Multiple Sclerosis:
A Summary

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Did you know...

Researchers performing population-based studies report that more than 100 Canadians per 100,000 have MS and that the prevalence of MS is substantially greater in Canada as compared to other developed countries.[1-3]

Point #1

Multiple sclerosis (MS) is a chronic, neurologic disease that is characterized by targeted destruction of myelin sheaths that surround the axons of the neurons in the central nervous system (CNS).

Point #2

At present, the autoimmune theory represents the most plausible and widely accepted explanation of disease pathology.

According to the autoimmune theory, circulating T-cells in the periphery (blood) become activated upon exposure to viruses and bacteria that share a similar amino acid sequence as that cont... well-kno... ...necrosis factor ...which are pivotal in the pathogenic immune response directed against CNS myelin. Furthermore, these cytokines are involved in the up-regulation of vascular lectins (ICAM-1, VCAM-1), which facilitate T-cell adhesion and migration through the blood brain barrier (BBB) into the CNS.

Once inside the CNS ... cytokines and che... by the T... ...per- ...disability. The evi- ...indicates that axonal destruction begins early in the disease course and is irreversible. On the basis of this information, disease treatment should be implemented in the early disease stage, if at all possible.

Point #3

The most characteristic clinical course of MS is relapsing-remitting, defined by disease relapses with full or partial recovery.

The periods between disease relapses are characterized by a lack of disease progression, where each relapse is defined as the acute or subacute onset of clinical dysfunction with minimal duration of at least twenty-four hours.

The other three forms of MS are…

1) Primary-progressive MS: Progression from the onset of the disease.
2) Secondary-progressive MS: Initially relapsing-remitting disease course followed by progression with or without relapses.
3) Progressive-relapsing MS: Progressive from the onset with clear acute relapses.

MS info...

Despite the inherent variability throughout the various geographical regions of Canada, the prevalence of MS in Brandon, Manitoba and Crowsnest Pass, Alberta reported counts as high as 203 per 100,000, representing a two-fold increase compared to most other areas of Canada as well as in other developed countries.[1-3]

Point #4

The signs or symptoms indicative of MS consist predominantly of:

- dysfunction of the optic nerve (such as optic neuritis) or corticospinal tract causing weakness,
- dysfunction causing problems with cerebellar co-ordination and/or
- long sensory tracts causing numbness and tingling, which is the most frequent initial presentation.

Point #5

The diagnosis of MS remains the clinical diagnosis. The neurologic examination and/or history must show evidence of at least two lesions disseminated in time and space in the CNS.

However, the most important tool to support the diagnosis of MS is magnetic resonance imaging (MRI). It is the most sensitive technique for visualizing lesions in the CNS. Its value in diagnosis provides the actual evidence of dissemination of lesions in space.

Cerebral spinal fluid samples and evoked potentials can also be a valuable addition to clinical information in the diagnosis of MS.

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AFFIRM findings...

AFFIRM was a randomized, double-blind, placebo-controlled, phase 3 trial involving the use of natalizumab in patients diagnosed with relapsing-remitting MS.

The treatment was associated with a 42% reduction (P = .0002) in the risk of disability progression and a 68% reduction in the rate of clinical relapses.[4] Unfortunately, treatment was voluntarily suspended in the US market and in all ongoing clinical trials.

The decision to voluntarily suspend treatment was based on reports of progressive multifocal leukoencephalopathy (PML), which is a frequently fatal, virally induced, demyelinating disease of the central nervous system in patients who develop PML.

The safety evaluation of this medication is currently ongoing.

Point #6

Recently, major advances have been made in the development of disease-modifying therapy for relapsing-remitting MS. Currently, available treatments, such as IFN-b, glatiramer acetate and mitoxantrone, have been found to have beneficial effects on disease activity. They decrease the frequency of relapses and the development of new T2 MRI lesions and have varied effects on disease progression.

Advances in biotechnology and multiple clinical trials have led to the development of new therapies for MS, one of which being natalizumab—a recombinant a4-integrin antibody to human a4B1 integrin. This drug is the first a4-integrin antagonist in its class of selective adhesion molecule inhibitors.

Natalizumab binds to a4 integrin on the surface of the activated T-cell and other mononuclear leukocytes, preventing adhesion between the T-cell and the endothelial cell.

Subsequently, this causes failure of mononuclear leukocyte migration across the BBB and initiation of inflammation in the CNS.

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References
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3. The Geography of Multiple Sclerosis: http://www.mult-sclerosis.org/facts.htt. Accessed on: February 24, 2005.
4. Multiple Sclerosis Express Report: Multiple Sclerosis—Continuum of Care. Based on the Date Presented at the 57th Annual Meeting of the American Academy of Neurology, April 9-16, 2005, Miami Beach, Florida.

Further references available—please contact *The Canadian Journal of CME* at **cme@sta.ca**.