

Multiple Sclerosis

*Diagnosis, Medical Management,
and Rehabilitation*

EDITED BY

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Demos

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caused by a deficiency of copper and/or molybdenum in their diet, leading to therapy based on this concept. Most recently, interest has been sparked in the media about bee venom therapy and the Cari Loder diet, but such alternative approaches occur frequently, fading slowly as the next one comes to the fore (212).

MULTIPLE SCLEROSIS SOCIETY

“It is possible that the cause of the disease lies buried somewhere in these lengthy protocols waiting to be found by anyone ingenious enough to unearth it.”

Dr. Henry Miller, 1972

An important impetus for change and encouragement for research in MS in the last half century has been the formation of MS societies in each country. By the end of World War II Putnam and others complained that the public, who knew so well the problem of polio, had little inkling of the MS that afflicted young adults. The public needed to be made aware of this illness and contribute to the efforts to find its cause and a cure.

The first step was taken by Miss Sylvia Lawry, who was distressed about her brother who had been diagnosed with MS and placed an advertisement in the *New York Times* on May 1, 1945 which stated: “Multiple Sclerosis. Will anyone recovered from it please communicate with the patient. T272 Times.”

From the responses it was apparent to Miss Lawry that there should be an organization to foster research into the cause, treatment, and eventual cure of MS. The organization was named the Association for the Advancement of Research into Multiple Sclerosis (AARMS) but a few months later it was changed to the Multiple Sclerosis Society (213).

Shortly afterward, Evelyn Opal, a Montreal housewife who had MS, heard of the New York group and began to raise funds, forming a chapter of the American group named for her physician, Dr. Colin Russel of the Montreal Neurological Institute. Another Montreal patient, Harry Bell, an engineer, also formed a group, the Canadian MS Research Organization. Lawry brought them together and in 1948 the Multiple Sclerosis Society of Canada was formed with Dr. Wilder Penfield as honorary chairman of the scientific advisory committee. The first grant went to Dr. Roy Swank and Dr. Donald McEachern for work on lipids and diet in MS. One grant per year was given for the first two decades, and then the support of research expanded each year.

In 1952 the Multiple Sclerosis Society of Great Britain and Northern Ireland was formed, with Dr. Dou-

glas McAlpine as chairman of the medical advisors. Each of these national organizations was formed with the encouragement and enthusiastic support of Miss Lawry. Each appointed society leading clinicians in MS to sit on the advisory committees that awarded the results of the first fund-raising efforts, and year by year these grants increased and encouraged more clinicians and later basic scientists to enter the field of MS research.

Sylvia Lawry was not finished organizing for MS. At the 8th International Conference of Neurology in September 1965 in Vienna, she proposed the formation of an international organization, supported by Dr. William Breed and Dr. Houston Merritt, which was formed the next year.

From a few thousand dollars to many million dollars per year these societies supported research into basic science, clinical research, epidemiology, psychosocial research, and clinical care. There is little question that the current vibrant research effort in all aspects of MS developed because an MS society in each country supported and funded the best efforts in research.

As I conclude this selective review of the early contributors to the understanding of MS, I acknowledge their pioneer efforts and vision and that of the MS societies of the world that support their work and introduce the reader to the coming chapters of this book, written by their worthy successors, the clinicians and researchers who are currently addressing the remaining questions about MS.

“The story of multiple sclerosis is not yet closed, but neither is the history of medicine.”

Tracey Putnam, 1938

Acknowledgments

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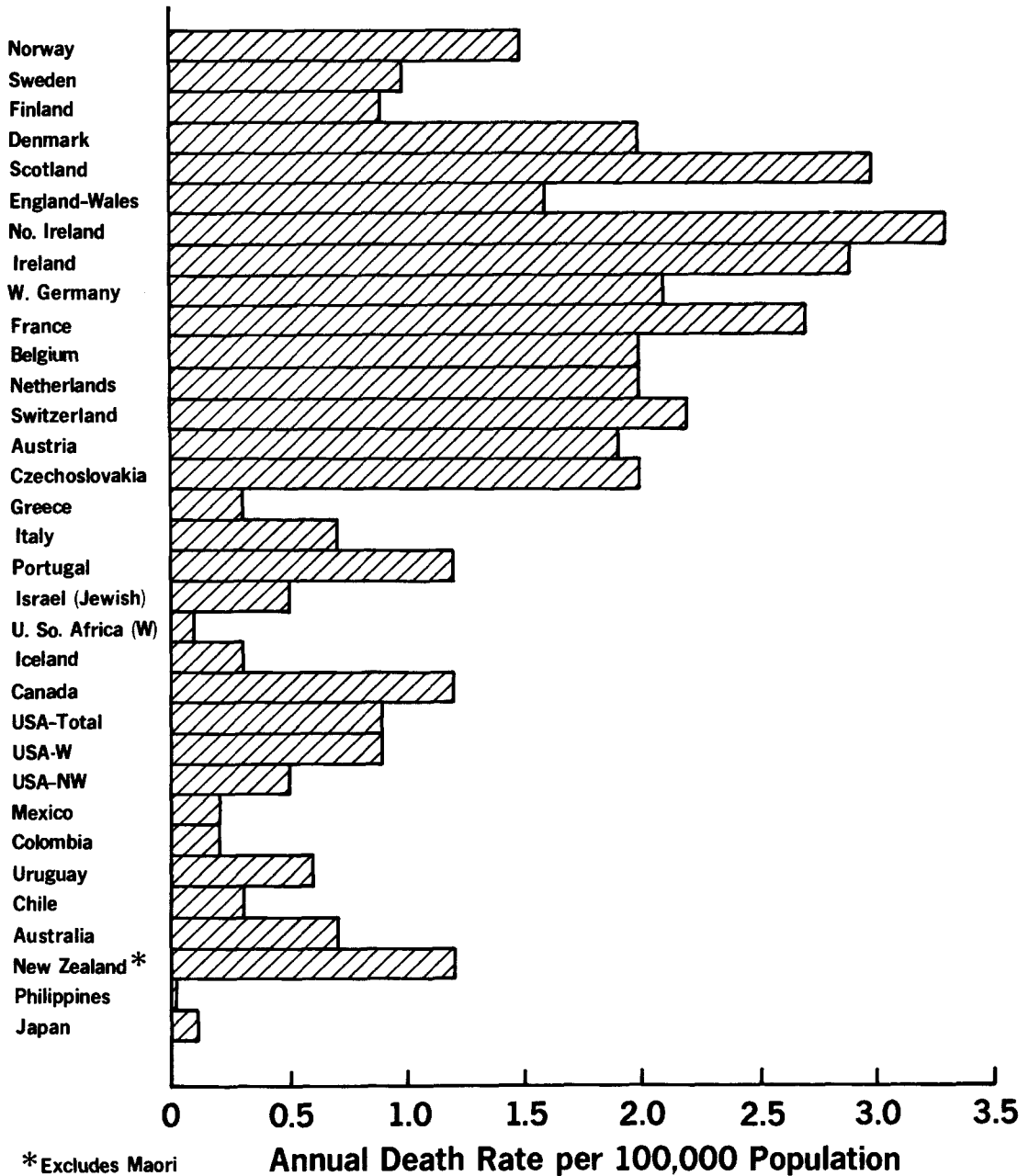


FIGURE 3-2

Average annual death rates per 100,000 population for MS by country, 1951-1958, with rates adjusted for age to the 1950 U.S. population. W = Whites, NW = Nonwhites. Modified from data of Goldberg and Kurland, 1962 (22); from Kurtzke, 1977 (2).

Worldwide Distribution

The general worldwide distribution of MS thus seems well described by a division into high prevalence (30+ per 100,000), medium prevalence (5 to 29 per 100,000), and low prevalence (under 5 per 100,000) regions, as proposed years ago. A “super high” class for prevalence of, say, 90+ seems not yet indicated. Figure 3-4 shows how scattered such regions would be in Europe. The most recent distribution is shown in Figure 3-7.

Sex and Race

Death rates in the United States indicate that nonwhites have MS recorded as a cause of death only half as often as whites, and both mortality and morbidity data demonstrate low frequencies of the disease in Asia. In fact, all the high-risk and medium-risk areas for MS have predominantly white populations. Regardless of residence in the United States, in the veteran series blacks or African Americans have only half the risk of white males (Table 3-1). Young white females have nearly twice the risk of MS as white males. The group consisting of the “Other” races suggests a paucity as well in Native Americans and

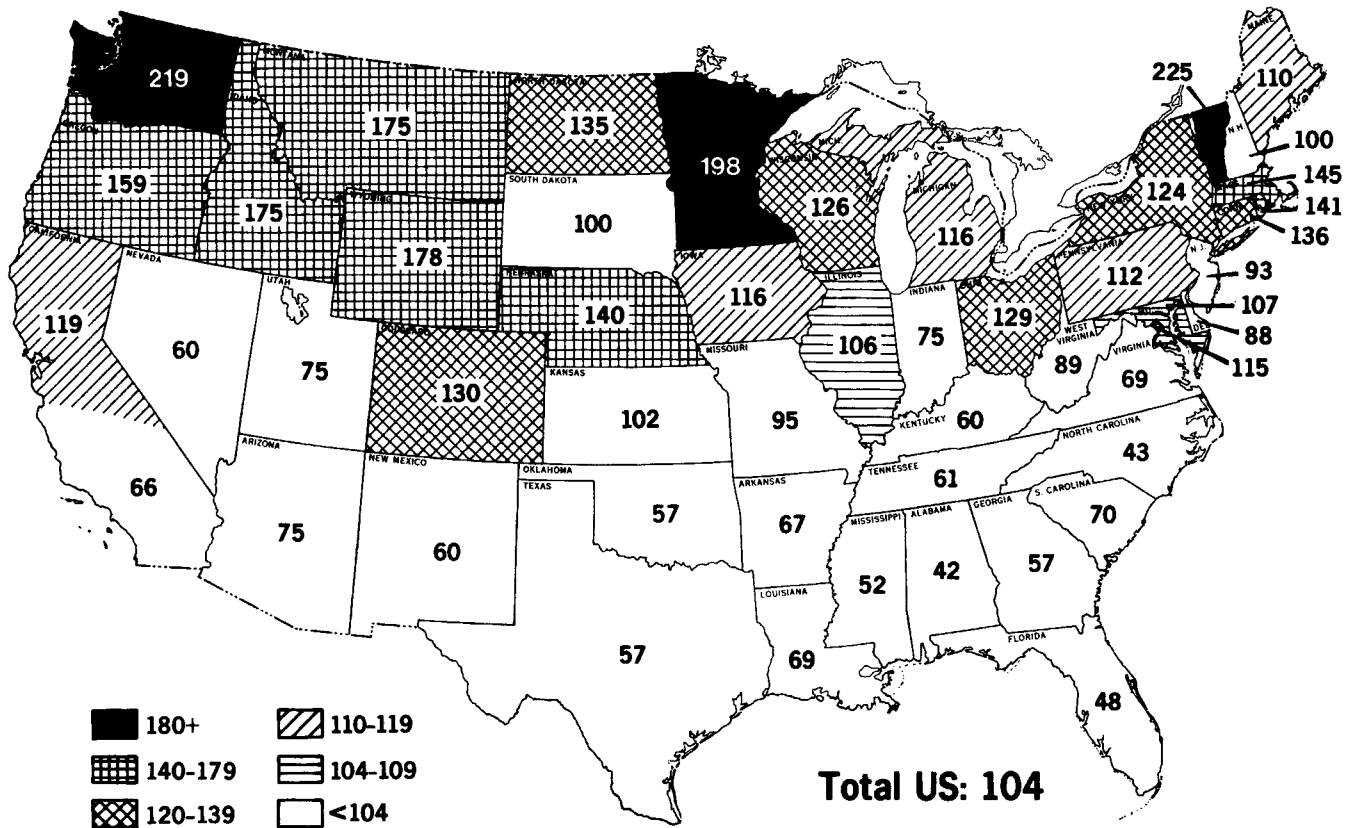


FIGURE 3-6

Case control ratios expressed as percentages for U.S. white male veterans of World War II according to state of residence at entry into active duty. Modified from Kurtzke et al., 1979 (30).

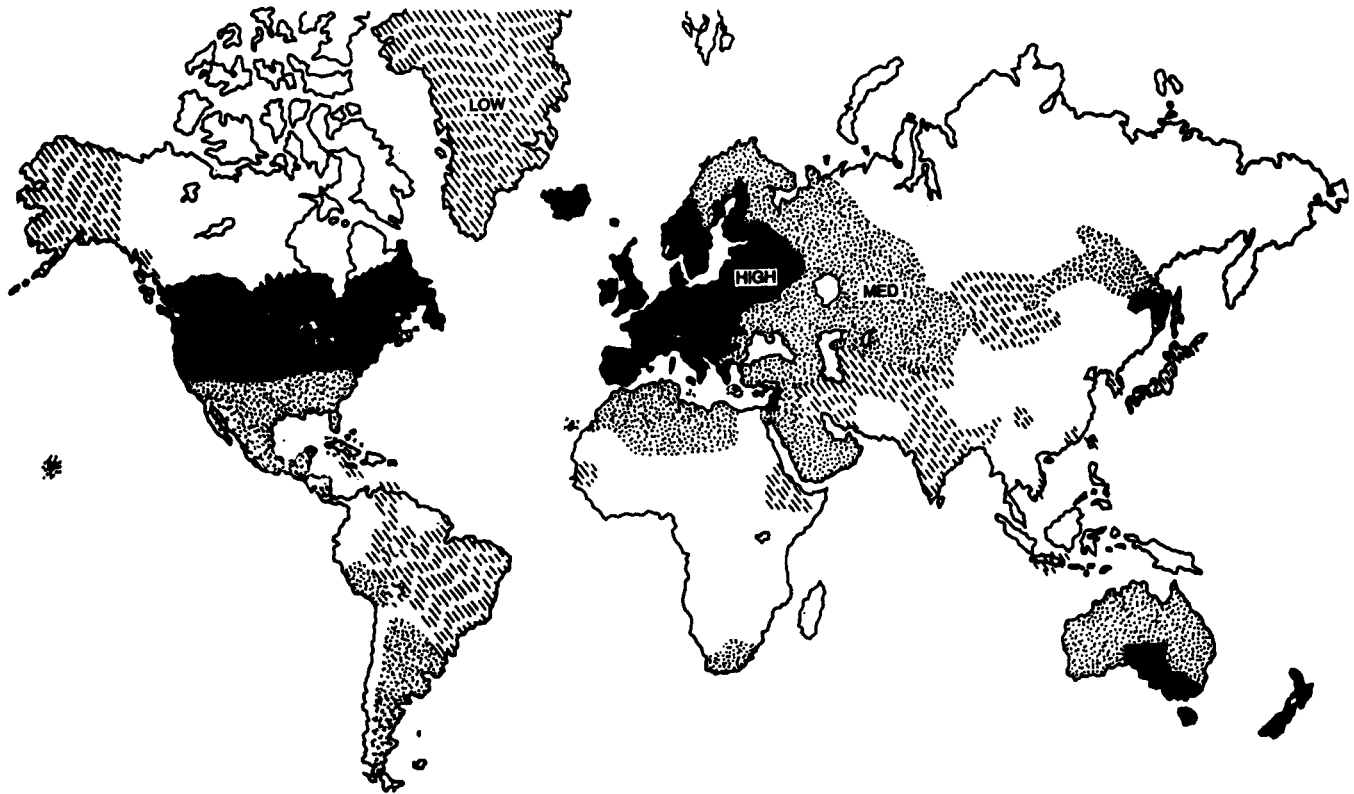


FIGURE 3-7

Worldwide distribution of MS as of 1998 with high (prevalence 30+; solid), medium (prevalence 5-29; dotted), and low (prevalence 0-4; dashed) regions defined. Blank areas are regions without data or people.

Marburg Variant

As noted previously, MS is a variable disease. At the far end of the clinical spectrum is an acute fulminant form called Marburg variant disease. This is most often a monophasic illness that occurs in young people and results in death within weeks to months. The first case in the literature, recorded in 1906, was a 30-year-old woman who died within a month of presentation (45). There have been a handful of other case reports, and in most instances the course has been rapidly progressive (46–48). Death generally occurs from brainstem involvement. The pathology is consistent with an acute MS process. It involves intense inflammation with diffuse infiltration by macrophages and to a lesser extent T cells (49). There is widespread often confluent demyelination, axonal damage, and edema, although multiple discrete lesions may also be found. Axon involvement is often extensive and more severe than in typical MS with actual necrosis. In one recent biopsy study the infiltrating macrophages showed a marked upregulation of messenger RNA coding for tumor necrosis factor α (TNF- α) and inducible nitric oxide synthase (iNOS), two factors that are known to damage myelin and oligodendrocytes as well as to cause conduction block (49). Infiltrating cells show marked expression of HLA class II antigens (50). In another recent autopsy study of a 27-year-old woman with a six-week course, CNS myelin basic protein was found to be developmentally immature and much less

PREGNANCY

Because MS affects so many women of childbearing age, pregnancy is a major gender-related issue. It is routine for patients to have questions not only about the effect of pregnancy on MS disease onset, activity, and prognosis, but also about whether MS in turn can affect the fetus and the birth process. Until 1949 pregnancy was considered to have a negative impact on MS and was discouraged. Over the next few years several studies were published that failed to confirm this widely held impression (29–31). Subsequent publications have addressed a variety of issues regarding pregnancy in MS (32–50). Overall, pregnancy does not increase the risk of developing MS. In fact, a recent Scandinavian study found that the risk of MS was higher for nulliparous women than for parous women, and that the risk ratio increased over time (51). The most compelling data on pregnancy and MS relate to the effect on disease activity. A recent European study of 254 women and 269 pregnancies noted that in the last trimester of pregnancy there was a 70 percent decline in the clinical relapse rate (52). This effect is more than twice as potent as the current disease-modifying therapies. This clinical benefit of late pregnancy is quite consistent with findings from a small study that reported a corresponding suppression of subclinical magnetic res-

Large placenta

Aspartame-Free Diet

Proponents for limiting aspartame claim that aspartame causes several medical conditions, including MS. They claim that there is a conspiracy between the pharmaceutical manufacturers and the FDA to keep aspartame on the market. Scientific evidence for these claims is lacking. Nonetheless, the Internet remains an active source of information to MS patients claiming the deleterious effects of aspartame.

Gluten-Free Diet

The gluten-free diet excludes wheat and rye because areas of the world that have a high volume of wheat and rye production and consumption also have a high incidence of MS. Studies on gluten-free diet have been uncontrolled, and this diet may result in inadequate protein intake. This diet is not recommended (11).

Allergen-Free Diet

Proponents of the allergen-free diet believe that MS is related to allergies to specific foods. After skin testing, certain foods are eliminated. No controlled studies on this diet have been published (11).

Evers Processed Food Elimination Diet

Joseph Evers proposed this diet for many diseases. This diet is based on the premise that the processing of food