

Fast Facts



Fast Facts: Multiple Sclerosis

George D Perkin and Jerry S Wolinsky

Second edition



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Declaration of Independence

This book is as balanced and as practical as we can make it.

Ideas for improvement are always welcome:

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Introduction

Until relatively recently, the diagnosis of multiple sclerosis (MS) was often subject to error. The advent of magnetic resonance imaging (MRI) made more accurate diagnosis possible, and for the first time it became possible to recognize the very early stages of the disease. In 2001, the International Panel on the Diagnosis of Multiple Sclerosis, chaired by Professor WI McDonald of the Royal College of Physicians, London, issued new diagnostic criteria that integrated the use of MRI findings to ensure rapid and accurate diagnosis of the disease. These criteria have recently undergone further review and revision, and are discussed in detail in Chapter 4.

Previously, the treatment of MS was largely confined to short-term injections or steroid tablets, alongside symptomatic measures. Now, the availability of interferon drugs and glatiramer acetate has enabled clinicians to alter the long-term natural history of the disease. Early data on natalizumab clearly indicate that an expanding armamentarium of more effective immunomodulatory agents based on the principles of molecular biology is on the way; however, such data also underscore the potential risks that immune manipulation may bring. This book gives a revised overview of the immunomodulatory drugs that reduce the risk of future attacks and may also slow the rate of acquisition of neurological dysfunction. It also covers steroid therapy for acute attacks and the range of treatments available for symptoms associated with the disease. There is updated information on pain management and discussion of the latest evidence on the role of cannabinoids.

The book examines the importance of a multidisciplinary team approach in providing MS patients with the best possible quality of life. Case histories punctuate the text and explore the lessons that can be learned from the experiences of patients coping with the disease.

We hope that this second edition of *Fast Facts: Multiple Sclerosis* will be a useful guide for all healthcare professionals working with patients who have this complex disease.

Multiple sclerosis (MS) is characterized by recurrent or chronically progressive neurological dysfunction. It is caused by perivenular inflammatory foci in the white matter of the central nervous system (CNS). Repeated episodes of inflammation result in characteristic widespread, demyelinated and sclerotic lesions, referred to as plaques, throughout the brain, optic nerves and spinal cord of affected individuals. An immune-mediated component is central to disease pathogenesis.

Epidemiology

MS is the most common non-traumatic, disabling neurological disease in young adults. Overall, the prevalence is about 100 cases per 100 000 people. This amounts to about 350 000 cases in the USA and Canada, and an almost equal number of cases in Europe, including the UK. However, the incidence of the disease varies markedly according to age, sex, location and genetic background.

Age, sex and ethnic origin. The age of onset peaks at about 30 years, with fewer than 10% of all cases starting before puberty or after the age of 55 years. Women are disproportionately represented in all patient series, with a ratio of about 2:1. White populations, particularly people of Scandinavian ancestry, have a high risk of the disease, though few ethnic groups are spared.

Geographic distribution. The disease shows a geographic gradient of prevalence, with more cases found at the northern latitudes of Europe and North America and at the southern latitudes of New Zealand and Australia (Figure 1.1). This variation strongly suggests the involvement of environmental factors in the pathogenesis of the disease. Despite research into possible environmental triggers, such as viral or bacterial infections, toxins, duration of sunlight, changes

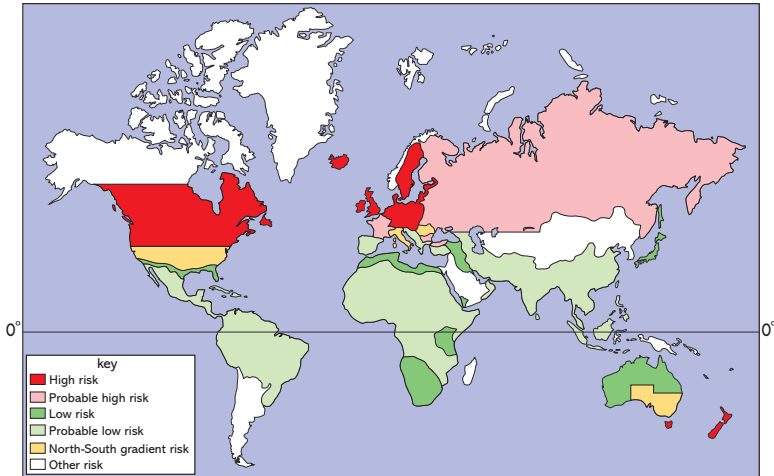


Figure 1.1 Geographic distribution of MS, showing patterns of risk in relation to region of residence. Areas of high risk are found at high latitudes. Reprinted from McAlpine et al. *Multiple Sclerosis: A Reappraisal*, 1965. Edinburgh: Livingstone. Copyright 1965, with permission from Elsevier.

in temperature and humidity, and diet, no specific environmental factor has been shown to cause MS.

Migration studies have shown that the risk of developing the disease can be attributed to the region of childhood residence. For example, it appears that an individual born in a high-risk area can acquire a lower risk if they relocate to a low-risk area before they reach 15 years of age. Reports of apparent disease epidemics in specific areas further support the hypothesis for a geographic influence on the disease.

Genetic factors. While increased MS risk is conferred by the *DRB1*1501 (DR2)* haplotype of the major histocompatibility complex, multiple genetic loci are likely to contribute interactively to the risk. Human leukocyte antigen (HLA)-DR molecules are critical in the immune system, where they present and process both foreign and self-antigens.

Table 1.1 gives an overview of the familial risk of the disease, which may be helpful when counseling family members of newly

3 The established condition

The features of established multiple sclerosis (MS) depend, to some extent, on the way in which the condition originally presented as well as its mode of progression. The disease course can be demonstrated in a visual format, in terms of the patient's disability against time, as shown in Figure 3.1.

For patients with benign MS, the established condition is, in a sense, not established at all. Even 15 or 20 years after presentation, these patients have little or no disability and little or no restriction of activity. In the UK at least, patients with benign MS seldom present themselves for medical attention.

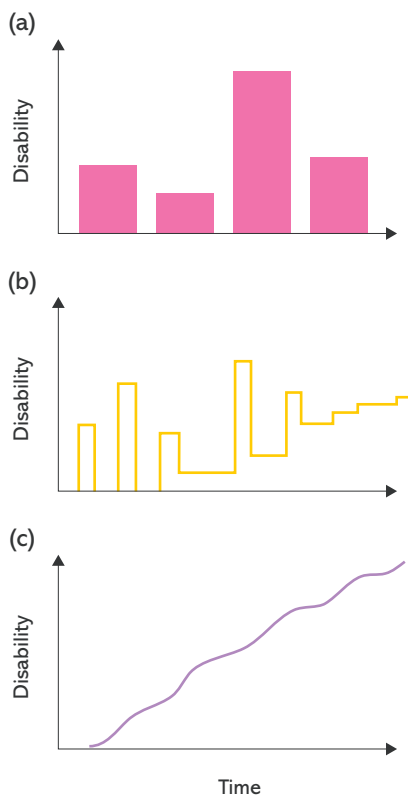


Figure 3.1 Relationship between severity of disability and duration of disease in (a) benign relapsing remitting MS, (b) relapsing remitting MS with secondary progression, and (c) primary progressive MS.

As discussed in Chapter 2, the majority of patients with MS present with a remitting relapsing form of the disease; however, many of these patients enter a secondary progressive phase, in which the frequency of relapses lessens, but residual disability emerges between attacks and then slowly progresses.

Most studies agree that relapse frequency is highest in the first few years of the disease. There is little evidence to show that relapse frequency influences outcome, but there are considerable data to indicate that the interval between the initial attack and the first relapse is significant; as this period lengthens, the likelihood of benign MS increases.

Eventually, in both primary progressive and secondary progressive MS, a fairly consistent pattern emerges, with an attendant level of disability (Figure 3.2). However, data on the disease's rate of progression and its effect on lifespan vary considerably.

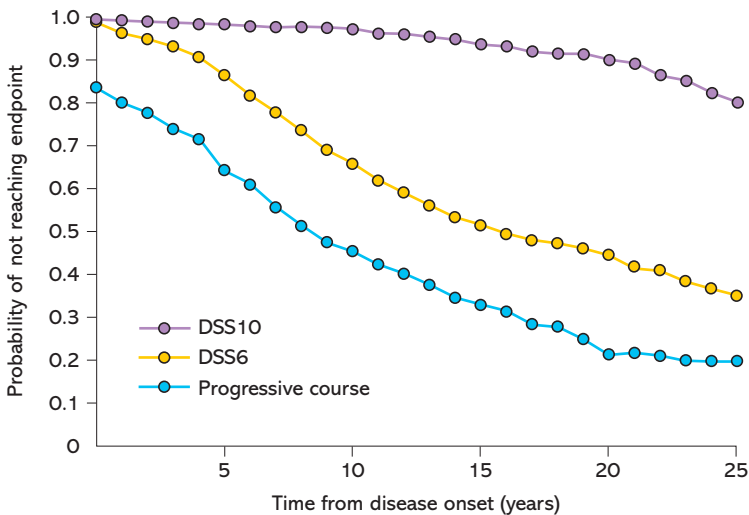


Figure 3.2 The rate at which certain endpoints are reached during the course of MS. Disability Status Score (DSS) 10, death related to the MS process; DSS 6, walking 100 m (330 ft) with assistance (e.g. with a cane or walker). Adapted from Runmarker and Andersen. 1993.