The prevalence of multiple sclerosis in Sicily II: Agrigento city

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SUMMARY The prevalence of probable multiple sclerosis in Agrigento city on the south-west coast of Sicily is at least 32 per 100 000. This is likely to be a considerable underestimate of the true prevalence because the study presented particular difficulties in that the city is far from the neurological centres of Palermo, Catania, and Messina. There is no neurological department at either the general or the psychiatric hospital in Agrigento and there was a low awareness of the disease among the doctors in the city. Most of the patients were diagnosed in other centres. Agrigento is a good example of the difficulties of studying multiple sclerosis in a rural city which has no special interest in neurological problems and is far from a neurological centre. Studies in such centres must be pursued with great enthusiasm and over a long period of time, and all available sources of information in the city, medical and lay, and in other cities, must be utilised if a high proportion of the patients is to be found.

Agrigento is a town on the south-west coast of Sicily, famous for its groups of ancient Greek temples. In 1976 the population was 49 979. There is a general hospital in the town but it has no neurological unit and no neurologists attached to it, and there is a large psychiatric hospital. Patients with neurological disorders generally go to Palermo or Catania, or farther afield, to establish the diagnosis. Nearly all the doctors in the town who were interviewed believed that multiple sclerosis (MS) was extremely uncommon; most of them claimed they had not seen a patient with MS resident in Agrigento city.

Method

No records could be found of any patients with MS at the general hospital, Ospedale Generale, in

Agrigento, but patients' records were not indexed by diagnosis. The husband of one of the nurses at the hospital suffered from MS and this patient was well-documented. Two patients with MS were known to the psychiatrists at the Ospedale Psichiatrica in Agrigento. Records were searched at the psychiatric and general hospitals in Palermo, Catania, Enna, and Messina for any MS patients resident in Agrigento city, and a search was carried out farther afield in Naples, Rome, and Bologna and at the Centro Studi Sclerosi Multipla in Gallarate, Milano. The records of the national health insurance groups were searched for possible MS patients and the clergy of Agrigento were asked if they knew of any patients with symptoms due to MS. The professor of neurology, Professor Agostino Rubino, Palermo, wrote to every doctor in practice in Agrigento asking

if they knew of any patients with MS because many of the doctors had studied in Palermo. None of the doctors replied in the affirmative. Lectures were given to the doctors at the general hospital on the diagnosis and epidemiology of MS. All the neurologists in the three university cities in Sicily and those in Naples, Rome, Bologna, and Milan collaborated in the study.

The study in Agrigento can be compared and contrasted with the studies in Enna city,¹ where there was a good neurological clinic, with an excellent records system, and with two neurologists; and in Monreale city,² which is close to the medical school and neurological clinics of Palermo. Patients from Monreale attended hospitals in nearby Palermo because there was no diagnostic hospital in Monreale. Agrigento, in contrast, proved an extremely difficult city in which to carry out an epidemiological study because of the absence of records in the hospitals or doctors' surgeries, the low awareness of the disease among the doctors, and the distance from a hospital with a neurological unit.

It is likely that more patients with MS resident in Agrigento city will be found in the next few years who had MS on prevalence day and who have been overlooked up to now.

Results

After visiting Agrigento every year for five years and screening the possible MS patients, whose names and addresses were generally found in other cities, 16 patients were considered to have probable MS, seven men and nine women, on prevalence day, 1 January 1975. An additional woman patient was considered to have possible MS and one patient had had retrobulbar neuritis only (Table 1).

Two of the men patients were father and son, otherwise there was no family history among the patients. The first symptoms among the 16 patients with probable MS were paresis in seven and paraesthesia, retrobulbar neuritis, and ataxia in three each respectively.

The average age of onset was 25.6 (21.9 for men and 28.9 for women) and the average age on prevalence day was 41.1 (40.4 men, 41.6 women). Four of the patients had had early onset of symptoms, man no. 3 at the age of 8, man no. 7 at the age of 11, woman no. 6 at the age of 16 and woman no. 7 at the age of 13.

All the patients except woman no. 8, who had had a rapid progressive course, had experienced remissions. One patient committed suicide and three other patients have died since prevalence day. All the patients with probable MS, except one, were born in Agrigento city. Two further long-established patients

have been found living in Agrigento now, but they were not resident there on prevalence day and were therefore excluded from the present study.

Sixteen patients with probable MS in Agrigento city in a population of 49 979 is a prevalence of 32.0 per 100 000. If the possible MS patient is included, the prevalence would be 34.0 per 100 000. It is believed that a number of patients with MS resident in Agrigento city, particularly patients with mild symptoms, have not yet been found because of the lack of awareness among the doctors of the symptoms of MS and the delay in making the diagnosis, and because the patients are seldom diagnosed as having MS until they are sufficiently ill to visit the neurological clinics in other cities, usually Palermo. The study in Agrigento will continue and it would appear to be likely that a further report will show a higher prevalence. Although a number of patients in Agrigento have undoubtedly been overlooked, the number of patients found, 16, is not significantly different from the expected number of patients with probable MS based on the prevalence found in Monreale, when the expected number would be 22, or the expected number based on the prevalence in Enna, when it would be 25 (Table 2).

Discussion

The higher prevalence of MS found in Monreale, Enna, and Agrigento cities, in comparison with previous studies in Italy and Sicily, is no doubt due to the deliberate choice of small populations which can be studied in depth. It is very difficult to find all, or nearly all, the diagnosed MS patients even in small populations. In Sicily, few doctors keep medical records and finding patients depends upon the use of many sources of information. Doctors in Sicily believe that MS is very rare and therefore the diagnosis is not likely to come to mind and, when it does, some vague term is often used to avoid naming the disease. The patients in this study were diagnosed in hospitals outside Monreale and not by their home doctor.

The high prevalence of MS found in three cities in Sicily, Monreale, Enna, and Agrigento, confirms the high prevalence found among Italian immigrants to London.³ The slightly lower number of hospitalised MS patients found in immigrants from Spain and Cyprus (Greek and Turkish Cypriots) compared with the expected number at the United Kingdom-born rates, age-corrected, resident in London, suggests that in the south of Italy and Sicily we may also expect to find a slightly lower prevalence than in northern Italy. The studies of MS prevalence in Enna, Monreale, and Agrigento provide evidence that the prevalence in Sicily is between 40 and 60 per

Table 1 Probable MS patients resident in Agrigento city, prevalence day, 1 January 1975

MEN							
No.	Age (years)	Date and first symptom		Remission	Relapse	Remission	Examination
1	56	1940	Unsteady gait	Complete	1948 Blurred vision rt. eye 1958 Weakness legs, could not walk without help 1963 Relapse 1974 Relapse	Yes Yes Partial	Pale discs, nystagmus, ataxia hands, spastic gait, hyperreflexia, Babinskis ↑↑
2	43	1961	Weakness rt. leg	Almost complete	1967 Weakness both legs, blurring of vision, arms ataxic		Discs pale, nystagmus, paraparesis R>L, ataxia arms, hyperreflexia R>L, clonus knee and ankle. MS diagnosed Rome, Bologna, etc
3	25	1958	(aged 8) Weakness rt. arm and rt. leg, rt. facial paralysis	Complete	1959 Relapse as in 1958. 1964 Bladder symptoms, incontinent, weakness both legs 1976 Severe relapse unable to walk, blurring vision lt. eye	Complete Improved Improved	Vision poor (cannot read), pale discs, nystagmus, ataxia arms and legs L>R, hyperreflexia, spastic legs, knee/ankle clonus Babinskis +, abdominals absent. (Son of man no. 4)
4	69	1930	Unsteady rt. arm	Complete	1952 Weakness in legs, difficulty in walking. 1966 Relapse, ataxia, difficulty in walking, Still walking however until stroke on 31/8/74	Improved	Nystagmus, ataxia, spastic, paresis, paraesthesia legs, hyperreflexia, Babinski ↑↑ (MS diagnosed Palermó, Rome, Padua, etc.). (Father of man no. 3)
5	33	1967	Blurring vision both eyes	Yes ACTH	1970 Blurred vision. 1972 Weakness legs, ataxia arms 1978 Vision cloudy, legs very weak, walking with aid 1979 Walking better. Vision again worse	Improved. Many attacks and remissions	Investigated Clinica Neurologica, Palermo, 1967 MS diagnosed. Also Germany MS, pale discs, spastic legs, ataxia arms, Babinski ↑↑
6	44	1974	Ataxic gait	Improved	1975 Relapse, ataxic gait, legs weak, walked with difficulty 1978 Legs very weak, walked only with aid		1975 Nystagmus, ataxia arms and legs, hyperreflexia, spastic legs L>R, rt. Babinski clonus ankles, protein 0.49 g/L, CSF Globulin ++, pandy ++, 2/4/78. Anisocoria, nystagmus, ataxia arms, legs spastic, hyperreflexia, Babinski rt., clonus ankles, incontinent, depressed. (Suicide November 1978)
7	13	1972	Weakness rt. face rt. arm, rt. leg	Complete ACTH	1979 Weakness legs, difficulty in walking, speech slurred, weak rt. arm, diplopia, two attacks blurred vision	Improved ACTH	1972 Ospedale Civico, Palermo, rt. Babinski, CSF protein increase, Globulin ++, MS diagnosed 1979 Pale discs, rt. face weak, hyperreflexia R>L, Babinski rt., ataxia rt. arm, ver delayed
WOMEN							
1	55	1954	Weakness rt. leg.	Complete	1955 Return weakness legs, Ataxia, attacks and remissions. 1977 Unable to walk. 1978 Walking again. Ataxic.	Yes Improved again	Scanning speech, nystagmus, ataxia arms, hyperreflexia, intention tremor, Babinskis +.

WOMEN

No.	Age (years)	Date and first symptoms	Remission	Relapse	Remission	Examination
2	36	1965 Burning sensation in legs.	Complete	1967 Weakness legs, in bed four months.	Yes	Walks with aids, nystagmus, intention tremor, hyperreflexia, knee/ankle clonus, Babinskis ↑↑ abdominals absent.
3	42	1962 Paraesthesia legs.	Yes	1971 Weakness legs, paraesthetic feet.	Yes ACTH	1978/79 Pale discs, nystagmus, hyperreflexia, clonus knee/ankle, abdominals -, Babinskis +. Can walk with unsteady gait. July 1980. No change.
4	56	1961 Paraesthesia legs, followed by paraparesis legs. Unable to walk.	Yes Almost complete.	Weakness arms and legs. 1972 Blurring vision. 1974 Difficulty in walking.	Partial. Many attacks and remissions	1979 Walks reasonably well, scanning speech, pale discs, hyperreflexia, abdominals -, lt. Babinski ↑
5	62	1953 Weakness legs.	Yes complete	1963 Diplopia. 1970s Weakness in legs.	Improves and deteriorates	Pale discs, nystagmus, hyperreflexia, clonus knee/ankle, abdominal reflexes absent, Babinski +, vibration sense absent in legs.
6	35	1956 Blurring vision both eyes. Lasted one year.	Yes	1970 Paraesthetic legs. 1975 Paraesthetic legs ++, vertigo, unsteady gait, ataxic hands L>R.	Yes ACTH	1978/79 Discs pale, nystagmus, ataxic arms L>R, hyperflexia, abdominals -, Babinskis +, IgG raised
7	16	1972 Blurring vision both eyes	Yes	1974 Could not distinguish hot and cold lt. leg. Some months later vertigo, vomiting attacks, weakness lt. leg. Diplopia. Many attacks and remissions up to 1979.	Yes ACTH	1977/79. Unable to walk, weakness both legs R>L, spastic legs, nystagmus, lt. hand paralysis, ataxic rt. hand, intention tremor pale discs, scanning speech. Pain touch diminished lt. side, vibration sense absent up to arms, abdominals -, hyperreflexia Babinskis +. July 1980. Deteriorating
8	37	1974 Weakness in legs Back ache	No	1976 After influenza legs very weak, ataxic and spastic, urgency micturition, incontinent 1978 Tetraparesis, unable to walk or feed herself, speech scanning ++ incontinent. Rapid course		Hyperreflexia, legs spastic, clonus ankles, Babinski ↑↑ CSF protein increased, Pandy ++, MS diagnosed England, Palermo Died November 1978
9	35	1963 Weakened rt. arm, dysgraphia, paraesthesia rt. arm	Yes	1964 Ataxia rt. arm, also paraesthesia and weakness. 1974 Vertigo, unsteady gait. 1975 Urgency micturition 1980 Difficulty in speech, ataxic gait, ataxic arms, urgency micturition, weakness rt. arm, both legs	Yes	1964 Hospital Frankfurt, Germany. Angiogram normal, encephalogram normal. 1969 Padua. Nystagmus, Ataxic gait, intention tremor, hyperreflexia R>L, Babinskis extensor pale discs. MS diagnosed. 1980 Pale discs, nystagmus, ataxia arms and legs, scanning speech, hyperreflexia, weakness legs L>R, Babinskis flexor

Table 2 Prevalence of probable MS in three cities of Sicily

Cities	Prevalence Day	Population	Probable MS			Rate per 100 000
			Male	Female	Total	
Enna	1 January 1975	28 189 (1976)	3	12	15	53.2
Monreale	30 June 1980	25 403 (1980)	6	5	11	43.3
Agrigento	1 January 1975	49 979 (1976)	7	9	16	32.0
TOTAL		103 571	16	26	42	40.6

100 000, which is of the same order of magnitude as that reported in central and northern Europe (Table 2). Other investigations have shown that MS prevalence increases with subsequent studies, because some patients are inevitably missed in the earlier study.^{4,5} Studies of the prevalence of MS are now required in small cities in other southern European countries such as Greece, Cyprus, and Spain.

The high prevalence in Sicily is in sharp contrast to the low prevalence, 4 per 100 000, in the islands of Malta.⁶ Sicily and Malta are therefore at a junction of high and low prevalence in the Mediterranean, and it is in these islands that the genetic and environmental factors responsible for MS may be unravelled.

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