefining the pattern of MS geographic distribution is still a difficult task. In fact, comparing prevalence studies of different areas and at different times implies a number of problems: (a) the variability of the surveyed populations in terms of size, age structure, ethnic origin and composition [1]; (b) the difference when determining the numerator, i.e. the recognition of benign and very early cases [2]; (c) the extent to which complete case ascertainment is achieved based on geographic and time variables, access to medical care, local medical expertise, number of neurologists, availability of and accessibility to new diagnostic procedures, degree of public awareness about MS, and on the investigators' zeal and resources [2,3]; (d) the use of different diagnostic criteria and the interobserver variability when applying them [1]. A description of MS geography worldwide is tentatively presented (for detailed references, see review by Rosati [4]).

2. Europe

The prevalence rates estimated for Scotland and its offshore islands over the last 25 years range from 145 to **193 per 100 000 and are the highest** so far detected anywhere in the world for large populations. In England and Wales, prevalence rates have varied from 74 to 112 in the last 15 years; 66 per 100 000 was the rate yielded by a nationwide survey in the Republic of Ireland in 1971, whereas a prevalence of 168 was estimated in northern Ireland. The highest frequencies of MS in the UK and mostly in Scotland support the hypothesis that the Scottish ancestry is associated with a high susceptibility to the disease, possibly on a genetic basis (Fig. 1).

A high risk for MS among Scandinavians is also well established although, it must be noted that the distribution of MS in Nordic countries is not homogeneous. In Norway there is a marked difference in MS risk between the northern Tröms and Finmark, with prevalence rates of 37 and 21 in 1983, and the southern Hordaland County and Oslo with rates of 75 and 132 in 1983 and in 1995, respectively. As a high proportion of the northernmost Norwegian populations are Samis, formerly known as Lapps, it is therefore likely that Samis are resistant to the disease. Gothenburg is the only area recently surveyed in Sweden based on a case register created in the early 1950s and updated in 1988, which yielded a rate of 96. The Danish nationwide prevalence of MS was updated in 1990 based on a case registry created in 1949, indicating a rate of 112. Danes, Norwegians and Swedes have an almost identical ethnic background, and may thus share a similar genetic susceptibility to the disease. The same ethnicity is also shared by the population of the Faroe Islands, which have been repeatedly assessed as to MS frequency by Kurtzke and Hyllested for almost 20 years. The most recent prevalence study [5] yields a rate of 66 per 100 000 in 1998. It has been claimed that MS appeared in the Faroes during the occupation by British troops in World War II and subsequently occurred in four separate epidemics, in support of the hypothesis that it is a widespread persistent asymptomatic infection. Being based on a small population and few cases, despite the Faroes' peculiar historical context and repeated surveys [6], the conclusion that MS is a transmissible disease somehow appears to be unwarranted [7,8]. The widespread asymptomatic illness that was then claimed as of infectious origin [6] may instead be viewed as a genetically based asymptomatic immune dysfunction which, when triggered by a non-specific viral infection [7,8], renders the general population at risk for devel-

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migrated from Northern and Southern Europe at different ages may persist, influencing the reported rates; in New Zealand, the south-to-north gradient observed may actually be justified by the presence of Maori ancestry up to 50% of the whites living in the north. In Australia, however, the highest prevalence rates reported from originally British, Scottish and Irish communities do not exceed half the frequency observed in most parts of the British Isles, and suggest that the role of environment cannot be ignored. In fact, the influential migration studies in South Africa, Israel and among West Indians migrating to the UK indicate that MS prevalence can vary with place of residence early in life irrespective of genetic factors; thus, twin studies show that almost 60% of monozygotic twins are not concordant for MS. Given that the increased MS frequency reported from different regions is, at least in part, real, a change of environmental conditions in susceptible populations should be reasonably assumed, because the genetics of a population per se would shape the disease at a much slower pace. The geography of MS could therefore be viewed in terms of a discontinuous distribution of genetic alleles of susceptibility, conferring risks that are subsequently modified and influenced by environment.

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The epidemiology of multiple sclerosis in New Zealand

Multiple sclerosis (MS) is a chronic inflammatory demyelinating disease of the central nervous system resulting in severe neurological disability. An accurate estimate of the number of people in New Zealand with MS is currently unknown, partly because hospital outpatient and private neurologist records (the majority of diagnostic care) are not centrally collected and administered.

The epidemiology of MS in New Zealand is of particular interest for several reasons outlined below.

An increasing disease prevalence has been consistently observed with decreasing latitude in both New Zealand and Australia.[1,2] Three explanations for this trend have been proposed: a concentration of genetically susceptible individuals, fewer sunshine hours in the south,[3] and unknown environmental factors associated with colder climates.[2]

Increasing incidence and prevalence of MS has been observed worldwide[4] without explanation. It has been postulated that improved diagnostic techniques such as magnetic resonance imaging (MRI) and an increase in the number of neurologists per population head make it easier to identify cases. However, the prevalence has continued to increase in areas even where there has been a reduction in the number of neurologists per population head, as was the situation in Novosibirsk, Russia in 2003, according to local neurologist Larisa Sperling (personal communication to Lou Gallagher, 2003).

Improved patient survival resulting from modern medical treatments has also been shown to be an insufficient explanation, as both incidence and prevalence have increased in areas where no treatment is available.

MS prevalence studies have been conducted in New Zealand since 1968. However, they are not directly comparable since there has been significant variation in case identification methods, clinical definitions of MS, demographic differences in the reference population studied, and inconsistent time periods during which the studies have been conducted. This is a common problem throughout the world, resulting in a situation where only the crudest of comparisons of MS prevalence by geographic region can be made.

According to previous studies, the prevalence of MS in New Zealand Maori seems to be substantially lower than in the European population.[5–8] Explanations for this apparent ethnic disparity in MS prevalence include differences in socioeconomic factors (Maori are less likely to present with MS symptoms to medical practitioners) and differences in environmental factors (Maori are less likely to live in areas with exposure to environmental triggers of MS). However, another plausible explanation is that differential susceptibility to MS between Maori and European groups is partially conferred by variation in genetic inheritance,[8] as has been observed among subpopulations overseas.[4] If Maori genetic inheritance confers some degree of immunity to MS, how much Maori ancestry is enough?, and what genetic variants are specifically protective for individuals with Maori

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Increasing frequency of multiple sclerosis in Padova, Italy: a 3 year epidemiological survey.

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OBJECTIVE: To determine the incidence and prevalence rates of multiple sclerosis (MS) and their temporal profiles over the last 30 years in the province of Padova (northeast Italy). BACKGROUND: In the early 1970s an epidemiological survey in the province of Padova showed a MS prevalence and incidence of 16/100 000 and 0.9/100 000 population, respectively; these figures are much lower than current estimates in other regions of Italy and Central Europe. METHODS: The population of the study area was approximately 820 000 (422 028 women, 398 290 men) in the 1991 census. All possible sources of case collection were used, but only clinically definite/probable and laboratory-supported definite/probable MS were considered in the analysis of incidence and prevalence trends from 1971 to 1999. RESULTS: On 31 December 1999, the crude prevalence rate was 80.5/100 000 (95% CI 70.3-90.7); prevalence was higher in women (111.1/100 000; 95% CI 99.0-123.1) than in men (49.7/100 000; 95% CI 41.3-58.1). This difference was significant (F/M = 2.43; z = 10.1, P < 0,00001); a rate adjusted for the European population was 81.4/100 000. On 31 December 1980 and on 31 December 1990 the estimated prevalence rates were 18/100 000 and 45.7/100 000, respectively. Thus, a fivefold increase in prevalence was observed from the 1970s. The mean annual incidence was 2.2/100 000 in the period 1980-89, 3.9 in the period 1990-94 and 4.2 in the period 1995-99. Thus, incidence increased more than fourfold from the 1970s through 1994 and remained quite stable in the last several years. Mean age at onset was 31.3 +/- 9.88 years. Mean diagnostic latency decreased significantly from 49.2 +/- 44.5 months in 1985 to 23.0 +/- 30.3 months in 1990, 12.9 +/- 15.61 in 1995 and 5.3 +/- 4.7 in 1999. CONCLUSIONS: The actual prevalence (80.5/100 000) and incidence (4.2/100 000) of MS in the province of Padova agree with the most recent epidemiologic estimates/trends observed in other Italian and European areas, except for

Sardinia and Scotland. The increase in both incidence and prevalence rates observed in much of this region over the last 30 years parallels the introduction of more sensitive diagnostic techniques and a highly significant decrease in diagnostic latency. These findings probably do not support a real increase in the frequency of MS in northeast Italy because recent estimates of incidence have increased only slightly (3.9 to 4.2, which is < 10% in five years) and increase in the prevalence rate was almost completely due to the accumulation of new incidence cases.

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