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Multiple Sclerosis

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Multiple sclerosis is characterized by central nervous system lesions causing neurologic dysfunction and other conditions, such as fatigue, pain, depression, and anxiety.

- Early disease is usually relapsing and remitting, but most persons develop secondary-progressive disease over time. No treatment has been shown to affect long-term outcome.
- Irreversible disability can occur, but life expectancy is generally not affected.

In persons with relapsing and remitting multiple sclerosis, glatiramer and azathioprine may reduce relapse rates, but have not been shown to affect disease progression. Toxicity associated with azathioprine means that 10 percent of persons cannot tolerate it at therapeutic doses.

- Interferon beta may reduce exacerbations and disease progression in relapsing and remitting multiple sclerosis, and may reduce the risk of conversion to clinically definite multiple sclerosis in persons experiencing a first demyelinating event.
- Intravenous immune globulin may prevent relapse after a first demyelinating event, but we do not know whether it is effective in persons with relapsing and remitting disease.
- Mitoxantrone may reduce exacerbations and disease progression.
- Natalizumab may increase the proportion of persons who are relapse-free at two years in relapsing and remitting multiple sclerosis.

Caution: Interferon beta and mitoxantrone have been associated with serious adverse effects. Natalizumab has been associated with progressive multifocal leukoencephalopathy, and the long-term benefits and risks are still unknown.

We do not know whether interferon beta, methotrexate, or intravenous immune globulin delays disease progression in persons who have secondary-progressive multiple sclerosis, because studies have given conflicting results.

Corticosteroids (methylprednisolone or corticotropin) may improve symptoms in persons with an acute exacerbation of multiple sclerosis compared with placebo.

- We do not know whether plasma exchange, intravenous immune globulin, or natalizumab is beneficial.
- We do not know whether amantadine, behavioral modification, modafinil, or exercise reduces fatigue. Exercise may help to maintain strength, fitness, and mobility, and to improve quality of life, but studies have been difficult to compare.
- We do not know whether botulinum toxin, gabapentin, intrathecal baclofen, oral antispasmodic drugs, or physiotherapy improves spasticity.

Inpatient rehabilitation may improve function in the short term, but we do not know whether outpatient rehabilitation is also of benefit.

Definition

Multiple sclerosis is a chronic inflammatory disease of the central nervous system. Diagnosis requires evidence of lesions that are separated in both time and space, and the exclusion of other inflammatory, structural, or hereditary conditions that might give a similar clinical picture.

The disease takes three main forms: relapsing and remitting multiple sclerosis, which is characterized by episodes of neurologic dysfunction interspersed with periods of stability; primary-progressive multiple sclerosis, in which progressive neurologic disability occurs from the outset; and secondary-progressive multiple sclerosis,

Clinical Questions

What are the effects of interventions aimed at reducing relapse rates and disability in persons with multiple sclerosis?	
Likely to be beneficial	Glatiramer (parenteral) in persons with relapsing and remitting or progressive multiple sclerosis
	Interferon beta in persons having a first demyelinating event or with relapsing and remitting multiple sclerosis
	Intravenous immune globulin in persons having a first demyelinating event
Trade-off between benefits and harms	Azathioprine
	Mitoxantrone in persons with relapsing and remitting multiple sclerosis
	Natalizumab in persons with relapsing and remitting multiple sclerosis
Unknown effectiveness	Interferon beta in persons with secondary-progressive multiple sclerosis
	Intravenous immune globulin in persons with relapsing and remitting or secondary-progressive multiple sclerosis
	Methotrexate
What are the effects of interventions to improve symptoms during acute relapse in persons with multiple sclerosis?	
Likely to be beneficial	Corticosteroids (methylprednisolone, corticotropin, or dexamethasone) vs. placebo
Unknown effectiveness	Corticosteroids (methylprednisolone, corticotropin, or dexamethasone) vs. each other (insufficient evidence to compare effectiveness)
	Intravenous immune globulin in persons with acute relapse of multiple sclerosis
	Natalizumab in persons with acute relapse of multiple sclerosis
	Plasma exchange
What are the effects of treatments for fatigue in persons with multiple sclerosis?	
Unknown effectiveness	Amantadine
	Behavioral modification
	Exercise
	Modafinil
What are the effects of treatments for spasticity in persons with multiple sclerosis?	
Unknown effectiveness	Baclofen (intrathecal)
	Botulinum toxin
	Drug treatments (oral) other than gabapentin
	Gabapentin
	Physiotherapy
What are the effects of multidisciplinary care on disability in persons with multiple sclerosis?	
Unknown effectiveness	Inpatient rehabilitation
	Outpatient rehabilitation

in which progressive neurologic disability occurs later in the course of the disease. Axonal loss is the major determinant of the accumulation of irreversible (progressive) disability as a result of inflammation during both the relapsing and remitting and progressive phases of multiple sclerosis, but also because of possible neurodegeneration through loss of trophic support.

The emergence of treatments for multiple sclerosis has led to the recognition of a first demyelinating event or clinically isolated syndrome, a single episode of neurologic dysfunction lasting for more than 24 hours, which can be a prelude to multiple sclerosis. Characteristic episodes include optic neuritis, solitary brainstem lesions, and transverse myelitis that, when associated with magnetic resonance imaging changes, result in a 30 to 70 percent risk of developing multiple sclerosis.

Increasingly recognized are other demyelinating syndromes thought to be distinct from multiple sclerosis; these include Devic disease (neuromyelitis optica), relapsing optic neuritis, and relapsing myelitis. Other than episodes of neurologic dysfunction, chronic symptoms produce much of the disability in multiple sclerosis. Symptoms include fatigue (the main symptom in two-thirds of individuals), spasticity, bladder/bowel problems, ataxia/tremor, visual problems, pain, depression/anxiety, dysphagia, and sexual dysfunction.

Incidence and Prevalence

Prevalence varies with geography and race. It is highest in white populations in temperate regions. In Europe and North America, the prevalence is one per 800 persons, with an annual incidence of two to 10 per 100,000, making multiple sclerosis the most common cause of neurologic disability in young adults. Age of onset is broad, peaking between 20 and 40 years of age.

Etiology and Risk Factors

The cause of multiple sclerosis remains unclear, although current evidence suggests that it is an autoimmune disorder of the central nervous system resulting from an environmental stimulus in genetically susceptible individuals. Multiple sclerosis is currently regarded as a single disorder with clinical variants, but there is some evidence that it may consist of several related disorders with distinct immunologic, pathologic, and genetic features.

Prognosis

In 90 percent of persons, early disease is relapsing and remitting. Although some persons follow a relatively benign course over many years, most develop secondary-progressive disease, usually six to 10 years after onset. In 10 percent of persons, the initial disease is primary-progressive. Apart from a minority of persons with "aggressive" multiple sclerosis, life expectancy is not greatly affected, and the disease course is often of more than 30 years' duration.

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