

# Multiple sclerosis in southern Europe

## I: Prevalence in Sicily in 1975

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**SUMMARY** Previous reports on large population groups have suggested that the prevalence of multiple sclerosis (MS) in Sicily and southern Italy is low, of the order of 4–8 per 100 000. In contrast, immigrants from Italy resident in Greater London, many of whom are from southern Italy and Sicily, had a hospitalised MS prevalence similar to that found among people born in the United Kingdom (1960–72). The present study shows that in Enna city (population 29 000) in central Sicily, the prevalence of probable MS was 53 per 100 000, which is of the same order of magnitude as has been reported from the United Kingdom and northern Europe. The high prevalence of MS found in Enna city may be due, at least in part, to the fact that the population studied was small. Because Enna is on high ground, similar studies are being undertaken in two small coastal towns of Sicily.

The prevalence of multiple sclerosis (MS) varies throughout the world. For example, Europe, Canada, and the northern part of the United States of America are areas of high prevalence, whereas Asia, Africa, and the West Indies are apparently areas of low prevalence. Those who migrate from a high-risk to a low-risk area keep their high risk unless they migrate when they are under 16 (Dean, 1967; Dean and Kurtzke, 1971).

Previous reports have suggested that the prevalence of MS in Sicily is very low—for example, 3.3 per 100 000 in Palermo city (Societa Italiana di Neurologia, 1975)—but these were studies of large populations. The high prevalence of MS among Italian immigrants living in London suggests that the prevalence of MS in Italy as a whole is not greatly different from that in the United Kingdom (Dean *et al.*, 1976; 1977). Many of the Italian immigrants are from Sicily and southern Italy.

Enna city in central Sicily, which had a population of 28 189 in 1971, is at a midpoint between the three university cities of Palermo, Catania, and Messina. It has a good hospital and neurological service and it appeared to be the best area for a preliminary study of MS prevalence sponsored by the European Economic Community. Enna at a height of 1000 m is

colder than cities on the coast; the average winter temperature is  $-1$  to  $+5^{\circ}\text{C}$ .

### Method

Full co-operation was obtained from the physicians at the Ospedale Umberto I, Enna, and from the 85 general practitioners in the town. Because patients with MS visit other centres for medical opinion and treatment, we also obtained a list of patients who were resident in Enna city and province from the studies that are being undertaken on the prevalence of MS at Palermo, Messina and Catania, the Multiple

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We regret that, owing to an error, the March 1979 issue of the *Journal of Epidemiology and Community Health* was given the wrong title throughout (as *Epidemiology and Community Health*). The name of the journal remains in fact that given it in 1978, and we apologise for any confusion that may have been caused.

Sclerosis Research Centre at Gallarate, Milan, and the collaborative study of the Italian Society of Neurologists.

The records were studied of patients admitted to the neurological department in the Ospedale Umberto I at Enna during a 16-year period. Patients with a diagnosis of MS, encephalitis, myelopathy, or optic neuritis were reviewed, and those who had been recorded as possible MS in the hospital records at Palermo, Messina, and Catania, and at the MS Research Centre at Gallarate, were included in the study. All of the patients who had not died or emigrated were seen by us, and each patient's clinical history was reviewed and the neurological examination repeated.

### Results

There were 15 patients with probable MS resident in Enna city who had the symptoms of the disease on prevalence day, 1 January 1975. Three of the probable MS patients were men and 12 were women (Table). In addition, there were two patients with a diagnosis of possible MS only.

Paraparesis was the first symptom in seven patients, paraesthesia in three patients, and impairment of vision in three. The remaining two patients presented with attacks of vertigo or of sciatic pain. The average age of the three men in the study on prevalence day was 36.3 and of the 12 women 37.5. The average age of onset was 26.4 and one patient had her first symptoms at the age of 8, another at 15. Fourteen of the 15 patients had at least partial remissions and only one patient (No. 1 in the 'females' section of the Table) had a non-remitting course; in her case, investigation in hospital in Milan and Bologna showed no other alternative pathology than MS to account for her symptoms.

Fifteen patients with probable MS out of a population of 28 189 is a crude prevalence of 53 (52.9) per 100 000: 22 (21.8) per 100 000 males and 82 (82.1) per 100 000 females. If these rates are age-standardised from the Enna population to the population of England and Wales, the expected rate for England and Wales would also be 53 (53.3) per 100 000. (There are three patients with MS in the neighbouring city to Enna, Calascibetta, population 5600).

### Discussion

The MS prevalence of 53 per 100 000 found in Enna city is the highest prevalence for MS that has yet been found in any community in Italy and it is several times greater than any previously reported in Sicily. It must be emphasised that this is a minimum prevalence

rate, not only because no doubt some patients with MS have been overlooked but also because some are likely to have been excluded as a result of our adherence to the strictest criteria for making the diagnosis. No one was included who did not have clear evidence of MS from the history and examination. The true prevalence of MS in Enna is therefore probably higher than we have established.

Studying the history and the clinical condition of the patients presented to us with identifiable disease, we were struck by the fact that MS appears to pursue a less benign course in this part of Europe. For example, all three men examined had a fixed disability, the first after six years, the second after an unidentifiable period, and the third after 10 years. Of the 12 women in the study, two (cases 5 and 6) had long remissions, one of 20 years and the other of 22 years. Only five of the 12 had had complete remissions. Ten of the 12 women had a fixed disability at an average time of just over six years after the onset of the illness and, if the two women with long remissions were included, at less than 10 years. This is quite contrary to usual experience in the north of Europe, where one would expect to find no evidence of disability whatsoever in over 50% of patients examined six years after the commencement of the illness nor in very nearly half of the patients when examined 10 years after the commencement. Of 335 patients seen consecutively by one of the authors (R.K.), 183 had a history going back for a minimum of 10 years without developing a fixed disability, and 74 (more than one-fifth of the total) had such a history going back more than 20 years (Kelly, 1972). We may, of course, have overlooked some patients in Enna with complete remissions and a more benign course.

The minimum prevalence of MS in Enna city, 53 per 100 000, is of the same order of magnitude as has been found in studies in northern Europe; for example, the reported prevalence of MS in Northern Ireland is 64 and in the Republic of Ireland 65 per 100 000 (Millar, 1971; Brady *et al.*, 1977). Enna is on high ground and is somewhat colder than the central cities of Sicily. A similar study is being undertaken in two small coastal cities.

The high prevalence of MS found in Enna is no doubt partly due to the fact that an intensive survey has been undertaken in a small population which has a good neurological service. The very low MS prevalence rates reported in many other Italian studies may be due to the difficulties of undertaking studies in large population groups. It is suggested that intensive surveys in small populations are likely to give more accurate prevalence rates than surveys in large groups.

There is little reason at present to believe that the genetic background, the standard of hygiene, or the

Table Probable multiple sclerosis patients in Enna city, 1 January 1975

MALES							
No.	Age (years)	Date and first symptom	Remission	Relapse	Remission	Examination	
1	23	1971	Paraesthesia left side	Complete	Diplopia; paraesthesia right side; walked with difficulty	Improved (ACTH)	Ataxia; bilateral Babinski+
2	39	For some years	Attacks of vertigo	Complete remissions (spleen removed 1976 for thalassaemia minor)	Sudden anaesthesia right face. Loss of power right arm and leg (1977)	Improved (ACTH)	Pallor left disc; nystagmus > left right arm paraesthesia; right leg spastic; right Babinski+; c.s.f. normal
3	47	1967	Left sciatic pain, followed by weakness left leg	Improved	Left retrobulbar neuritis 1972; left leg spastic 1975; left eye vision failed 1975; right leg dragging 1977	Improved (ACTH)	Temporal discs pallor, nystagmus; spastic paraparesis; abdominals-; ataxia right
FEMALES							
No.	Age (years)	Date and first symptom	Remission	Relapse	Remission	Examination	
1	46	1960	Loss power right leg	No	Paraplegia investigated Milan 1966-67; complete paraplegia 1968	Improved	Legs spastic right > left; bilateral Babinski+; abdominals- discs pale, myelogram, etc. (Milan) normal
2	34	1972	Impaired vision both eyes; months later loss of power right leg; difficulty in urination	Complete	Lost power both legs; partial loss vision right eye	Improved	Spastic paraparesis; right Babinski+; c.s.f. normal
3	26	1972	Paresis left face; lost power left arm and leg	Complete	Lost power right side 1973; complete loss vision right eye 1977	Partial	Right disc pale; spastic left; adiadocho - kinesia right hand; left Babinski +; c.s.f. normal
4	28	1974	Paraesthesia right hand; lost power both legs	Complete	1975 return weakness legs; spastic gait; 1977 third attack similar symptoms	Improved	Bilateral Babinski +; spastic gait; ataxia both arms
5	48	1942	Paraesthesia both legs; walking difficult	Improved	1962 lost vision left eye (3 months)	Improved	Left disc pale; spastic left leg; right foot clonus; absent vibration left leg; abdominals -; c.s.f. normal
6	31	1952	Cloudiness of vision (aged 8); (? following injury) electric sensation both legs (aged 16)	Complete	1974 diplopia; four further attacks; dysarthria; vertigo; hypersomnia; loss of power in legs	Complete	Nystagmus; paresis VII right; dysmetria; loss of power right leg; Babinski left +; abdominals -
7	59	1957	Cloudiness vision both eyes	Complete	Blind left eye; loss of power both legs; walks with difficulty	Improved	Pallor left disc; nystagmus; spastic legs; right > left
8	34	1963	Lost power right leg	Recovered	1965 loss of power both legs	-	Spastic paresis; pallor both discs; left Babinski +; abdominal -; walks with great difficulty
9	45	1968	Lost power both legs	Improved	Relapsed to complete paraplegia	-	Pallor discs; nystagmus; dysmetria; spastic paraparesis; c.s.f. pandy +
10	20	1971	Lost power both legs; difficulty with micturition	Improved	Relapsed vertigo, ataxia in walking	Improved	Discs pale; nystagmus; ataxia arms; paraparesis; bilateral Babinski +; abdominals -; c.s.f. pandy +; cells increased
11	55	1955	Lost power both legs	Improved	Relapse 1958; complete paralysis both legs; partial loss vision both eyes (1958); difficulty with micturition	Improved	Spastic paraplegia; discs pale; could not walk since 1973; c.s.f. negative
12	24	1971	Weakness in right leg	Improved	Spastic paraparesis	Improved	1976 left disc pale; right leg paresis; right Babinski +

way of life of the people of Enna are greatly different from those of people in other parts of Sicily but these factors need to be examined further. A somewhat colder climate is unlikely by itself to account for a high prevalence of MS; for example, MS is uncommon in northern Japan, an area much colder than Enna.

The studies which are being undertaken in the southern tip of Europe, in Sicily, Malta, and perhaps in North Africa—the probable meeting area of high prevalence and low prevalence MS—should help to illuminate the genetic and environmental factors involved in the aetiology of this disease.

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#### References

- Brady, R., Secerbegovic, S., Secerbegovic, A.M., and Dean, G. (1977). Multiple sclerosis in the Republic of Ireland. *Journal of the Irish Medical Association*, **70**, 500–506.
- Dean, G. (1967). Annual incidence, prevalence, and mortality of multiple sclerosis in white South African-born and in white immigrants to South Africa. *British Medical Journal*, **2**, 724–730.
- Dean, G., and Kurtzke, J. F. (1971). On the risk of multiple sclerosis according to age at immigration to South Africa. *British Medical Journal*, **3**, 725–729.
- Dean, G., Brady, R., McLoughlin, H., Elian, M., and Adelstein, A. M. (1977). Motor neurone disease and multiple sclerosis among immigrants to Britain. *British Journal of Preventive and Social Medicine*, **31**, 141–147.
- Dean, G., McLoughlin, H., Brady, R., Adelstein, A. M., and Tallett-Williams, J. (1976). Multiple sclerosis among immigrants in Greater London. *British Medical Journal*, **1**, 861–864.
- Kelly, R. E. (1972). Clinical trials in multiple sclerosis. *Pahlavi Medical Journal*, **3**, 518–529.
- Millar, J. H. D. (1971). *Multiple Sclerosis. A Disease Acquired in Childhood*. Charles C. Thomas: Illinois.
- Societa Italiana di Neurologia. (1975). *XIX Congresso Nazionale, Genova, 3 Dicembre 1975*.