Multiple sclerosis

Prof. M. GAVRILIUC

Multiple Sclerosis

Multiple? **Disseminated!**

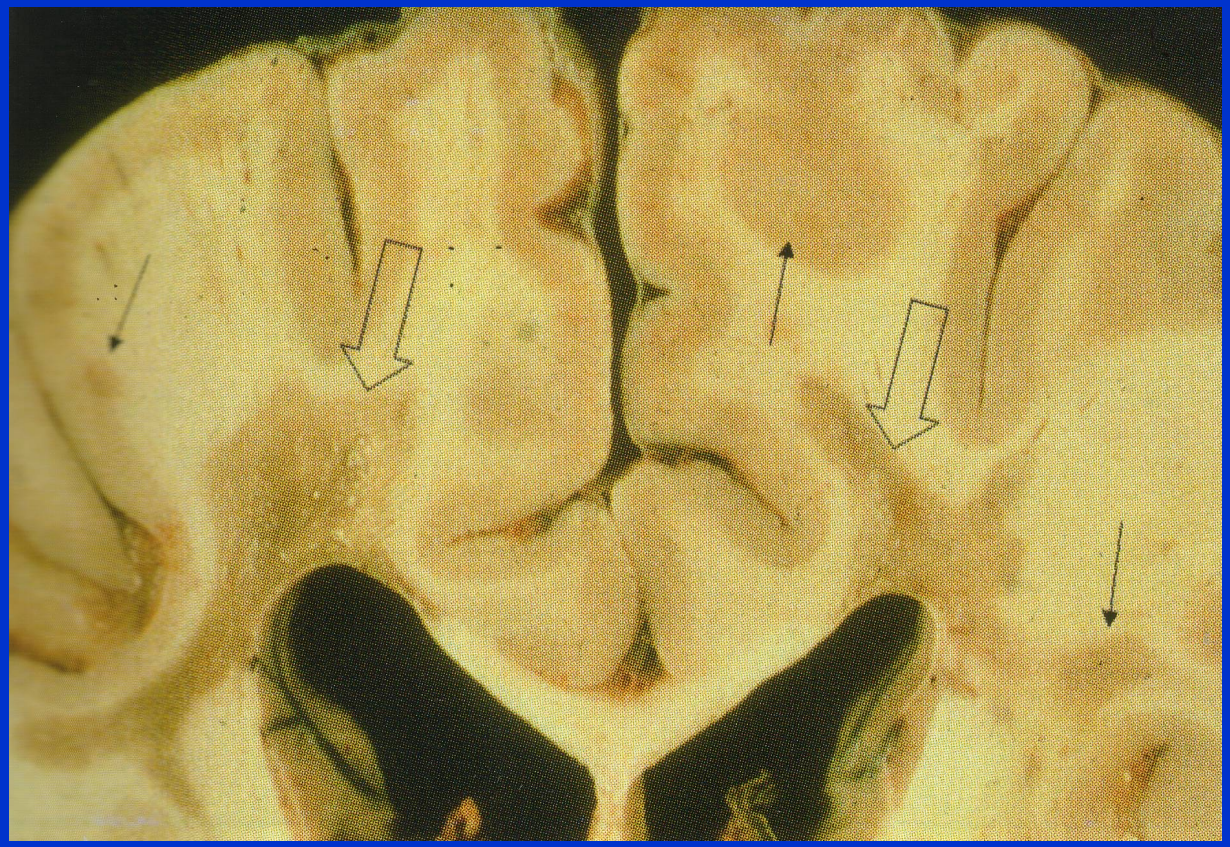
Sclerosis? ***Demyelinating Plaques evolution in*** **Scar / Cicatrice**

Where?

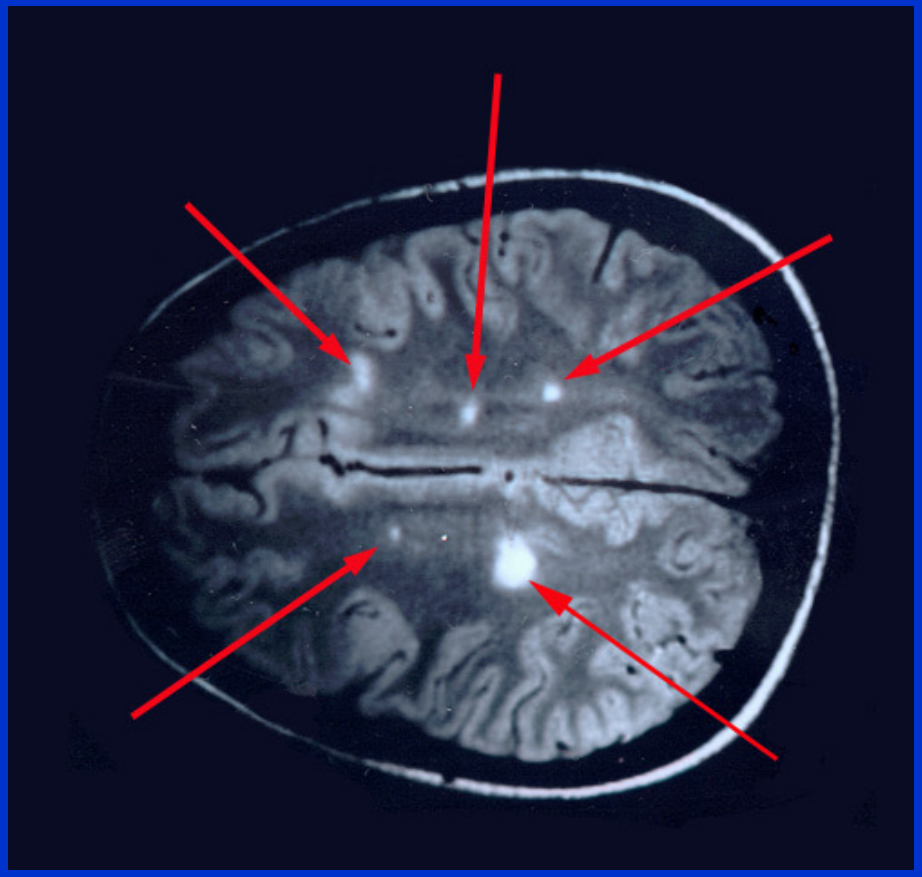
Everywhere: CNS and/or PNS!

PATHOLOGY

- Gross appearance of the MS brain autopsy: coronal section of a brain from an MS patient.
- Note the following: (1) enlarged lateral ventricles, (2) bilateral periventricular (dark brown) confluent plaques (open arrows), (3) scattered (dark brown) plaques in the hemispheric white matter bilaterally (small arrows).



Demyelination in Cerebral Hemispheres - MRI Scan



Overview

- Characterized by patches of **demyelination** in the brain and spinal cord, resulting in multiple neurological symptoms
- Autoimmune disorder of the CNS

Symptoms

- Weakness and clumsiness Stiffness and gait disturbances
- Visual defects
- Mental defects, including lack of judgment, emotional liability, sudden weeping or laughter

Overview

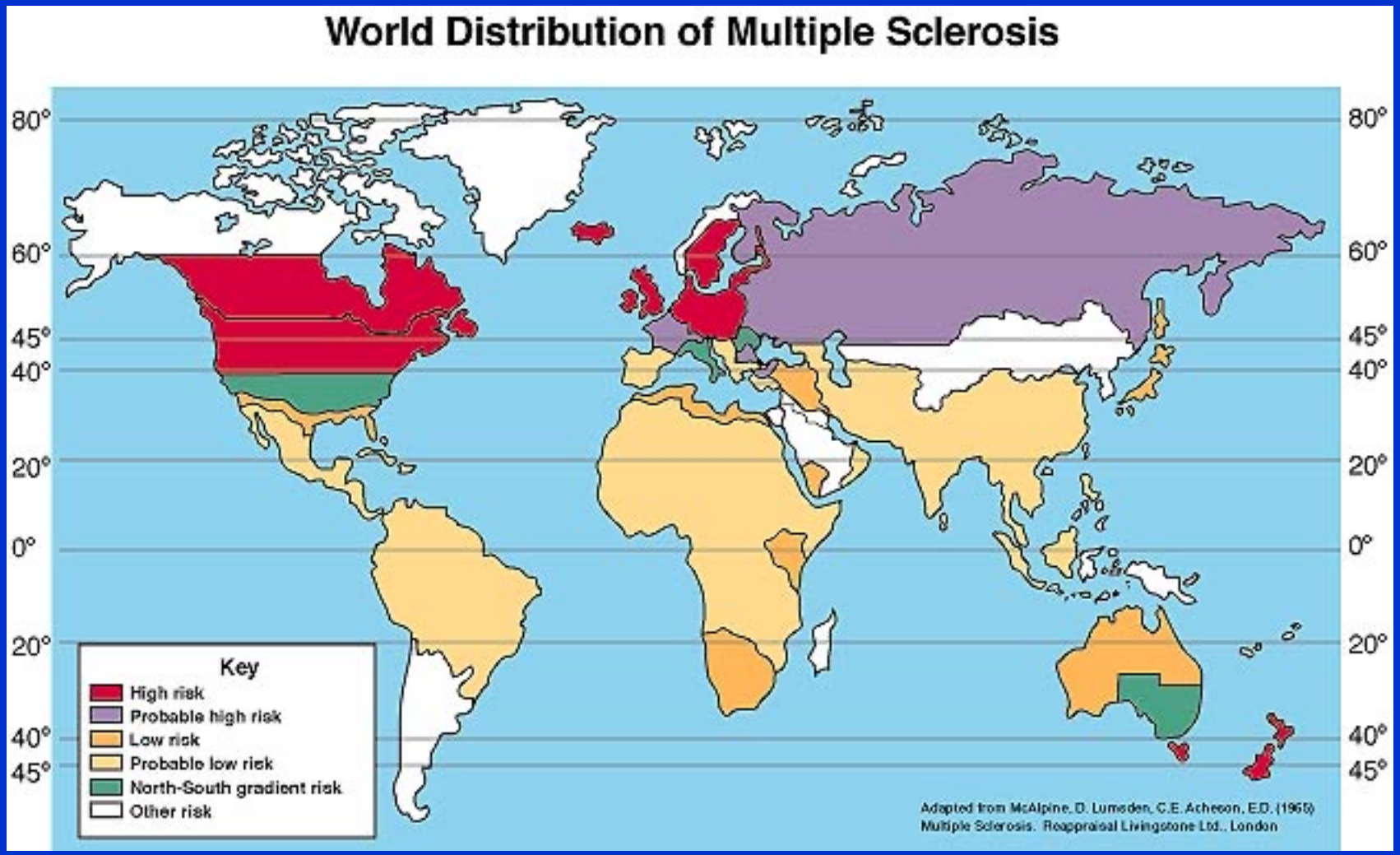
Multiple Sclerosis (**MS**) is a chronic disease of the central nervous system, which predominantly affects young adults during their most productive years. Viral and autoimmune etiologies are postulated. Genetic and environmental factors are known to contribute to MS, but a specific cause for this disease is not identified.

Disseminated white matter lesions of the CNS were first described by a French neurologist Charcot in late XIX. century. On histological sections these lesions were demonstrated to contain **perivascular inflammation and demyelination**. These features now are pathological hallmarks for MS.

Multiple sclerosis affects around 2.5 million people worldwide: it is one of the most common neurological disorders and cause of disability of young adults, especially in Europe and North America. There is a lack of epidemiological studies from Asia where the prevalence is reported to be low, though, with the availability of more neurologists and magnetic resonance imaging, a larger number of patients are being diagnosed.

MS: epidemiology

- Affects mainly Caucasians (N. Europe)
- Most common neurodegenerative disease of young adults (1 per 400)
- Average age at onset 28(f)/30(m) years.
- **Female : male ratio = 2:1**
- Etiology – Unknown
- Autoimmune attack (of T cells and B cells) against **oligodendrocytes**


World Distribution of Multiple Sclerosis
80°
60°
45°
40°
20°
0°
20°
40°
45°
Key
High risk
Probable high risk
Low risk
Probable low risk
North-South gradient risk
Other risk
Adapted from McAlpine, D. Lumsden, C.E. Acheson, E.D. (1965)
Multiple Sclerosis. Reappraisal Livingstone Ltd., London

MS in Israel

(...) However, analysis of subgroups suggested that the European immigrants to Israel had a higher socio-economic status than Afro-Asian immigrants. As multiple sclerosis has been shown to be five to 10 times more prevalent in Europeans than Afro-Asian in Israel (...). Further analysis suggested that the degree of urbanization of a region might influence the susceptibility of different socio-economic groups to multiple sclerosis. It was speculated that in rural regions, those individuals with lower socio-economic status might be more susceptible, whereas in urbanized regions those from higher socio-economic strata may be more susceptible.

Antonovsky A., Leibowitz U., Medalie J. M. *et al.* Epidemiological study of multiple sclerosis in Israel. *J Neurol Neurosurg Psychiatry.* 1967 Feb; 30(1): 1-6.

Multiple sclerosis frequency in Israel's diverse populations

Results: Prevalence rate of MS per 10^5 population on June 30, 2000, for each of these groups in the order listed was 61.6, 53.7, and 27.9 for the Jewish groups and 35.3, 14.7, 10.9, and 17.3 for the non-Jewish groups. Three tiers in MS prevalence were apparent. The highest rates were in Israeli-born Jews and in Jewish immigrants from Europe/America (significantly higher in the former than the latter). Jewish immigrants from African/Asian countries and Christian Arabs had intermediate MS rates (significantly lower than in the first two groups but not significantly different from each other). Moslem Arabs, Druze, and Bedouins had the lowest rates of MS (significantly lower than in the intermediate group but not significantly different from each other).

Conclusion: Diverse ethnic groups living in the same geographic area may have significantly different frequencies of MS.

Alter M, Kahana E, Zilber N, *et al.* *Neurology* April 11, 2006 vol. 66 no. 7 1061-1066.

Israel Multiple Sclerosis Society

The Israel Multiple Sclerosis Society is a non – profit organization, whose objectives are to provide support and treatment required by persons with multiple sclerosis (MS) and their families, who number over 5,000 persons.

For more information: http://www.mssociety.org.il/

يوم التصلب المتعدد العالمي

يوم توعية للأشخاص الذين يعيشون مع المرض

ستة آلاف وجه للتصلّب المتعدد

لأننا كثيرون! موحّدون في مواجهة التصلّب المتعدد (MS)

إذاً... ما موضوع هذا المعرض؟ همّه أن نكون جزءًا من المجتمع...
مجتمع غير مُسَيّج بتلك التسخيصات "الجميلة"
التي تبتسم دائما وتنتصر دائما، والتي تحبّ وسائل الإعلام تقديمها لنا!
إنه معرض من أجل النصف الثاني... أولئك الذين يشعرون أحياناً بأنهم غير مرغوبين...
أولئك الذين يُسمّون مرضى، مساكين، حُرْجًا، مقعدين على كرسي حجلات، أو "مجرد"
أشخاص غير ملائمين...

لكن دعونا نسمّي أنفسنا: الأبطال المميّزين! لأننا نقع، ولكننا نقف من جديد!
لنقف موحّدين في مواجهة هذا المرض صاحب آلاف الوجوه...!
ستكون هذه منصتنا... وسنبدأ بوجوهنا وأسرارنا...
الهدف هو: ٦٠٠٠ بطل مميّز من كل أنحاء إسرائيل!
تم خلال هذه الحملة جمع وترتيب البطاقات، العبارات والبوستات ضمن عرض تقديمي عنوانه:
«سري الأبيض – رحمة، أمل وتفهّم»
(نشرنا صورا مظلّلة للأبطال المميّزين!)

الأبطال المميّزون بحاجة لدعمكم! وسواء تبرعتم أم لا. رجاءً عمّموا البشرى
مع شكرنا الجزيل!
اضغطوا هنا لمشاهدة العرض التقديمي للبطاقات: التصلب وسري الدفين

ETIOLOGY

There appears to be an "autoimmune" attack against myelin and myelin-forming cells in the brain and spinal cord. Multiple etiologies for multiple sclerosis have been proposed. These include (1) viruses; (2) bacteria; (3) defective function or repair in oligodendroglia; (4) diet (affects membrane composition, macrophage function, and prostaglandin synthesis); (5) genetic (predisposition to respond to brain antigens, decreased control of the immune response to brain antigens); and (6) various other mechanisms (toxins, endocrine / catecholamine /stress interrelations).

ETIOLOGY

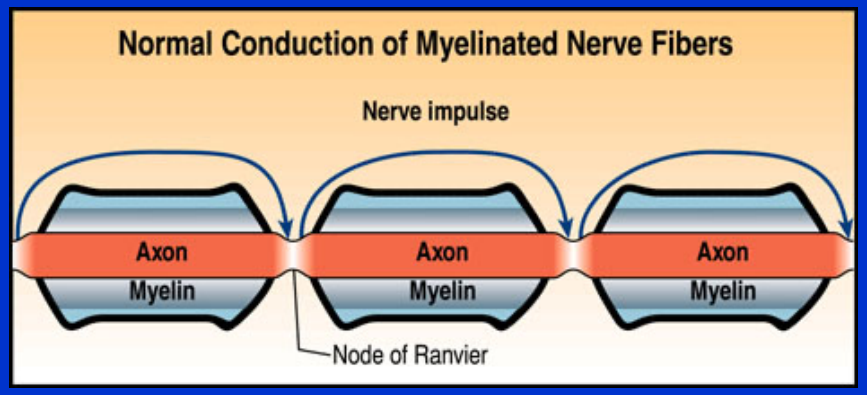
Despite intensive efforts at finding the source of the disease, no etiologic agent for MS has been identified. The disease presumably can be exacerbated by hormonal changes during the postpartum period. Some argue that MS could be a heterogeneous disorder triggered by several different environmental agents. In fact, only 1 of every 4 MS attacks is associated with an intercurrent infection.

ROLE OF MYELIN

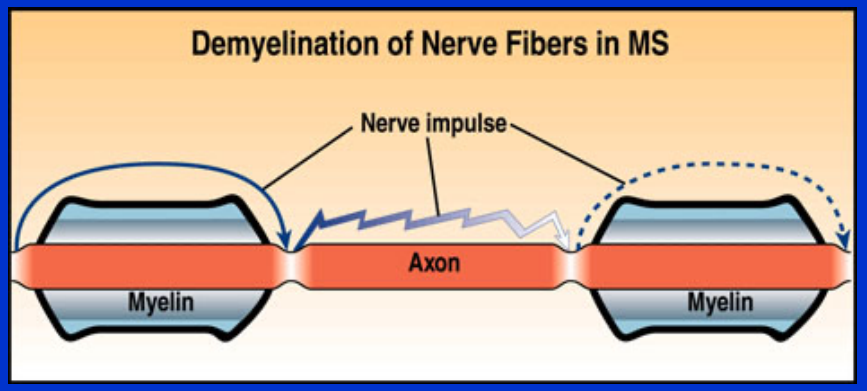
Myelin provides insulation for axons and is necessary for saltatory conduction. It is composed of tightly wrapped lipid bilayers with specialized protein constituents. Peripheral nervous system (PNS) myelin is formed by the extension of Schwann cells, and central nervous system (CNS) myelin is produced by oligodendrocytes.

ROLE OF MYELIN

Normal conduction



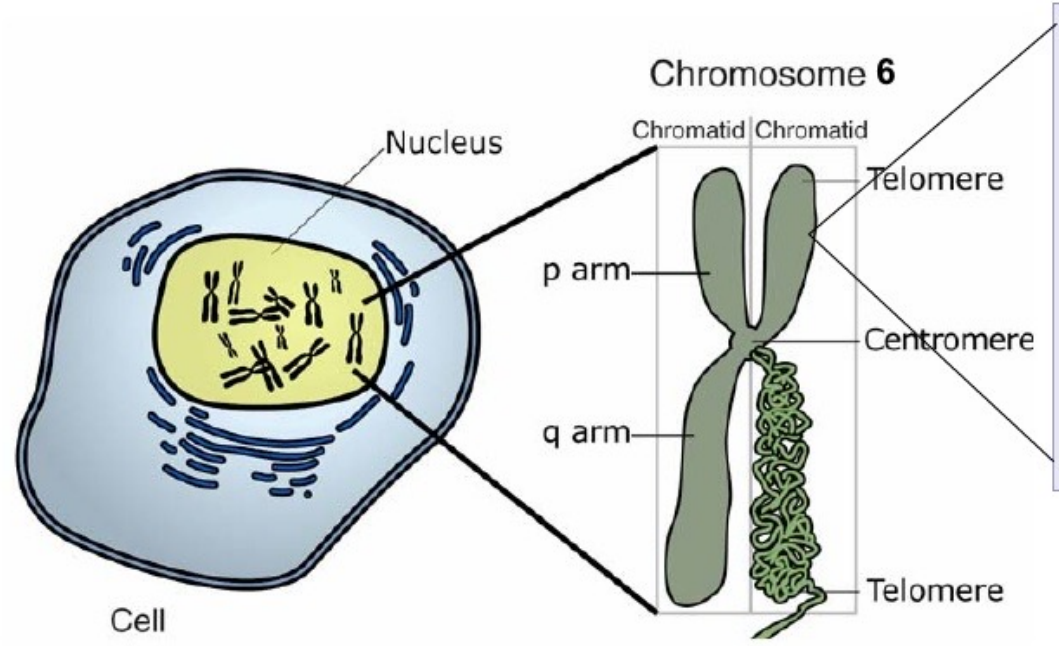
Conduction with Demyelination in MS



PATOPHYSIOLOGY

MS is characterized by perivenular infiltration of lymphocytes and macrophages in the parenchyma of the brain, brain stem, optic nerves, and spinal cord. Expression of adhesion molecules on the surface seems to underlie the ability of these inflammatory cells to penetrate the blood-brain barrier. The elevated immunoglobulin G (IgG) level in the cerebrospinal fluid (CSF), which can be demonstrated by an oligoclonal band pattern on electrophoresis, suggests an important humoral (ie, B cell activation) component to MS. In fact, variable degrees of antibody-producing plasma cell infiltration have been demonstrated in MS lesions

PATOPHYSIOLOGY



- The **major histocompatibility complex** (**MHC**)
  - **Class I, II, & III**
- A cluster of genes encoding cell-surface **antigen-presenting proteins**

The major histocompatibility complex (MHC)

- Plays pivotal role in the immune system
- Contains **140** genes coding for **class I**, **II**, and **III** proteins
- Found on antigen-presenting cells (**APCs**)
- They display an **epitope** of a foreign antigen to T cells, via the T cell receptors (TCRs)
- **T cells** should ignore **self peptides** while reacting appropriately to the **foreign peptides**
- **A subset of genes in MHC region implicated in MS**

MHC Class II

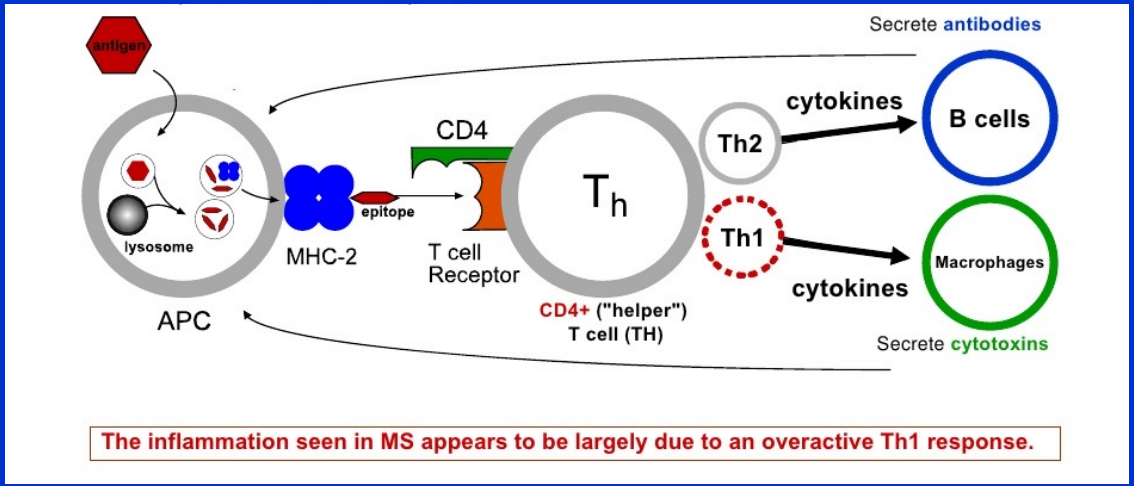
Found on specialized antigen-presenting cells (APCs) - **macrophages**

Interact with **CD4+** ("helper") T cells (Th).

Antigen is digested in lysosomes

An epitope is displayed by MHC-II

Th cells divide rapidly and secrete small proteins called **cytokines** that "help" the immune response



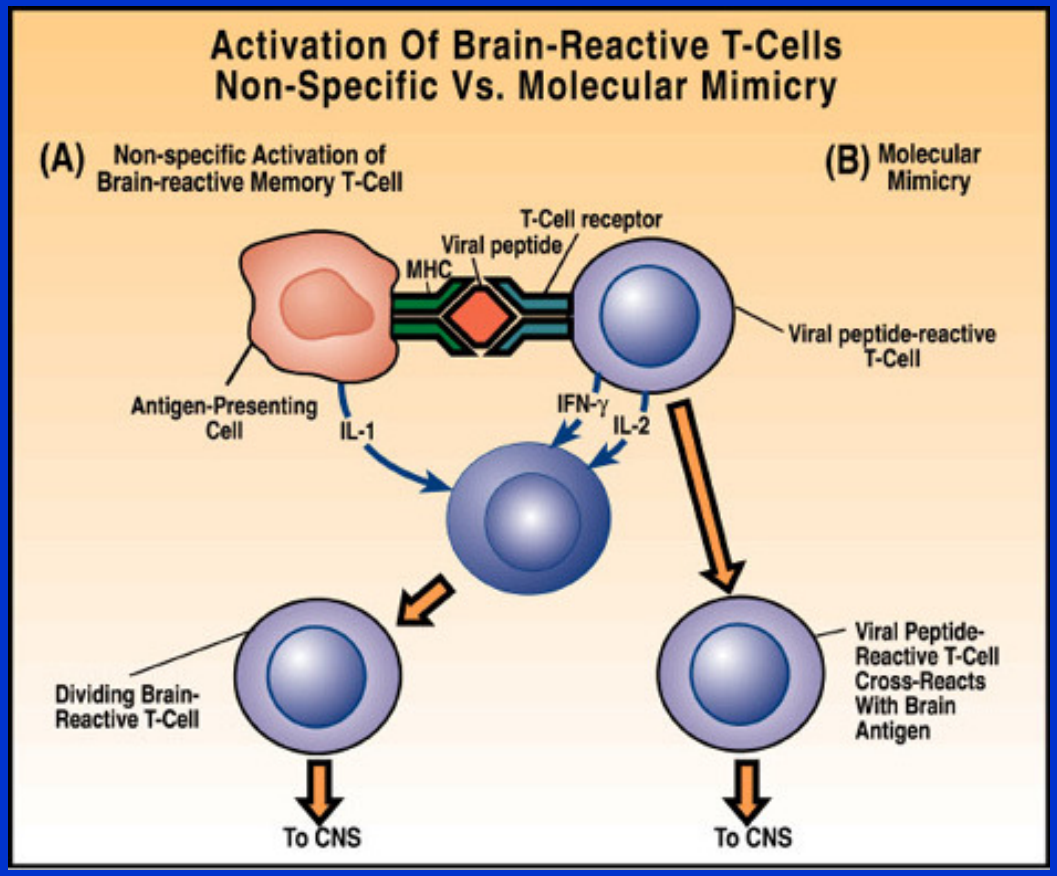
Immunologic abnormalities in CSF, whole blood and serum in MS patients:

CSF	Serum	Blood
↑IFN-gamma	↑IFN-gamma	↑IFN-gamma
↑IgG & oligoclonal bands	↑TNF	↑IL-2
↑TNF	↑IL-2	↑IL-4
↑activated CD4+ cells	↑IL-2 receptors	↑IL-1
	↓PGE-2 release by macrophages	
	↓CD8+ cells	

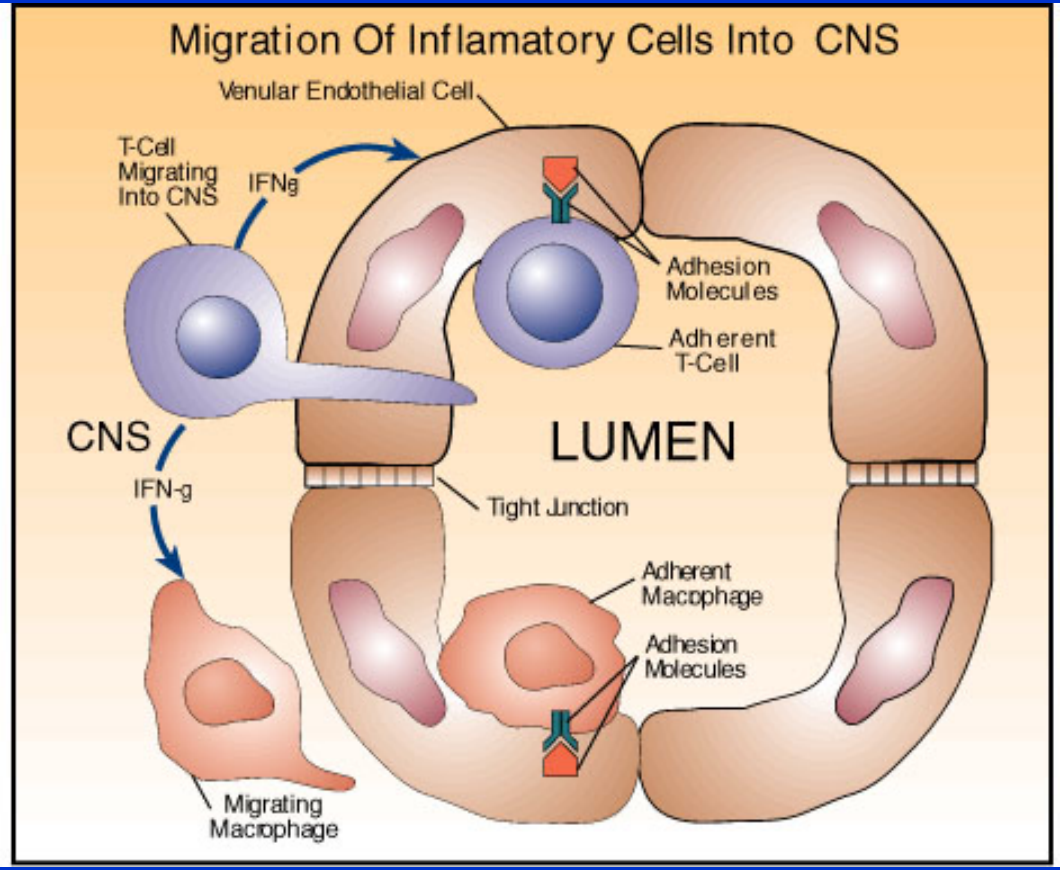
Abbreviations:

- IFN-gamma - *interferon gamma*
- IgG - *immunoglobulin G*
- TNF – *Tumor necrosis factor alpha or alpha & beta*
- CD4+ - *Major Histocompatibility Complex Class II restricted T-cells*
- CD8+ - *Major Histocompatibility Complex Class II restricted T-cells*
- IL-2, IL-4, IL-1 - *interleukins*
- PGE-2 - *prostaglandin E*

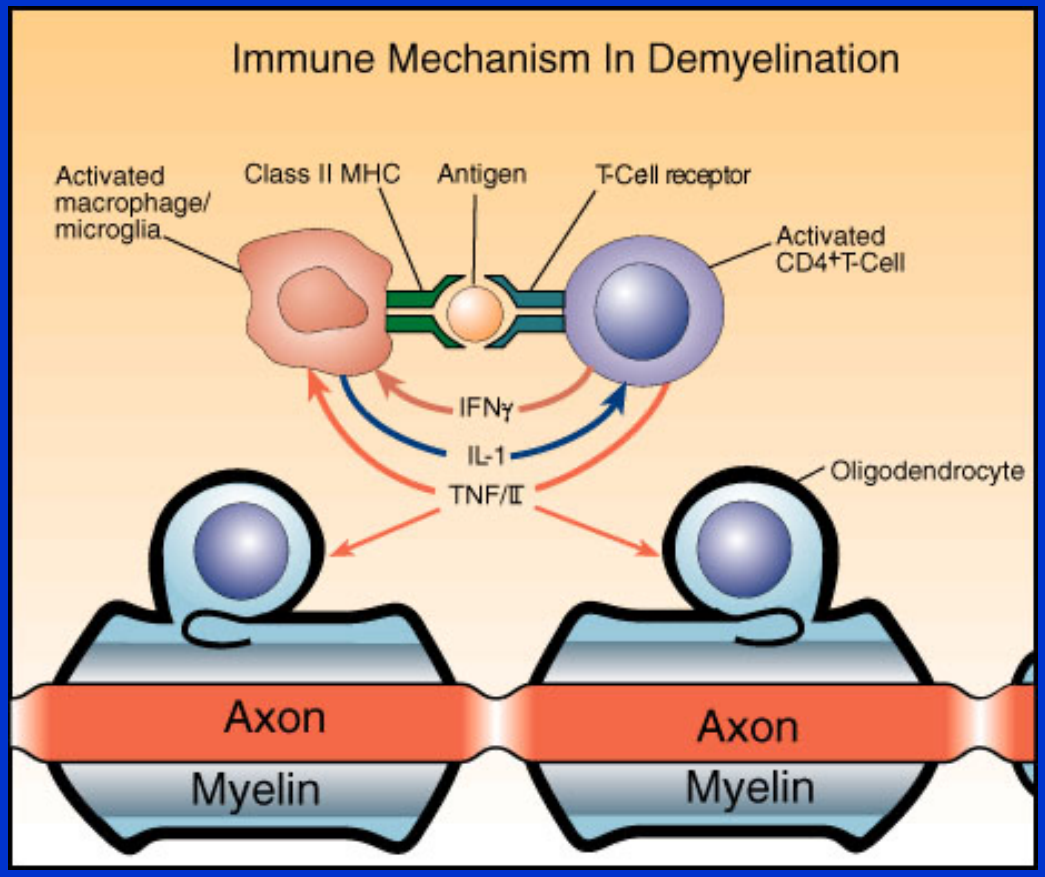
Possible Etiologic Mechanisms of Demyelination in CNS - T-cell Activation



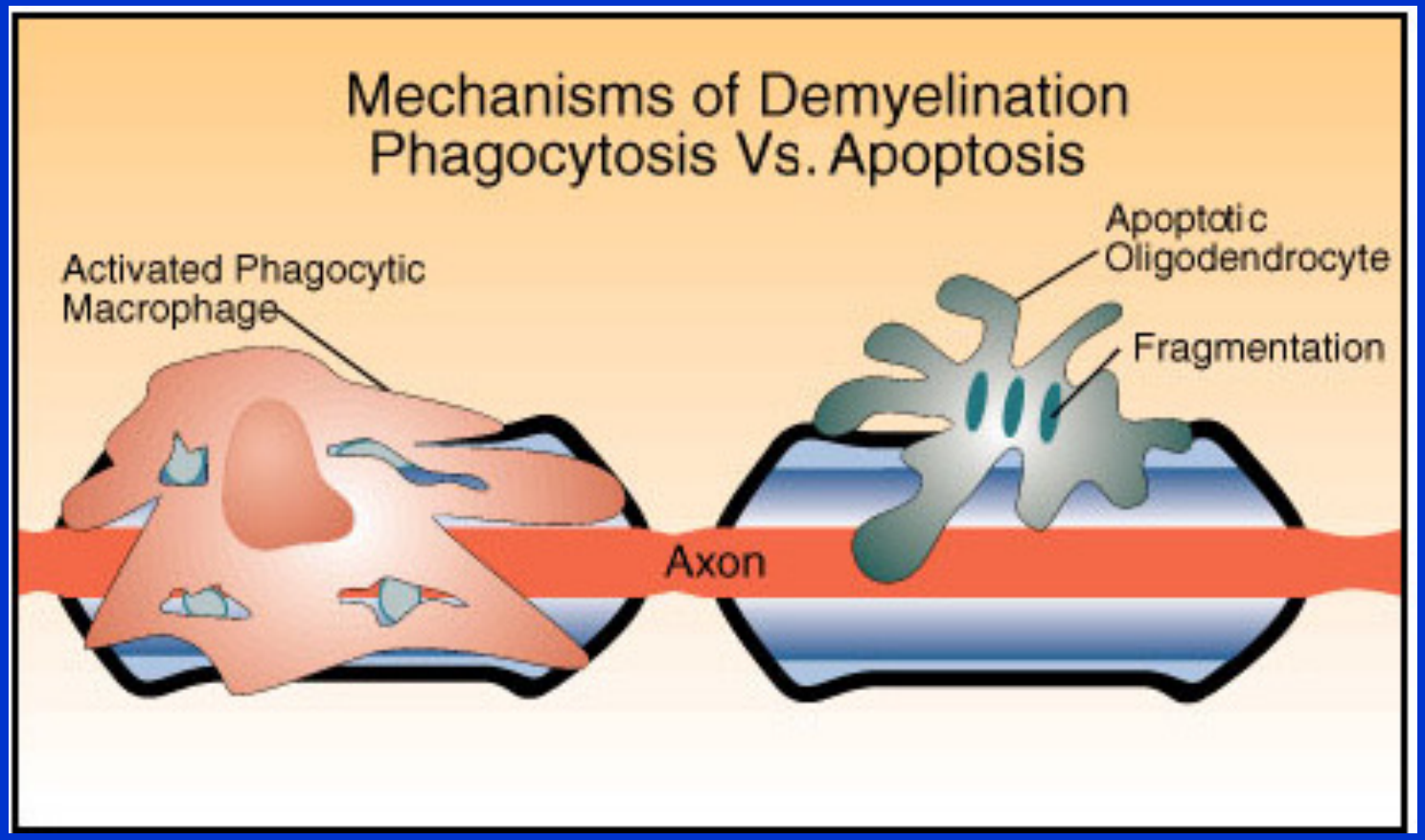
Possible Etiologic Mechanisms of Demyelination in CNS - Inflammation

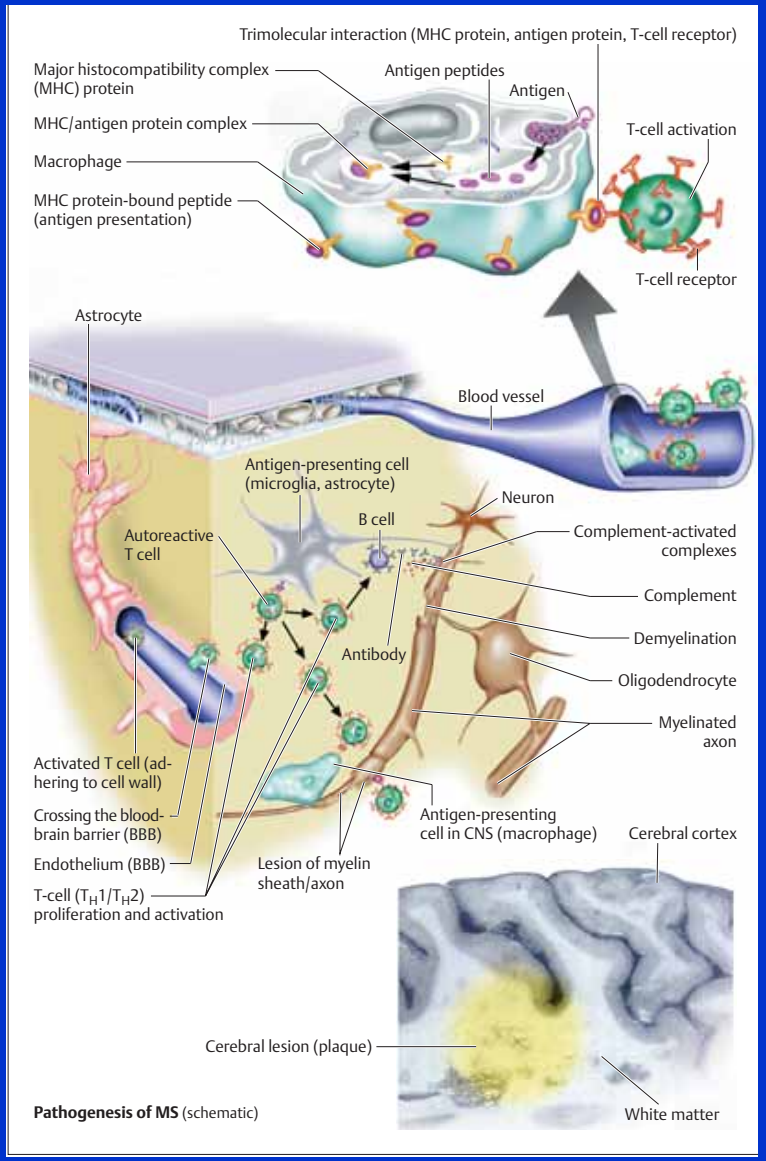


Possible Mechanisms of Demyelination in CNS - Immune Cell Activation



Possible Mechanisms of Demyelination - Phagocytosis Apoptosis





Pathogenesis of MS (schematic)

Phases and mechanisms of MS pathophysiology

Pathomecanisms involved in MS:

- Inflammation/immune disfunction: activation of microglia, T cells, B cells, plasma cells, macrophages, complement and antibody deposits, release of mediator

- Alteration of the blood-brain barrier

- Oxidative damage and excitoxicity

- Demyelination

- Remyelination, neuroregeneration

- Gliosis
- Neurodegeneration, axonal damage

PATOPHYSIOLOGY

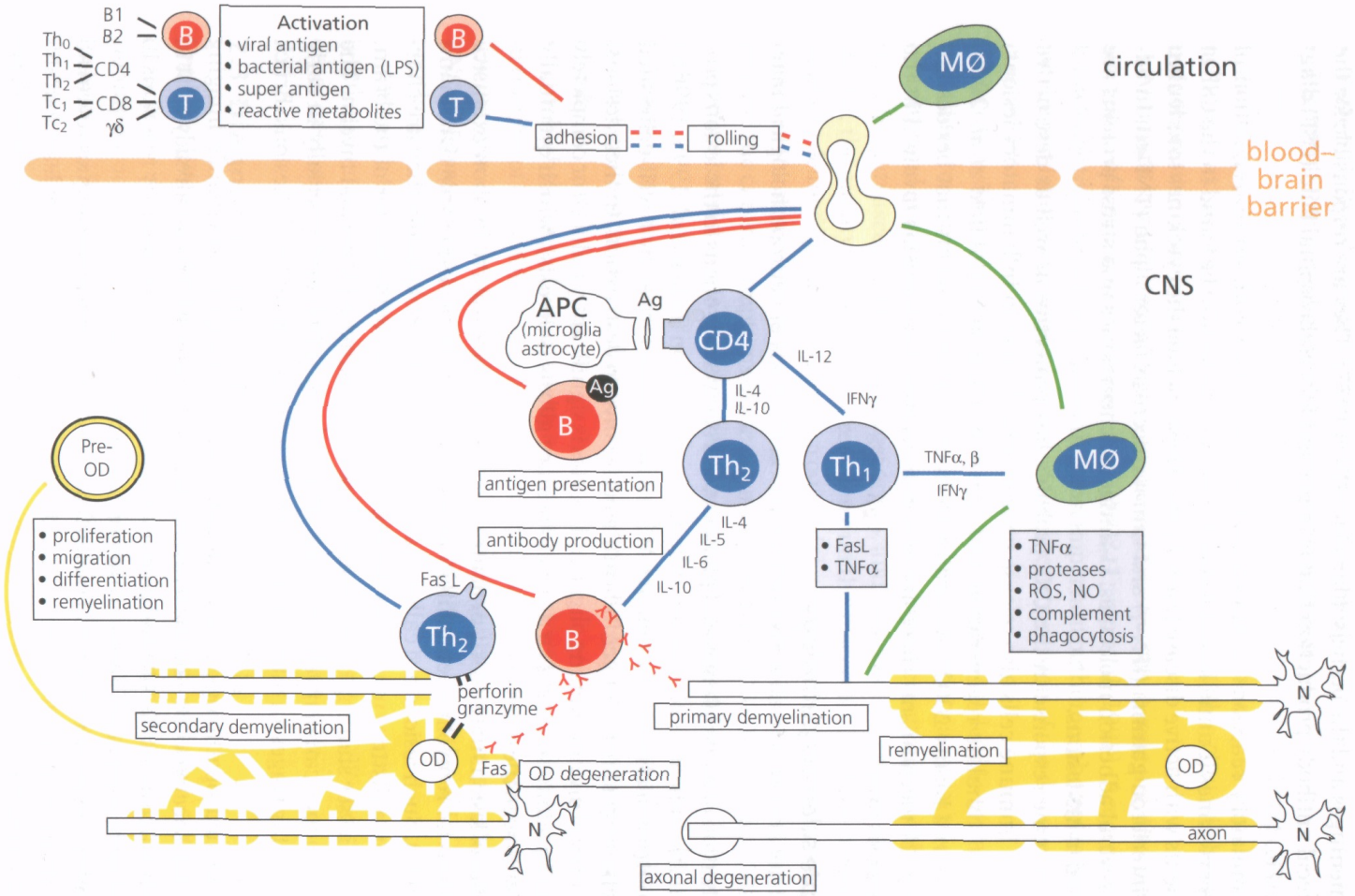
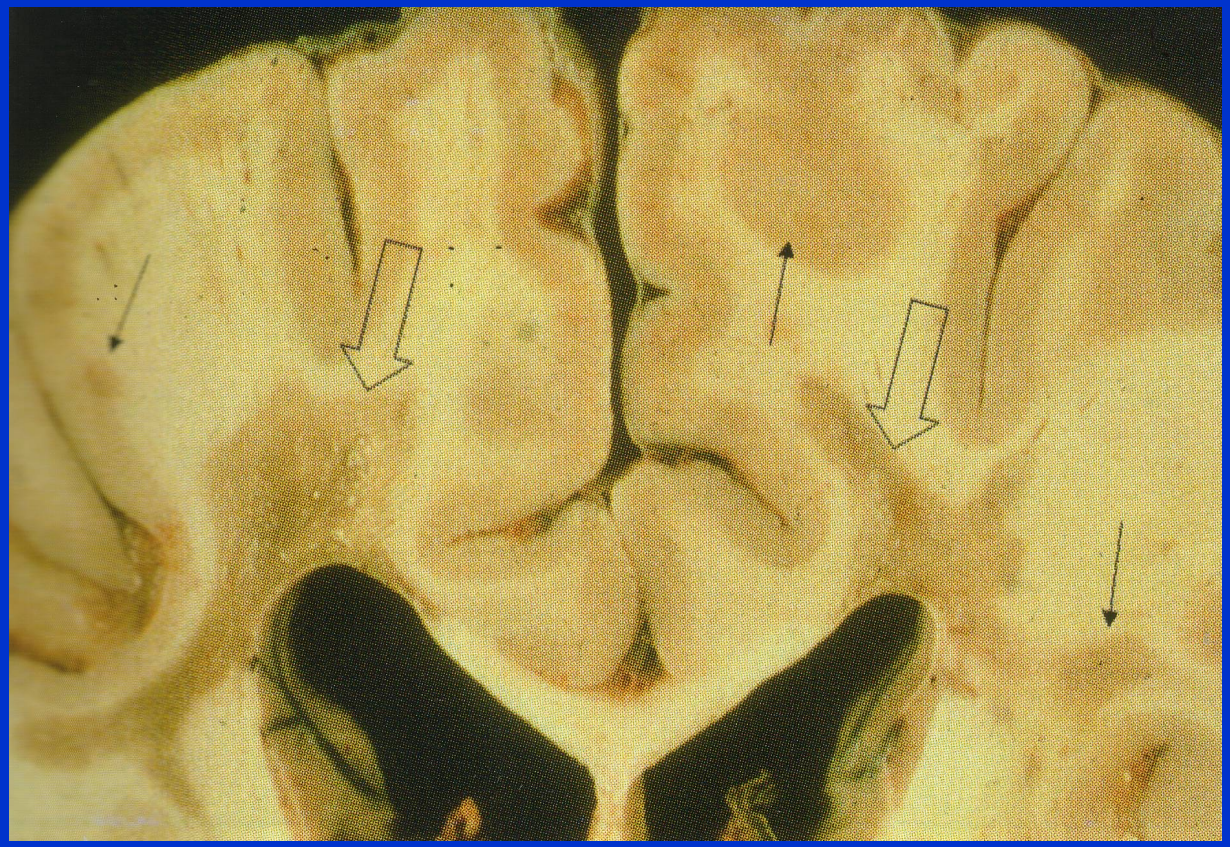


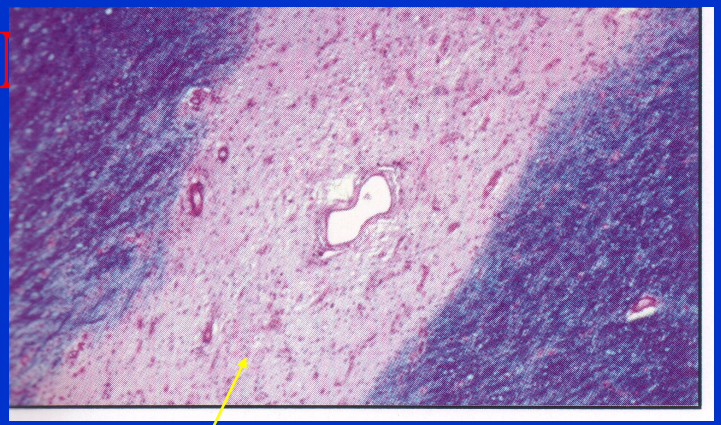
Fig. 1 *Schematic illustration of factors potentially involved in the immune-mediated destruction in multiple sclerosis (MS) lesions.* Abbreviations: Ag, antigen; APC, antigen-presenting cell; B, B cell; B1, B cell, fetal type; B2, B cell, adult type; Fas, CD95 molecule; FasL, Fas ligand; γδ, γδ+T cell, fetal type; IFNγ, interferon-gamma; IL, interleukin; LPS, lipopolysaccharide; MO, monocyte/macrophage; N, neuron; NO, nitric oxide radicals; OD, oligodendrocyte; ROS, reactive oxygen species; T, T cell; Tc, cytotoxic T cell; Th, T helper cell; TNFα, tumour necrosis factor-alpha.

PATHOLOGY

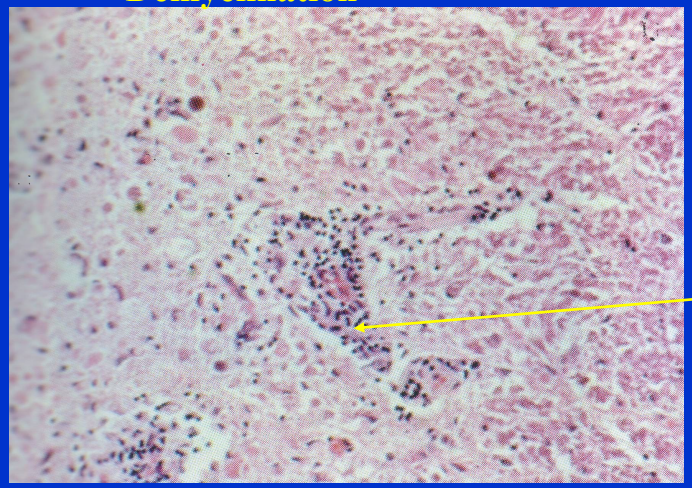
- Gross appearance of the MS brain autopsy: coronal section of a brain from an MS patient.
- Note the following: (1) enlarged lateral ventricles, (2) bilateral periventricular (dark brown) confluent plaques (open arrows), (3) scattered (dark brown) plaques in the hemispheric white matter bilaterally (small arrows).



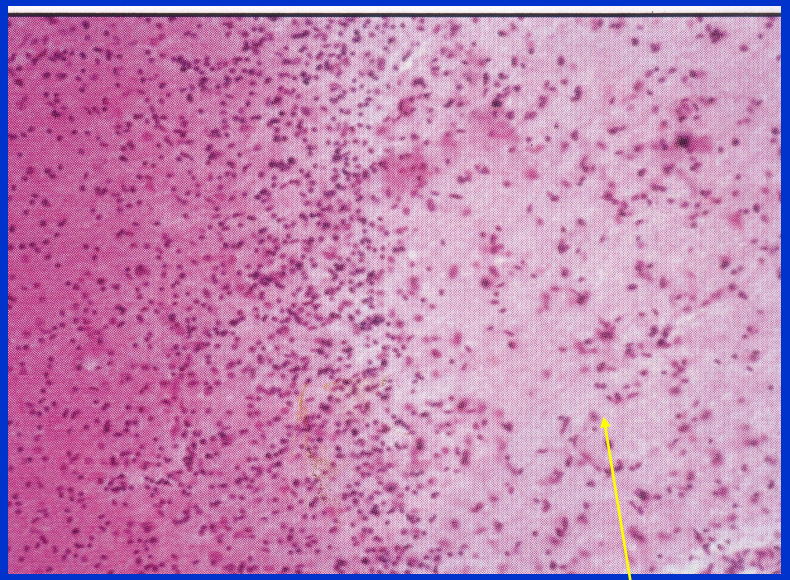
PATHOLOGY



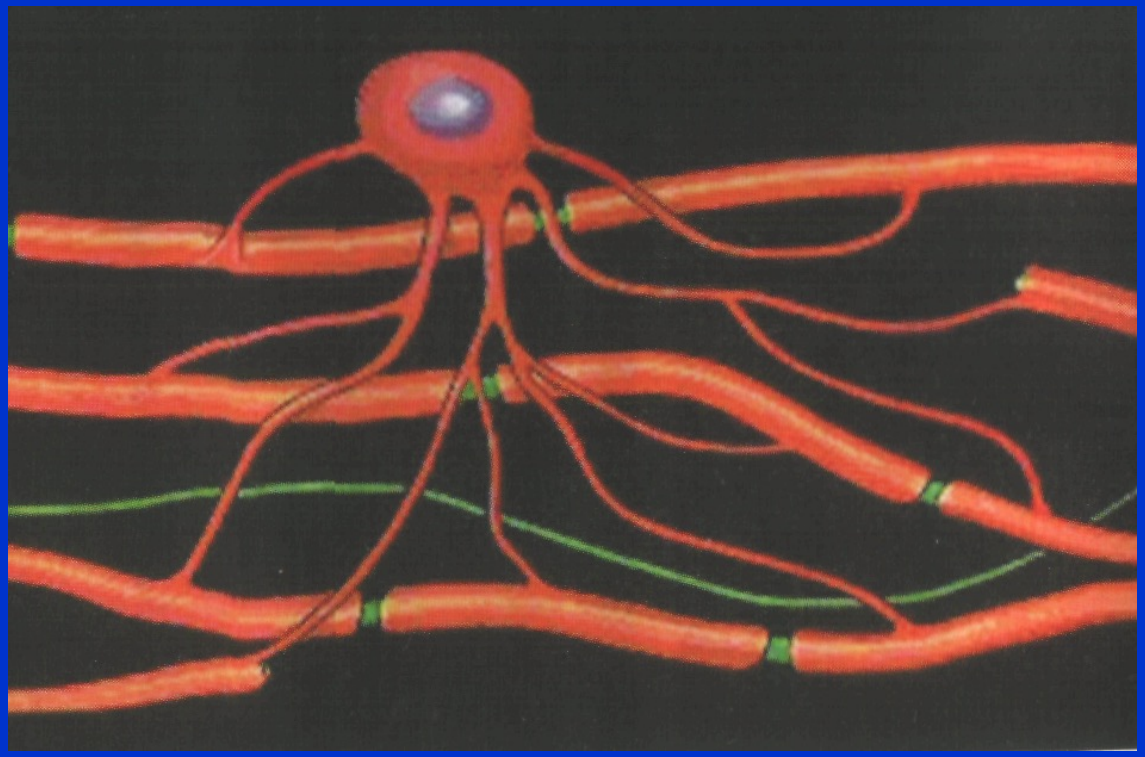
Demyelination



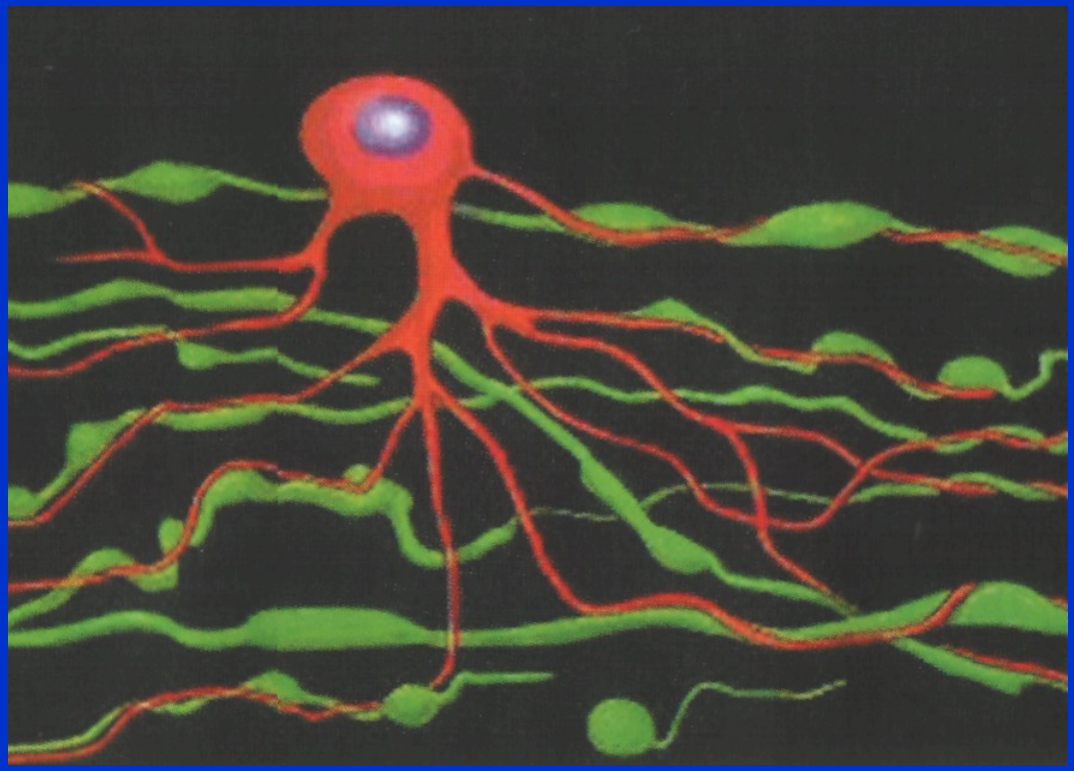
The cellular infiltration is minimal in some acute plaques



A plaque consists of a well-demarcated area with myelin loss, inflammatory cells, and relative but partial preservation of axons and neurons.

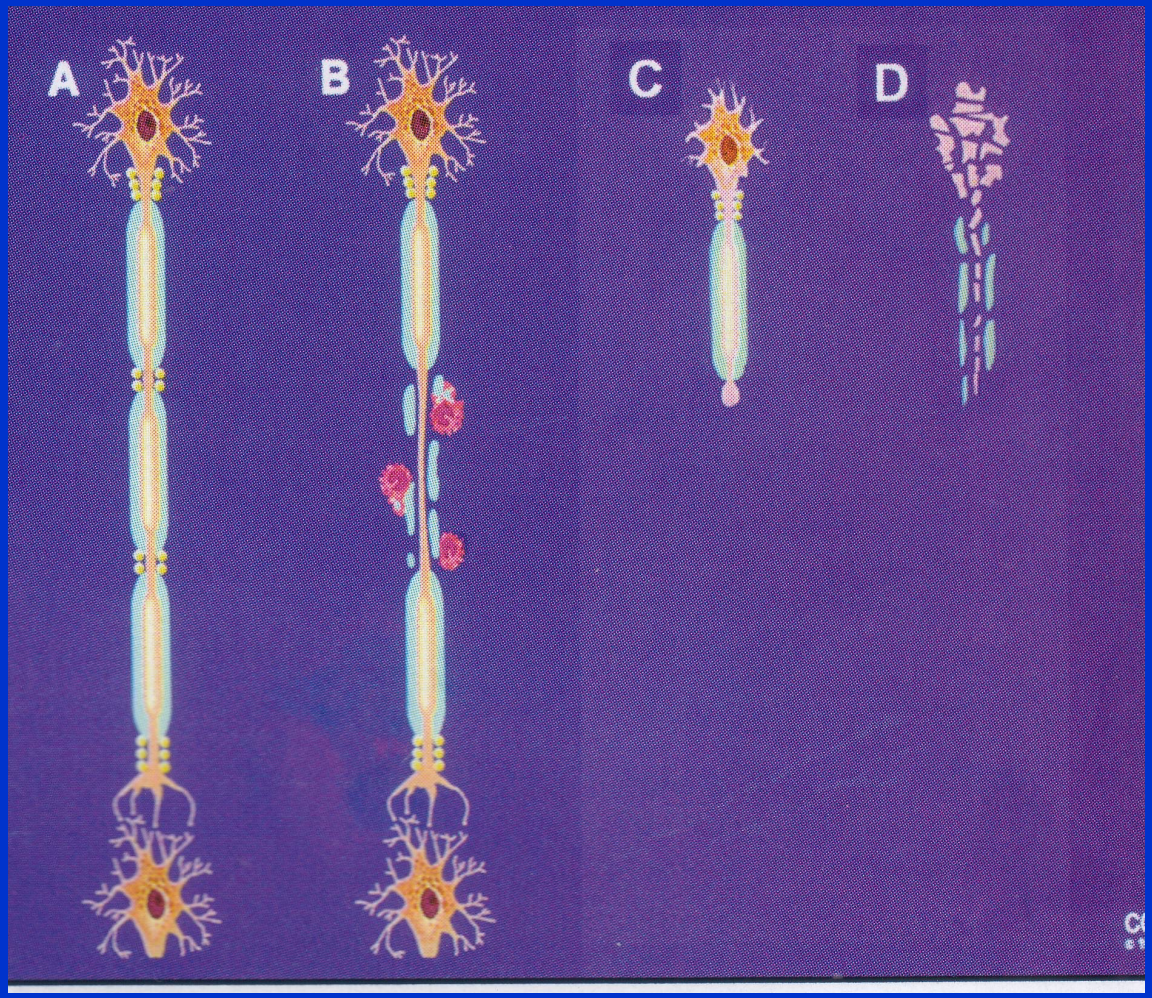


Axons are damaged in multiple sclerosis.



Severe axonal loss

NATURAL HISTORY



Pathological subtypes depend on the degree of inflammation, myelin destruction, and oligodendroglial preservation.

CLINICAL MANIFESTATIONTS

Multiple sclerosis lesions in the brain and spinal cord can damage every function of the central nervous system. The clinical presentation varies from mild to aggressive symptoms and from relapsing-remitting to progressive disease. The protean symptoms include fatigue as well as disturbed function in sensory, motor, bladder, bowel, sexual, cerebellar, brainstem, optic nerve, and cognitive realms.

SYMPTOMS

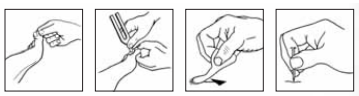
Symptoms of MS vary in severity and duration, and manifest in differing combinations, depending on the area of the nervous system affected. Complete or partial remission, especially in the early stages of the disease, occurs in approximately 70% of MS patients. Patients often present with visual changes indicative of optic neuritis, sensory disturbances or focal muscle weakness.

SYMPTOMS

Symptoms of MS include:

- visual changes;
- focal muscle weakness;
- fatigue;
- depression;
- bowel/bladder/sexual dysfunction;
- gait problems/spasticity;
- paresthesias;
- heat intolerance;
- dysarthria/scanning speech/dysphagia;
- Lhermitte's sign;
- neuritic pain;

SYMPTOMS



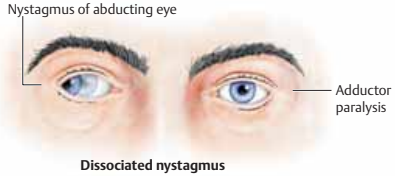
Sensory disturbances

Motor disturbances
(central paresis, spasticity, abnormal fatigability)

Test for visual field defects (confrontation test)

Central scotoma (optic neuritis)

Nystagmus of abducting eye



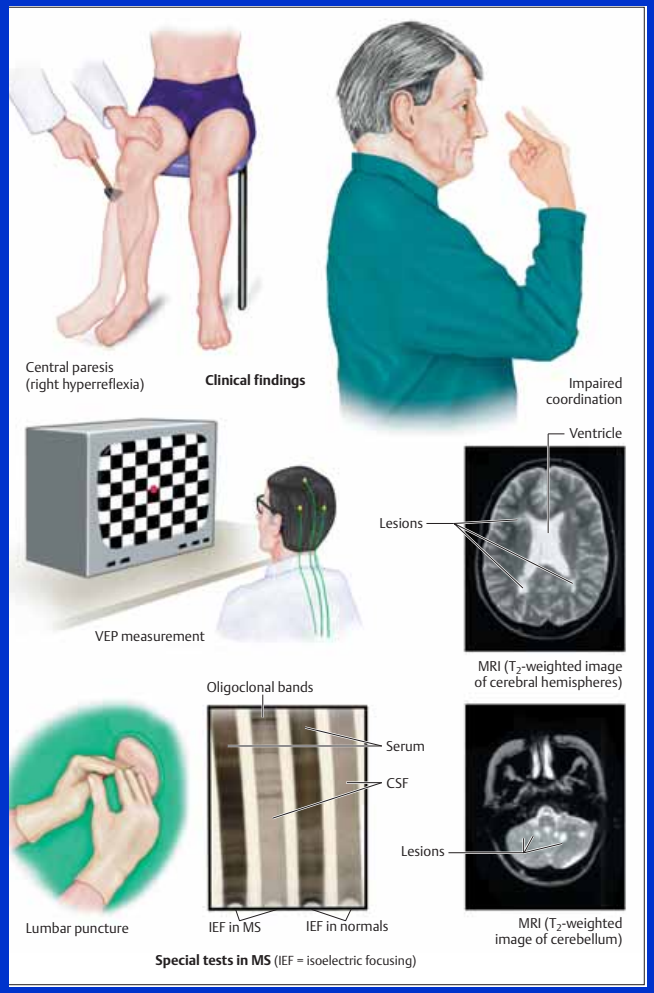
Adductor paralysis

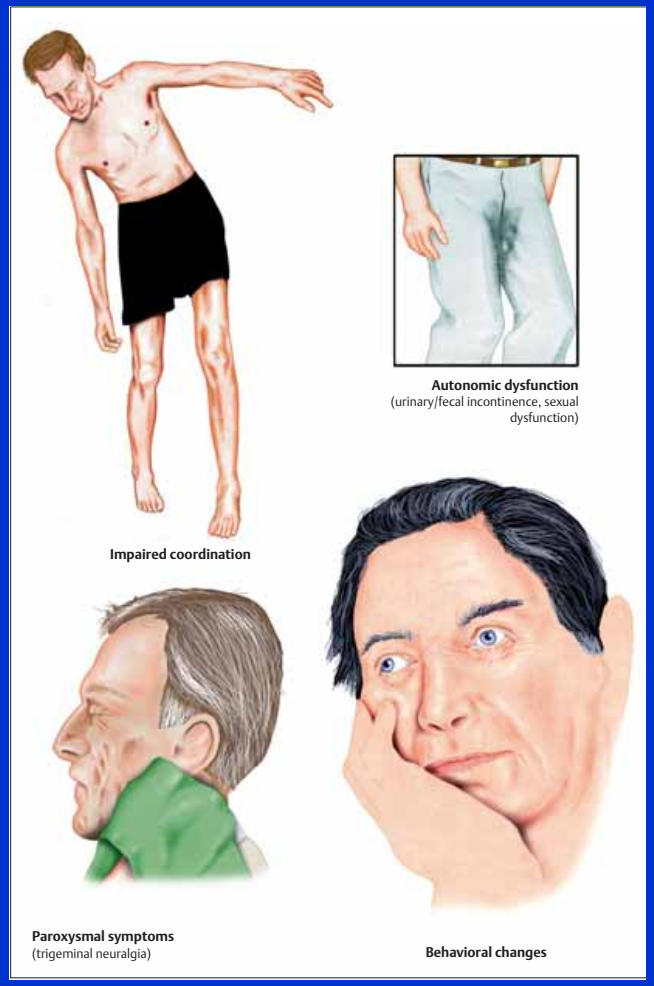
Dissociated nystagmus
(internuclear ophthalmoplegia, patient looking to right)

Atrophy

Temporal papillary atrophy
(after optic neuritis)

SYMPTOMS


Central paresis
(right hyperreflexia)
Clinical findings
Impaired
coordination
Ventricle
Lesions
VEP measurement
MRI (T_2-weighted image
of cerebral hemispheres)
Oligoclonal bands
Serum
CSF
Lesions
Lumbar puncture
IEF in MS
IEF in normals
MRI (T_2-weighted
image of cerebellum)
Special tests in MS (IEF = isoelectric focusing)


Impaired coordination
Autonomic dysfunction
(urinary/fecal incontinence, sexual
dysfunction)
Paroxysmal symptoms
(trigeminal neuralgia)
Behavioral changes

Clinical.

What is a relapce?

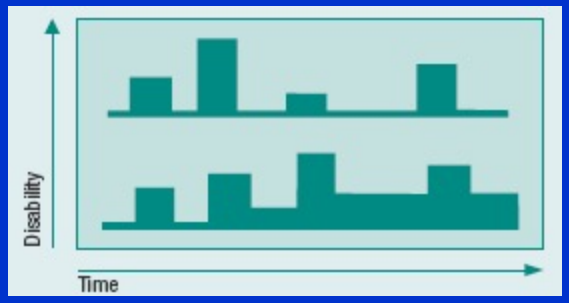
- New symptoms that reflect CNS involvement of inflammatory and demyelinating nature
- Duration ≥ 24 hours (anamnestic or actual result)
- No associated infections or fever
- Exclusion of a pseudo-relapse: Uhthoff phenomenon or paroxysmal events (e.g. tonic spasm)
- Minimum timespan between two episodes: 30 days between the onset of the first attack and the onset of the second attack

Clinical Tools for measurement of mobility related abnormalities

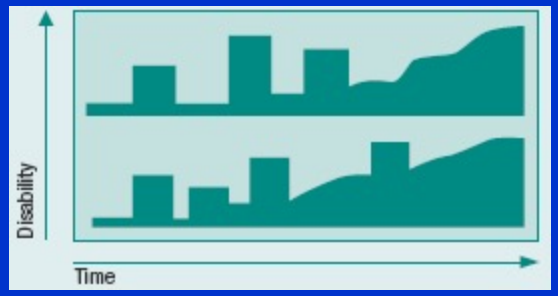
- Kurtzke's Expanded Disability Status Scale (EDSS) – Primary clinical outcome measure

- Multiple Sclerosis Functional Composite (MSFC) – includes clinical dimensions of arm, leg and cognitive function

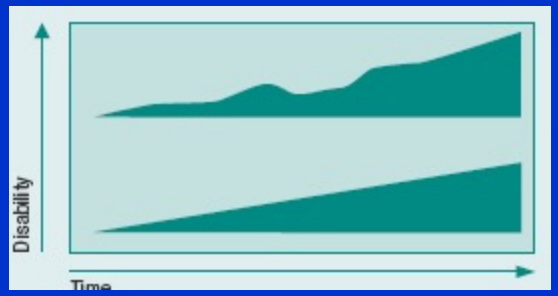
COURSE AND OUTCOME



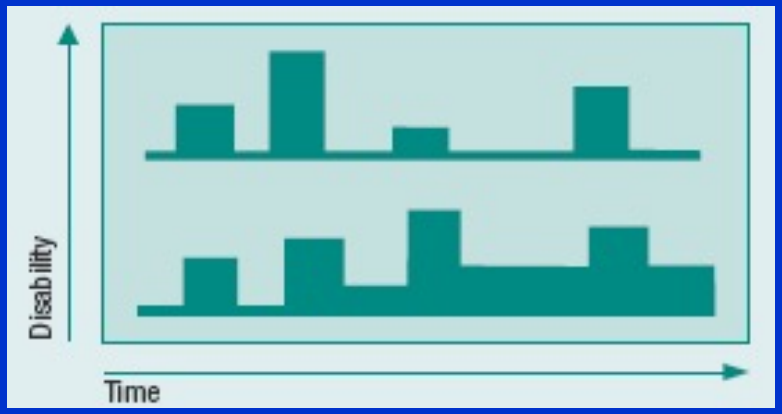
Relapsing/remitting (RRMS)
2 typical courses



Secondary progressive (SPMS)
2 typical courses



Primary progressive (PPMS)
2 typical courses



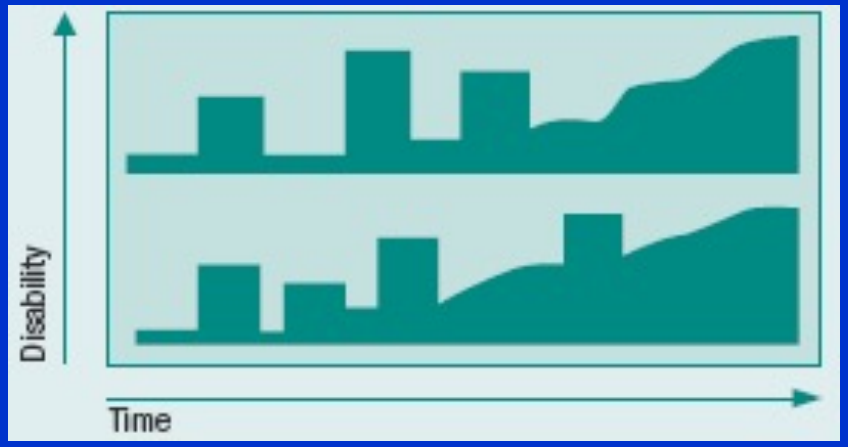
Relapsing - remitting MS

Approximately 80% of patients will initially present this form of MS.

The disease may appear to be clinically inactive for months or years, though MRI studies show that asymptomatic inflammatory activity is usually more frequent.

Over time, however, symptoms may become more severe with less complete recovery of function after each attack, possibly because of gliosis and axonal loss in repeatedly affected plaques.

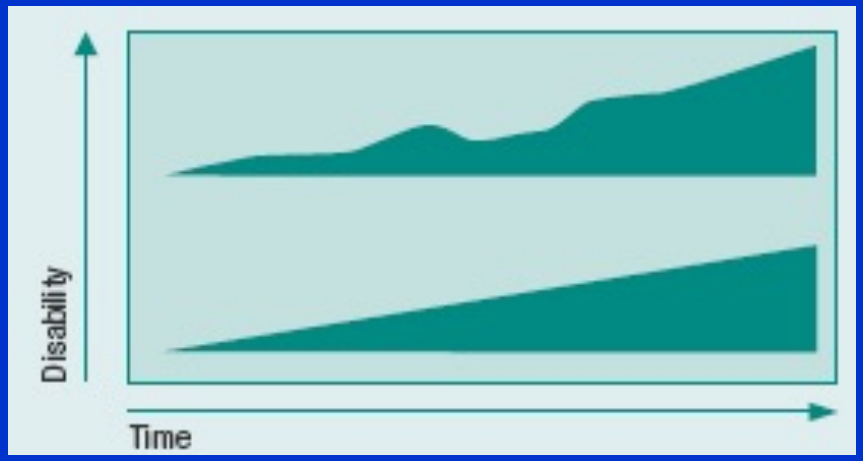
People with MS may then enter a progressive phase, characterized by a step-like downhill course.



Secondary progressive MS

Secondary progressive MS is characterized by progression that is not relapse related.

Approximately
50% of patients with relapsing/remitting MS will develop secondary progressive MS within 10 years, and 80% will have developed this form of MS within 20 years of disease onset.



Primary progressive MS

Primary progressive MS, which affects around 10–15% of all MS patients, is characterized by a lack of distinct attacks, but with slow onset and then steadily worsening symptoms.

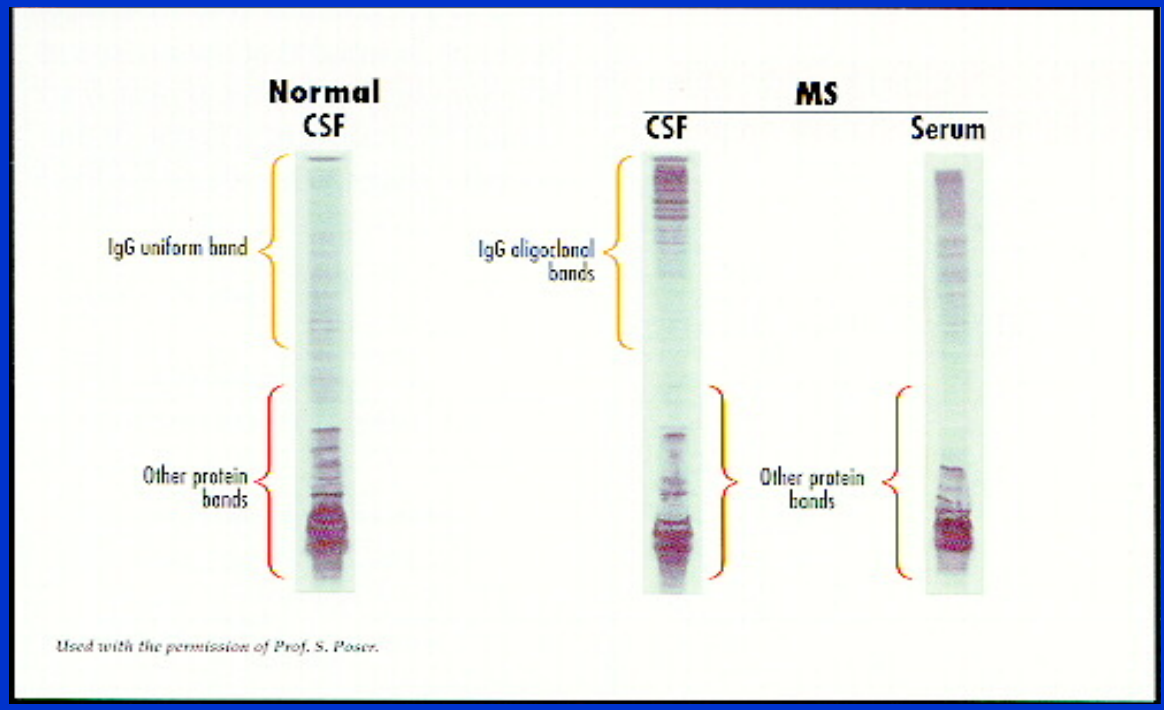
There is an accumulation of deficits and disability which may level off at some point or continue over years.

Clinically isolated syndrome (CIS)

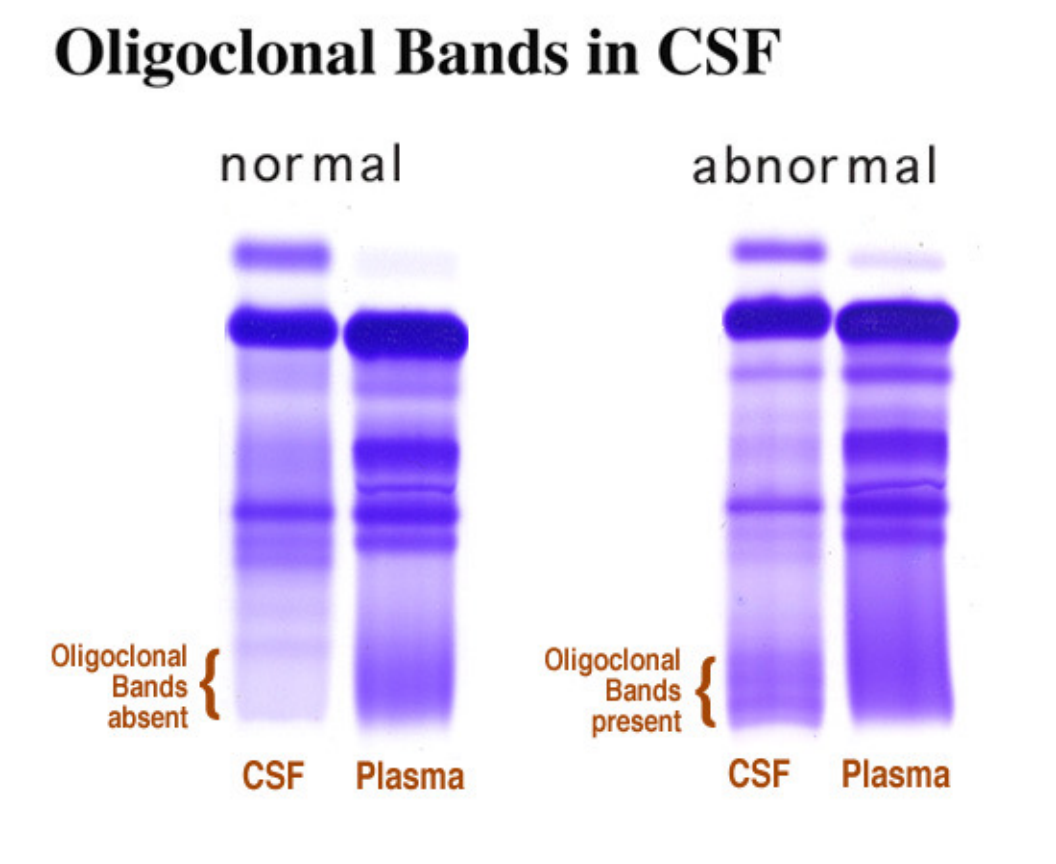
- is a term that describes a first and single neurologic episode of inflammation or demyelination (loss of the myelin that covers the nerve cells) in the central nervous system (CNS) lasting at least 24 hours.

WORKUP

Oligoclonal bands are distinct electrophoretic patterns that reflect substantial elevation of IgG produced by a restricted set of plasma cells and are demonstrated in CSF samples of approximately 85% of patients with MS.



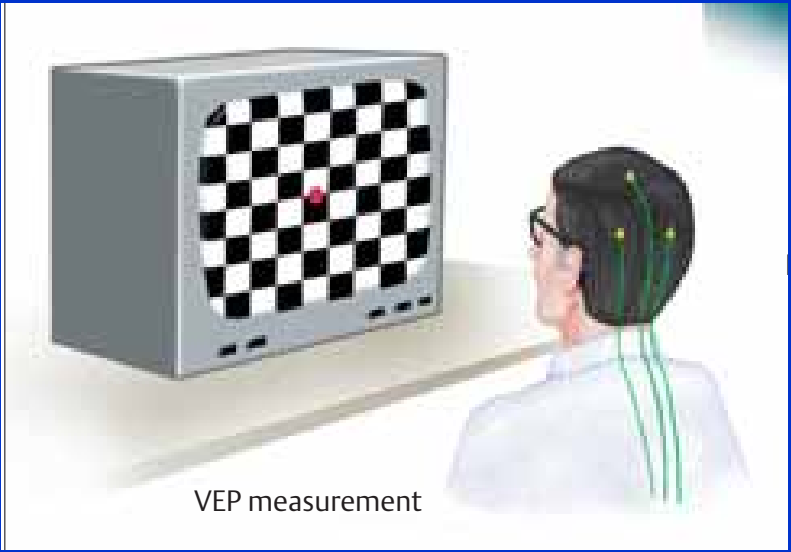
Oligoclonal Bands in CSF in a Patient with Multiple Sclerosis

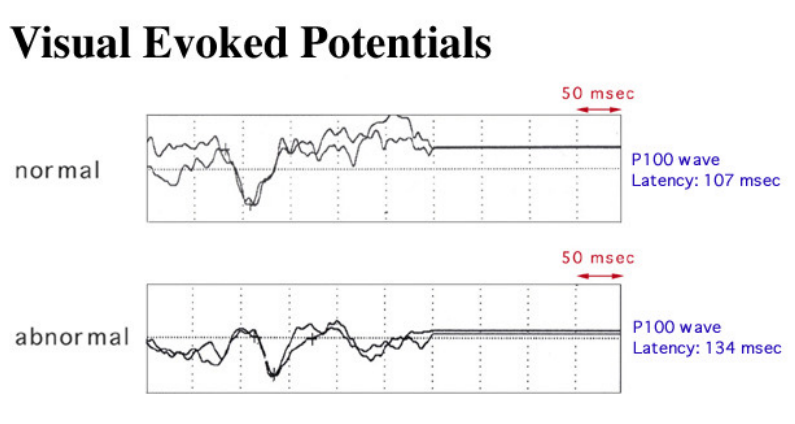


EVOKED POTENTIALS

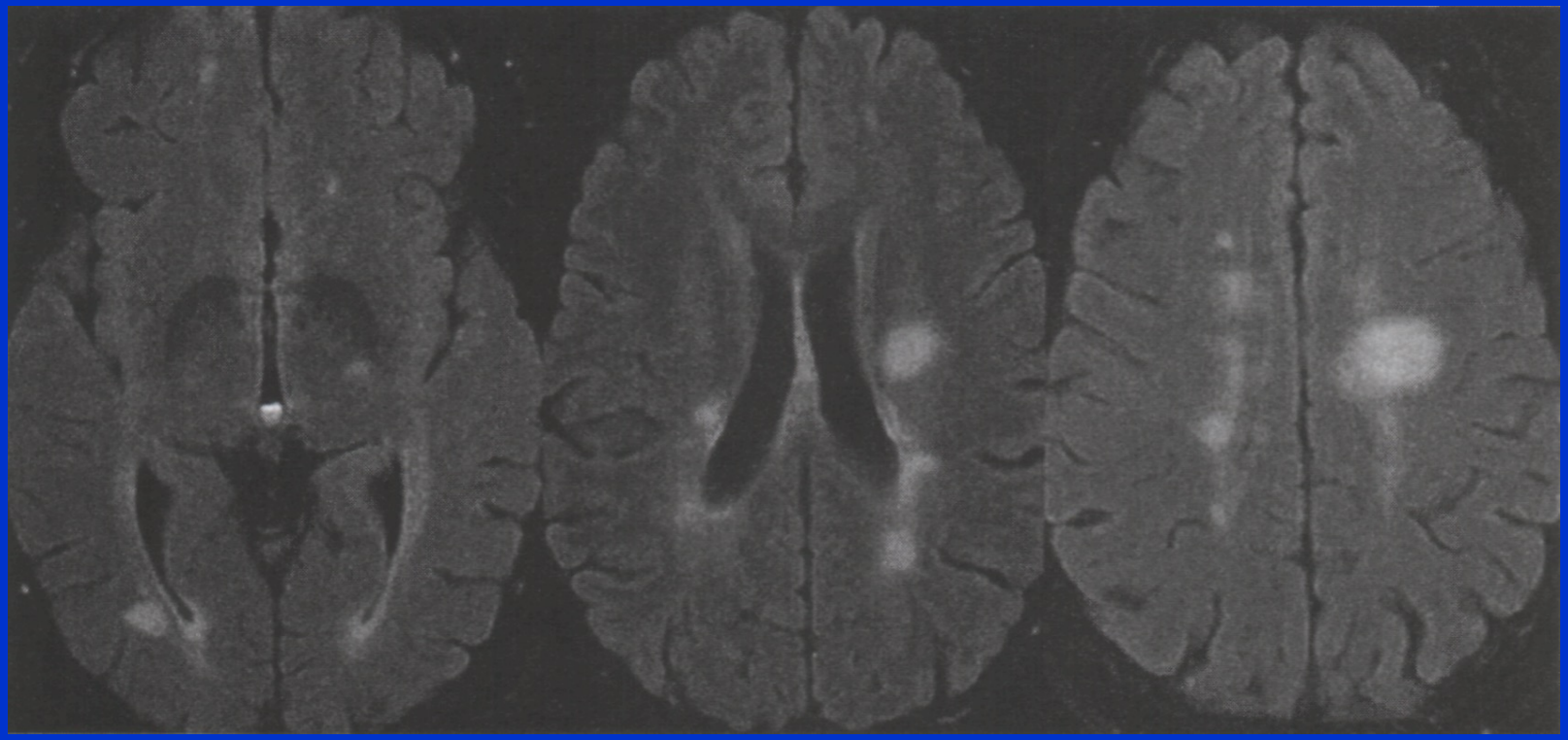
Evoked potentials are valuable to detect silent lesions in the optic nerves, or somatosensory, or auditory, or motor pathways. They are used to confirm dissemination within the CNS or to determine whether a symptom is accompanied by objective neurologic defictits when the neurologic examination is normal.

Visual Evoked Potentials in a Patient with Multiple Sclerosis


VEP measurement



IMAGING STUDIES

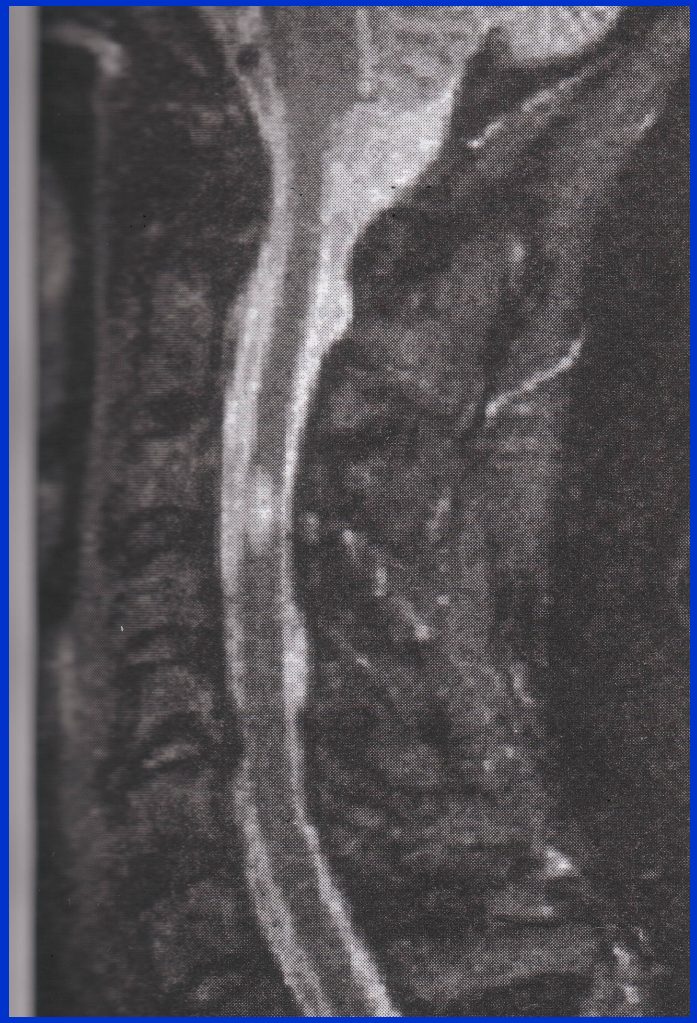


FLAIR (Fluid Attenuated Inversion Recovery sequence).

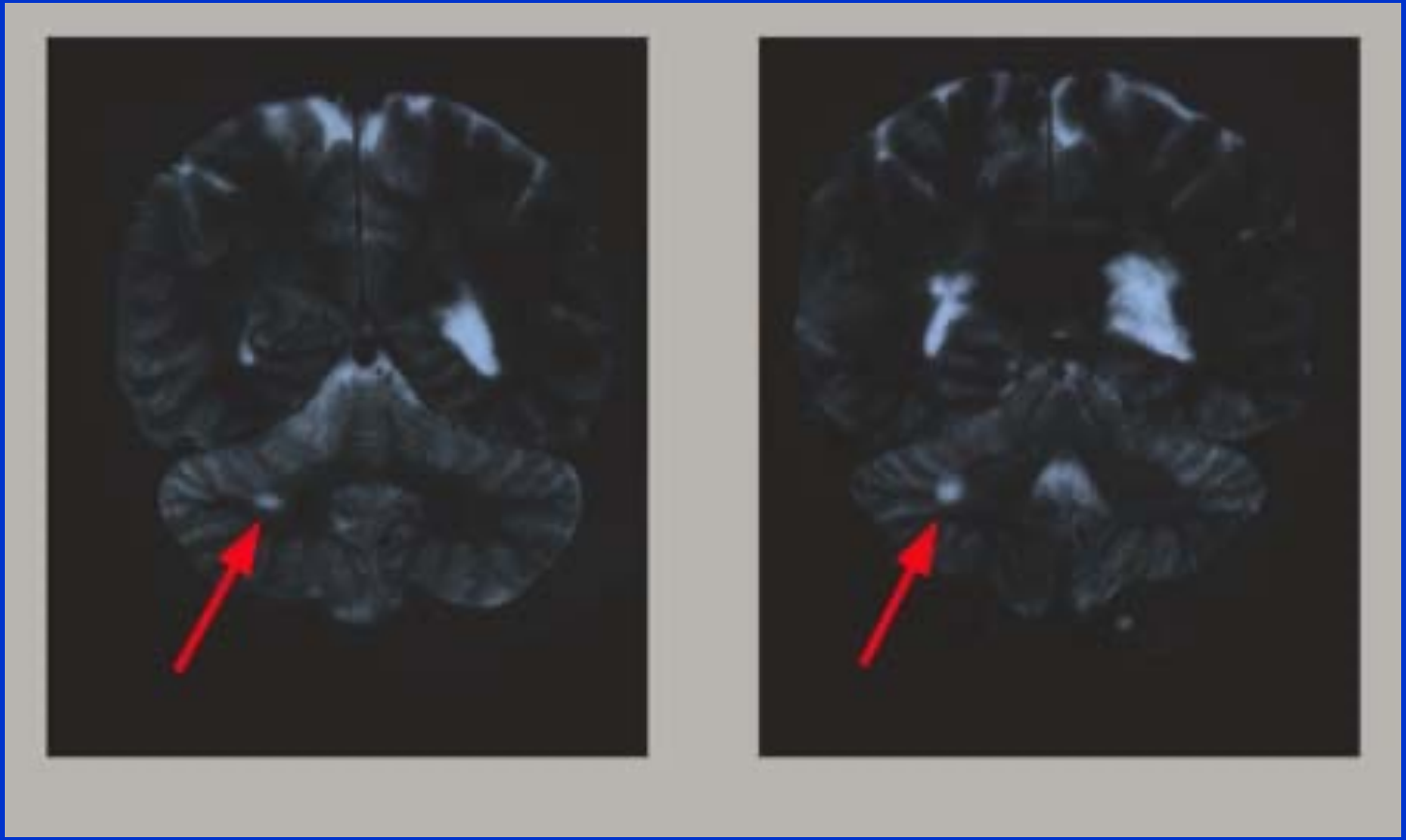
Typical MS lesions appear as T2 hyperintensities in the periventricular regions; they have an ovoid appearance with their largest axis oriented perpendicular to the ventricular surface; they typically involve only the white matter, and several arise from the corpus callosum

IMAGING STUDIES

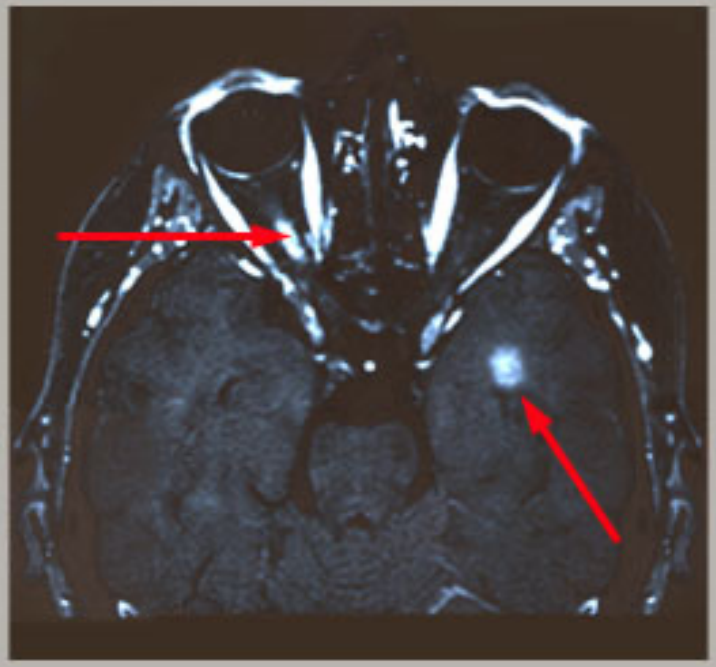
T_2 hyperintense lesion within the cervical spinal cord



Area of Demyelination in Cerebellum - MRI scan



Optic neuritis - MRI



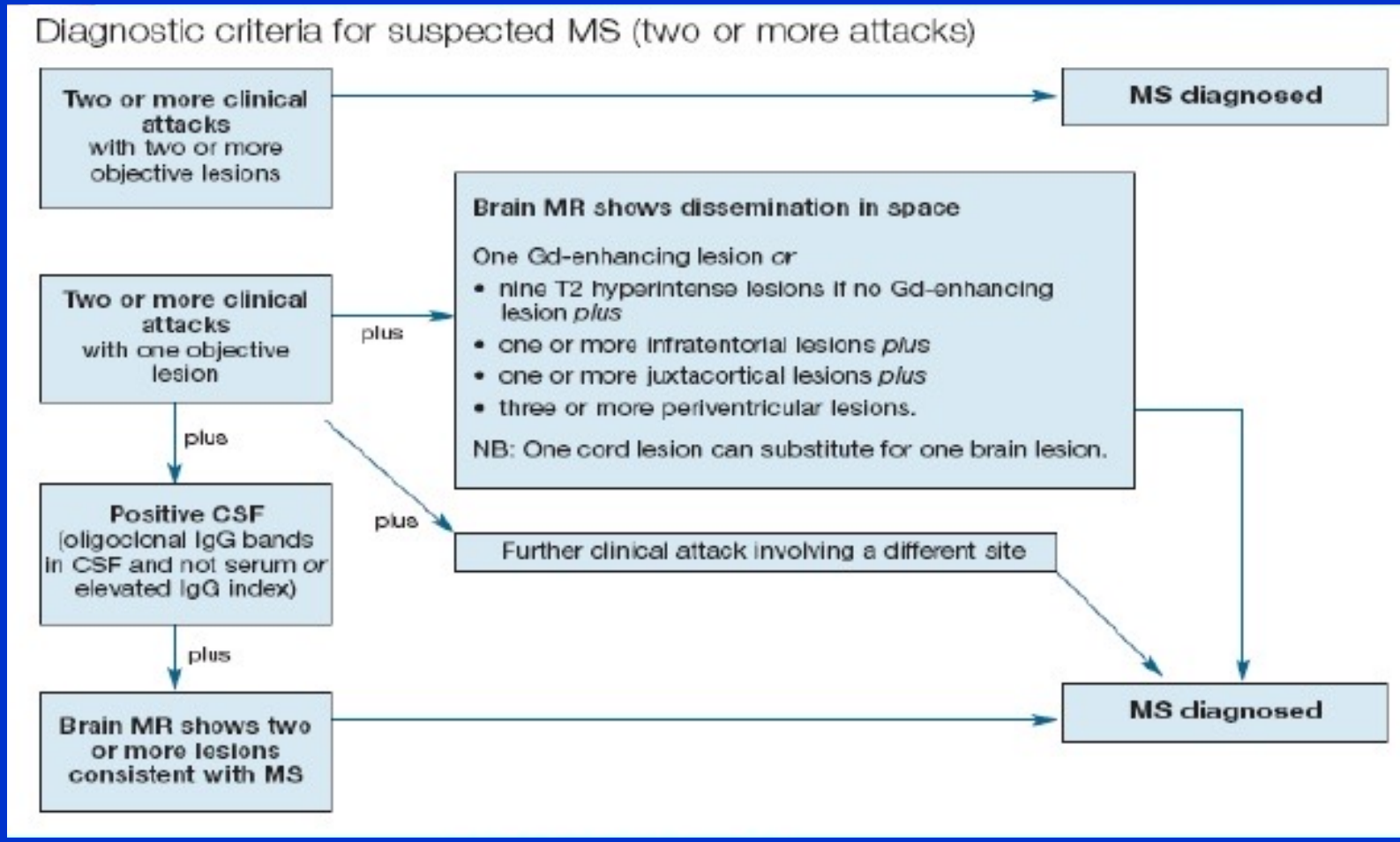
This MRI scan from a patient with acute opticneuritis. This MRI scan shows enhancement of involved area in optic nerve (left top arrow).

A second area of contrast enhancement is seen in the contralateral lobe (right lower arrow).

DIAGNOSING

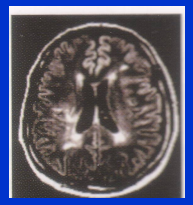
- No single test can diagnose MS.
- The medical history, neurologic exam and lab tests help physicians rule out other diseases and confirm the MS diagnosis.

McDonald Criteria for MS Diagnosis

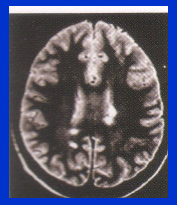


MRI criteria for dissemination in space

1 gadolinium-enhancing lesion



or

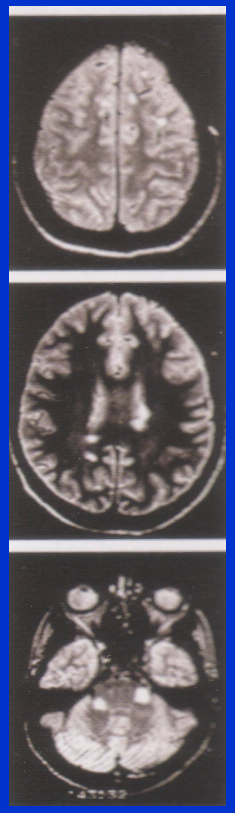


9 hyperintense T2 - lesion

1 juxtacortical lesion

3 periventricular lesions

1 infratentorial lesion



DIFFERENTIAL DIAGNOSIS

Acoustic neuroma. Acute disseminated encephalomyelitis. Acute ischemic optic neuropathy. Acute necrotizing encephalopathy. Intrcacranial aneurysm.

Autoimmune thyroid disease
Behcet disease
CADASIL
Carcinomatous polyradiculopathy
Cerebellar degeneration
Cerebrotendinous xanthomatosis
Cervical compression
Charcot-Marie- Tooth disease
Chemotherapy
Chronic inflammatory demyelinating polyradiculo-neuropathy
Cogan syndrome

Congenital adrenal hyperplasia
Connective tissue diseases
Copper deficiency
Cortical blindness
Cranial arteritis
Eales disease.
Guillain-Barré Syndrome
Hereditary spastic paraplegia
Hypo-thyroidism.
Increased intracranial pressure

Inflammation or infection
Inflammatory bowel disease with brain lesions Lyme disease
Maculopathy
Metastasis
Metronidazole
Migraine
Miller-Fisher syndrome
Myasthenia gravis
Myotonic dystrophy
Neoplastic
Neuroretinitis
Nutritional neuropathy
Optic nerve glioma

Orbital pseudotumor Paraneoplastic Pelizaeus- Merbacher disease. Progressive necrotizing myelopathy. Pseudotumor cerebri. Pseudoxanthoma elasticum. Radiation necrosis.

Reversible posterior leukoencephalopathy. Sarcoidosis Sjögren syndrome. Storage diseases. Subacute myelo-optic neuropathyfrom halogenated hydroxyquinolines. Subacute sclerosing panencephalitis. Susac syndrome. Syphilis. Thyroid ophthalmopathy. Tobacco-alcohol amblyopia. Tolosa-Hunt syndrome. Trauma . Vaccination. Vascular disease lesions. VasculitisViruses ore viral encephalitis

Vitamin B12 deficiency

TREATMENT

Acute exacerbations

No highly effective treatment is currently available to counteract MS attacks after their onset. The most widely used treatment is intravenous methylprednisolone, 1 g IV qd for 3-5 days. This medication may help expedite the timing of recovery but will not affect the actual degree of recovery.

High-dose steroids may work more effectively than oral steroids for the acute attack, and home therapy is recommended if the patient does not require hospitalization. Alternatively, high-dose oral methylprednisolone should be used, when feasible.

TREATMENT

Acute exacerbations

Complications of steroid treatment may include nonspecific immunosupression leading to opportunistic infections, fluid retention, hyperglycemia, hypokalemia, behavioral disturbances, peptic ulcers, osteoporosis, hypertension and increased risk of cataract development. Supplementation of steroid therapy with H-2 blockers, Potassium and vitamin D with calcium is frequently useful to reduce side-effects. Avoidance of salt or sugar during steroid therapy is recommended.

TREATMENT

Prevent relapses or disease progression by using the immunomodulatory drugs

Drug	Manufacturer	Dosage and administration	Indication
BETASERON® INF β - 1b	Berlex laboratories	250 µg via SC injection every other day	Relapsing forms
AVONEX ® INF β – 1a	Biogen IDEC	30 µg via IM injection weekly	Relapsing forms First clinical episode and MRI consistent with MS
COPAXONE ® (glatiramer acetat for injection)	Teva Neuroscience	20 mg via SC injection daily	RR MS
REBIF ® INF β – 1a	Serono / Pfizer	22 µg or 44 µg via SC injection three times weekly	Relapsing forms
NOVANTRONE ® (mitoxantrone)	Serono	12 mg / m^2 via IV infusion every three months (lifetime maximum 140 mg / m^2)	SPMS, PRMS, and worsening RRMS

COPAXONE


NDC 68546-317-30
℞ only
SINGLE-USE PRE-FILLED SYRINGES
COPAXONE®
(glatiramer acetate injection)
Contains 30 single-use PRE-FILLED Syringes
and 33 Alcohol Preps (Swabs)
STORAGE CONDITIONS:
KEEP REFRIGERATED (36°-46°F/ 2°-8°C)
AND PROTECTED FROM LIGHT
TEVA NEUROSCIENCE
FOR SUBCUTANEOUS INJECTION ONLY
U.S. Patent Nos. 5981589, 6054430, 6342476, 6362161, 6620847, 6939539, 7199098.
Manufactured in Israel by TEVA Pharmaceutical Industries Ltd., Kfar-Saba 44102, Israel
Manufactured for: TEVA Neuroscience, Inc., Kansas City, MO 64131

TREATMENT

Modifying the disease course (FDA-approved)

Injectable medications	Oral medications	Infused medications
Avonex (interferon beta-1a)	Aubagio (teriflunomide)	Lemtrada (teriflunomide)
Betaseron (interferon beta-1b)	Gilenya (fingolimod)	Novantrone (mitoxantrone)
Copaxone (glatiramer acetate)	Tecfidera (dimethyl fumarate)	Tysabri (natalizumab)
Extavia (interferon beta-1b)		
Glatopa (glatiramer acetate – generic equivalent of Copaxone 20 mg dose)		
Plegridy (peginterferon beta 1a)		
Rebif (interferon beta-1a)		

TREATMENT

Treatment of symptoms

Education of patients *is an important first step. The second intervention should be to avoid drugs that cause symptoms such as fatigue, weakness, or confusion. Some symptoms are primary--from CNS inflammation and damage, others are secondary--social disruption, muscle deconditioning, and drug side effects.*

TREATMENT

Treatment of symptoms

Fatigue. *The most common complaint in multiple sclerosis is fatigue. Sleep problems, limitation of mobility and spasticity, pain, deconditioning, depression, infections, drugs, other medical disorders (anemia, hypothyroidism), pain, deconditioning, and depression cause "secondary fatigue" (Krupp and Christodoulou 2001).*

TREATMENT

Exercise

Appropriate exercise program is very beneficial for the patients with Multiple Sclerosis. Simple exercises such as normal walking, swimming, using exercise bike may be of considerable value to the patients. All patients should be strongly advised against overheating (saunas, hot tubs, sunbathing, etc.) to prevent declines in neurologic function. Exercising in a cool, well aerated environment is strongly encouraged.

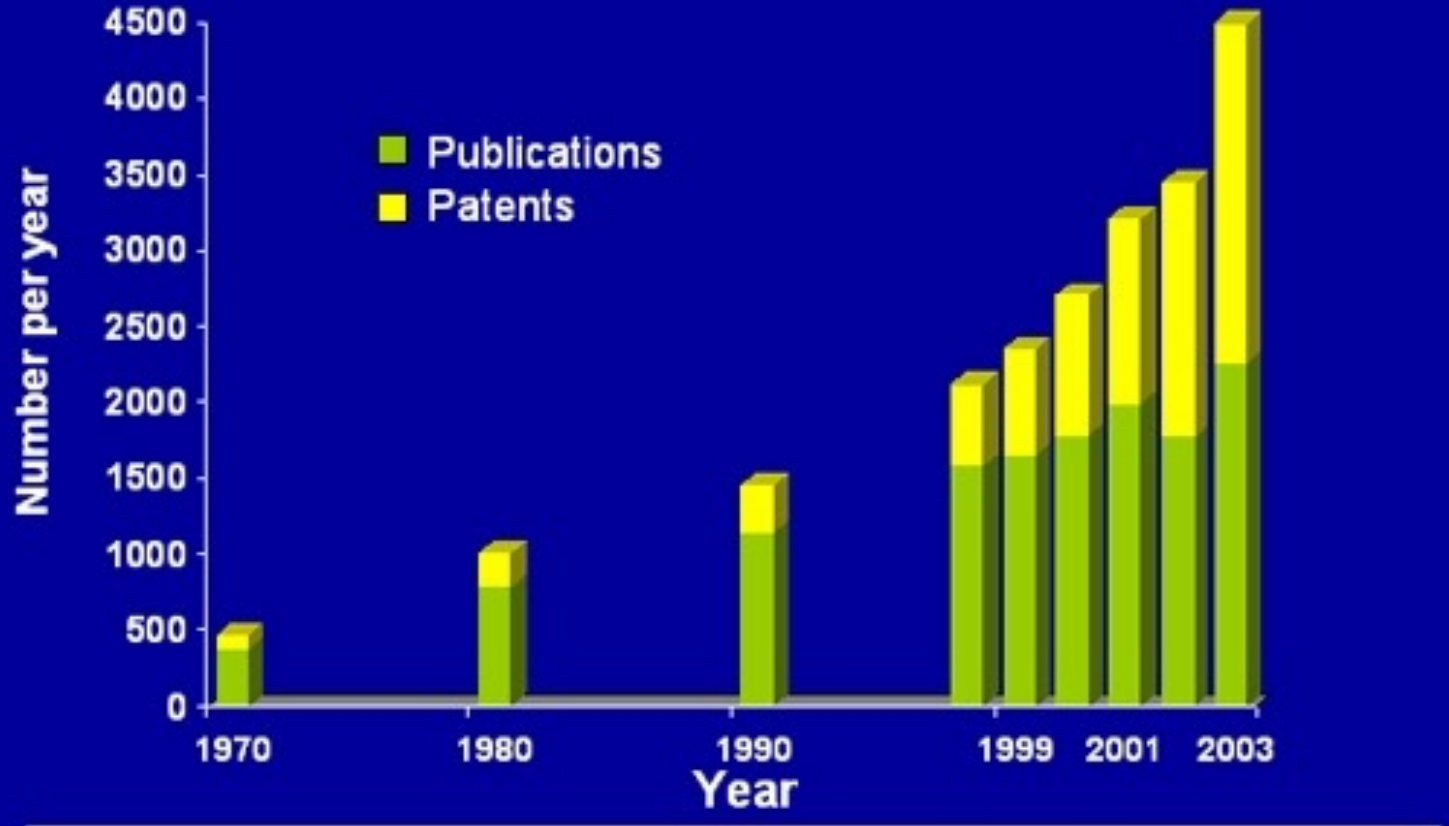
NUTRITION

- Multiple Sclerosis Society recommends the low fat, low cholesterol diet adopted by American Heart Association.
- Balanced diet is important in patients with MS.
- Some patients with medullary lesions and difficulty swallowing may require feeding tubes to prevent aspiration and resulting pneumonia.

PREGNANCY and MOTHERHOOD

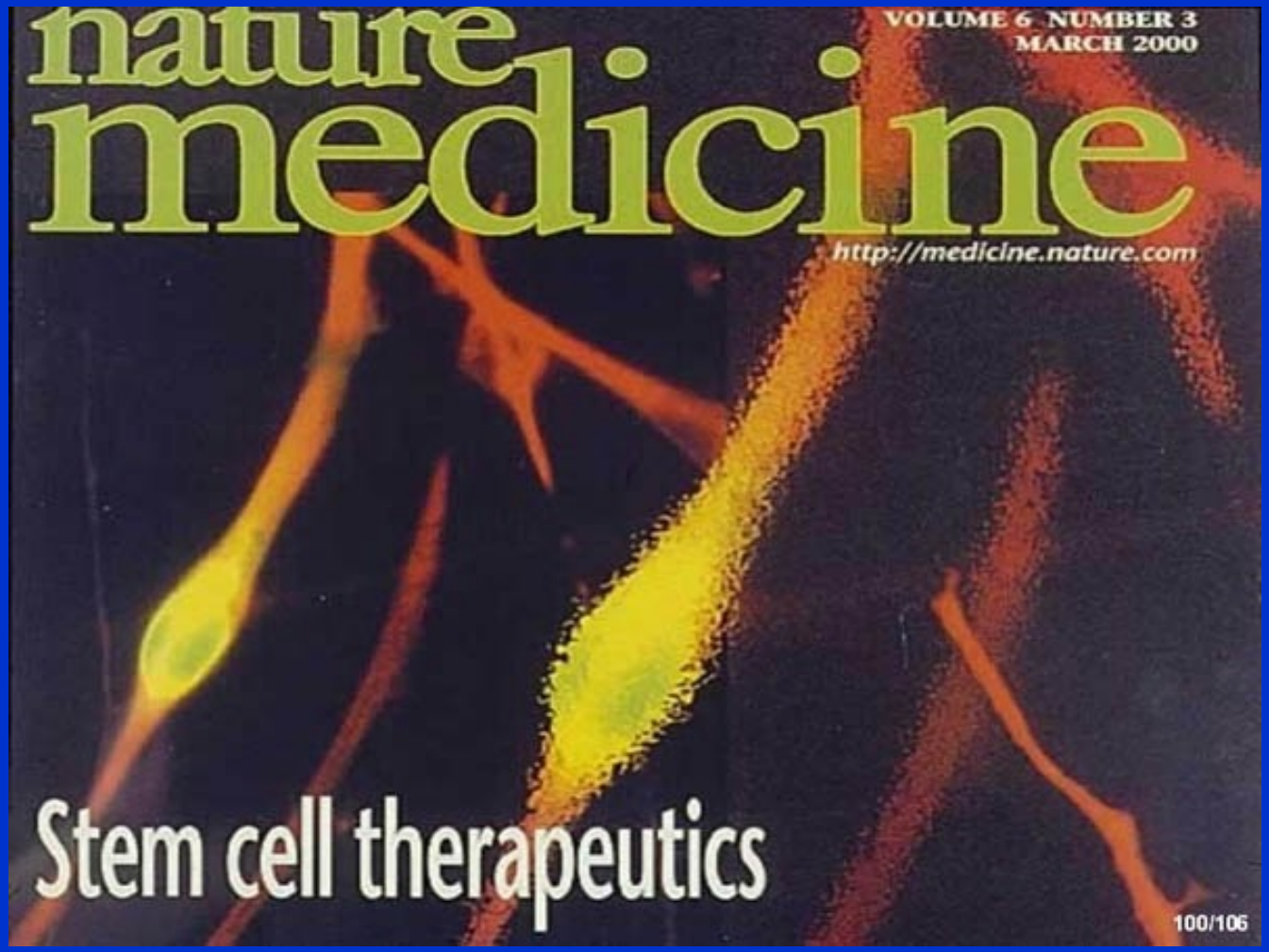
- The risk of exacerbation(s) during pregnancy itself is reduced due to increased immune tolerance.
- There is an increased risk of exacerbation(s) in the first several month postpartum due to return to normal "pre pregnancy" immune tolerance.
- According to numerous studies, overall long term disability does not appear to be changed by pregnancy.
- Female patients in childbearing age need to be aware of problems related to infant or child care due to potential disease-related disability.
- All of these issues should be addressed before the patient reaches her decision about pregnancy and motherhood.

Growth in MS Scientific Publications and Patents



Sources: Medline, Embase, World Patent Index

Noi strategii de tratament



What news?

- Israeli Researchers: Trials Are On for New MS Treatment
- Researchers in Israel are working on a new treatment they hope will slow down the progressive deterioration suffered by patients with multiple sclerosis and other autoimmune diseases.