Multiple Sclerosis
Epidemiologic, Clinical, and Therapeutic Aspects

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KEYWORDS

• Multiple sclerosis • Symptoms • Treatment

KEY POINTS

- Multiple sclerosis is a chronic autoimmune and degenerative disease of the central nervous system that affects young people, with a prevalence of 33 per 100,000.
- Multiple sclerosis will develop in genetically susceptible individuals exposed to different triggering environmental factors.
- Based on symptoms onset and their evolution, different phenotypes are described. About 15% of patients will present with a primary progressive course and 85% with a relapsing–remitting course.
- An increasing number of disease-modifying treatments has emerged. Although encouraging, the broad number challenges the clinical neurologist because each treatment has its own risk–benefit profile.
- Patients should be involved in the decision-making process to ensure a good treatment and safety-monitoring adherence.

INTRODUCTION AND EPIDEMIOLOGY

Multiple sclerosis (MS) is a chronic autoimmune disease of the central nervous system (CNS) in which inflammation, demyelination, and axonal loss occurs from the very early stages of the disease. It mainly affects young people, between 20 and 40 years of age, with a female predominance.[1,2]

The global median prevalence of MS is 33 per 100,000 people, with a great variance between different countries. North America and Europe have the highest prevalence (with 140 and 108 per 100,000 people, respectively), and Asia and sub-Saharan Africa countries have the lowest prevalence (2.2 and 2.1 per 100,000 people, respectively).[3]

The ultimate cause of MS is unknown and a multifactorial etiology is accepted. Thus, MS will develop in genetically susceptible individuals exposed to different triggering environmental factors (such as Epstein–Barr virus, tobacco use, and vitamin D).[1–4]

CLINICAL MANIFESTATION AND NATURAL COURSE

MS symptoms vary depending on the area of the CNS affected. Based on symptoms onset and their evolution, 4 MS phenotypes were initially described: relapsing–remitting MS (RRMS), secondary-progressive MS, primary-progressive MS, and relapsing-progressive MS.[5] This classification has been recently reviewed: this last phenotype (relapsing-progressive MS) has been eliminated and the clinically isolated syndrome (CIS) has been added into the classification[6] (**Fig. 1**). Moreover, additional descriptions of clinical and radiologic disease activity was defined to add information into a static classification based

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Neuroimag Clin N Am 27 (2017) 195–204
http://dx.doi.org/10.1016/j.nic.2016.12.001

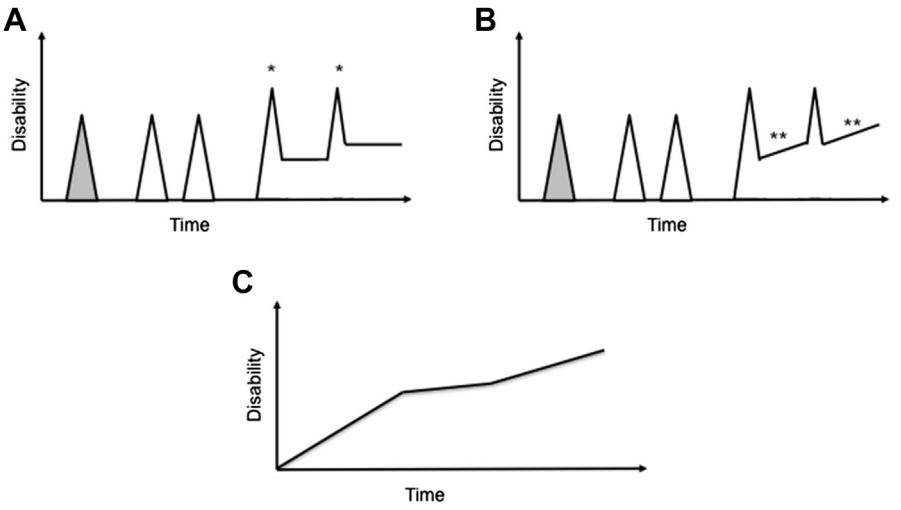

Fig. 1. Multiple sclerosis (MS) phenotypes. The figure shows the different MS phenotypes. In relapsing-remitting MS (*A*), after the first event or clinically isolated syndrome (*light gray*) new relapses will occur. The recovery of these relapses may be complete or partial (*asterisk*). After this initial period, some patients enter a progressive phase of the disease (*double asterisks*), with or without superimposed relapses, that constitutes the secondary progressive MS (*B*). In primary progressive MS (*C*), patients present a sustained and progressive neurologic impairment since onset. (*Adapted from* Lublin FD, Reingold SC. Defining the clinical course of multiple sclerosis results of an international survey. Neurology 1996;46(4):907–11; with permission.)

on symptoms evolution. Thus, patients may be also classified as presenting with or without disease activity based on the presence (or absence) of relapses, progression, new or enlarging T2 lesions, and gadolinium (Gd)-enhancing lesions.[6]

About 15% of patients with MS present with a primary-progressive MS. This phenotype is characterized by a slow progressive neurologic disability from the beginning of the disease (see **Fig. 1**). Most of these patients (80%) present with a gait disorder owing to an spastic paraparesis, which may be accompanied with sensory symptoms and sphincter dysfunction.[7]

In the majority of patients with MS (85%), the disease starts with the RRMS phenotype[8] and they develop relapses (defined as a subacute onset of new neurologic symptoms that last for at least 24 hours in the absence of fever or infection) followed by symptom recovery (see **Fig. 1**). CIS is a term that refers to the first clinical manifestation of the disease that by definition is isolated in time or not preceded by any neurologic event. It usually affects the optic nerves (20%), the brainstem (10%–20%), or the spinal cord (40%) causing an optic neuritis, a brainstem syndrome, or an incomplete transverse myelitis, respectively[8,9] (**Table 1**). These symptoms may also occur in subsequent relapses. Relapse recovery may be complete or lead to neurologic sequelae; in this last scenario, other neurologic signs and symptoms may appear owing to irreversible CNS damage[2] (see **Table 1**). The accumulation of disability is

Table 1
Neurologic symptoms of multiple sclerosis

Relapse neurologic symptoms	
Optic nerve	Mononuclear painful vision loss
Spinal cord	Hemiparesis, mono/paraparesis Hypoesthesia, dysesthesia, parasthesia Urinary and/or fecal sphincter dysfunction
Brainstem and cerebellum	Diplopia, oscillopsy Vertigo Gait ataxia, dismetria Intentional/Postural tremor Facial paresis and/or hypoesthesia
Cerebral hemisphere	Facio–brachial–crural hemiparesis Facio–brachial–crural hemihypoesthesia
Other clinical manifestations	Paroxistic symptoms Painful spasms/spasticity Dysarthria/dysphagia Neuropathic pain Sexual dysfunction Spastic gait Ataxic gait Fatigue Cognitive impairment Depression Seizures