

New Therapies for Multiple Sclerosis

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How Do We Diagnose MS?

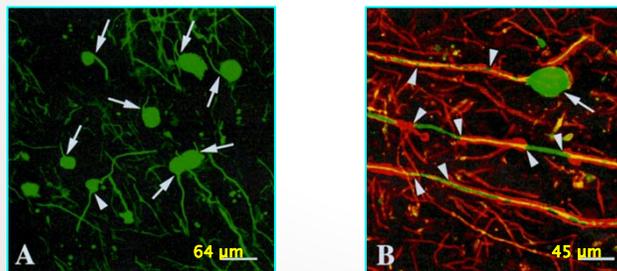
- ▶ History of “typical MS” presenting symptoms of more than 24 hours duration
- ▶ Objective neurological evidence on examination
- ▶ Dissemination of CNS lesions in time and space
- ▶ Supportive paraclinical tests: MRI or VEPs
- ▶ Laboratory: CSF-oligoclonal bands; ↑ IgG
- ▶ Exclusion of other causes

(CMSC, 2013)

Typical Presenting Syndromes of MS

- ▶ **Optic Neuritis**
 - Unilateral
 - Typically painful
 - Retrobulbar
 - Recovery expected
 - No retinal exudates or disc hemorrhages
- ▶ **Brainstem/Cerebrum**
 - Ocular motor syndromes
 - Hemisensory, crossed sensory
 - Hemiparesis
 - Trigeminal neuralgia
 - Hemifacial spasms
- ▶ **Myelitis**
 - Partial sensory or motor
 - Bowel and bladder dysfunction
 - Thoracic band-like sensation
 - L'hermitte sign
- ▶ **Cerebellum**
 - Cerebellar tremor
 - Acute ataxia
- ▶ **Paroxysmal Symptoms**
 - Tonic spasms
 - Paroxysmal dysarthria/ataxia

Frohman EM et al. *Neurology*. 2003;61:602-611.

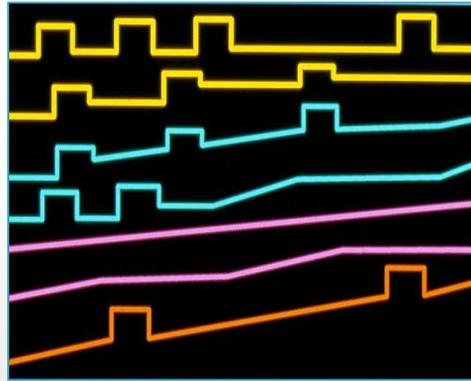


- ▶ 50–80% axonal loss in chronic lesions
- ▶ Immune-mediated inflammation is continuous, even during periods of apparent remission

Lovas G, et al. *Brain*. 2000;123 (Pt 2):308-317.
Trapp BD, et al. *N Engl J Med*. 2000;343:278-285

Clinical Patterns of MS

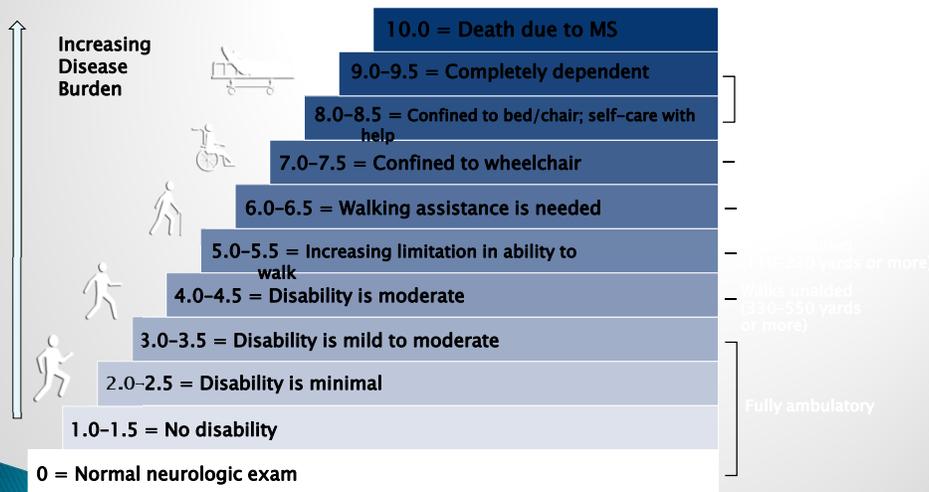
Relapsing–remitting
Secondary progressive
Primary progressive
Progressive relapsing



Time

Adapted from Lublin F, et al. *Neurology*. 1996;46:907–911.

Measuring Disability—EDSS (cont)



Kurtzke JF. *Neurology*. 1983;33:1444–1452.

Considerations When Making a Treatment Choice

- ▶ Effectiveness
- ▶ Patient's lifestyle
- ▶ Needle phobia
- ▶ Support system
- ▶ Financial concerns
- ▶ Trials
- ▶ Adverse-effect profile

(CMSC, 2013)

Disease Modifying Therapies

- ▶ **Avonex®** (*interferon beta-1a*)
- ▶ Once a week; intramuscular (into the muscle) injection; 30 mcg.
- ▶ **Betaseron®** (*interferon beta-1b*)
- ▶ Every other day; subcutaneous (under the skin) injection; 250 mcg.
- ▶ **Copaxone®** (*glatiramer acetate*)
- ▶ Every day; subcutaneous (under the skin) injection;
- ▶ 20 mg (20,000 mcg).
- ▶ **Extavia®** (*interferon beta-1b*)
- ▶ Every other day; subcutaneous (under the skin) injection; 250 mcg.
- ▶ **Rebif®** (*interferon beta-1a*)
- ▶ Three times a week; subcutaneous (under the skin) injection; 44 mcg.

The MS Disease-Modifying Medications General information
(NMSS, 2013)

Side Effects of Injectable Therapy

- ▶ **Avonex®**
- ▶ Flu-like symptoms following injection, which lessen over time for many. (See "Managing side effects" below.) Less common: depression, mild anemia, liver abnormalities, allergic reactions, heart problems. (See "Avonex Warnings" on page 12.)
- ▶ **Betaseron®**
- ▶ Flu-like symptoms following injection, which lessen over time for many. (See "Managing side effects" below.) Injection site reactions, about 5% of which need medical attention. Less common: allergic reactions, depression, liver abnormalities, low white blood cell counts. (See "Betaseron Warnings" on page 13.)
- ▶ **Copaxone®**
- ▶ Injection site reactions. Less common: vasodilation (dilation of blood vessels); chest pain; a reaction immediately after injection, which includes anxiety, chest pain, palpitations, shortness of breath, and flushing. This lasts 15–30 minutes, typically passes without treatment, and has no known long-term effects. (See "Copaxone Warnings" on page 13.)
- ▶ **Extavia®**
- ▶ Flu-like symptoms following injection, which lessen over time for many. (See "Managing side effects" below.) Injection site reactions, about 5% of which need medical attention. Less common: allergic reactions, depression, liver abnormalities, low white blood cell counts. (See "Extavia Warnings" on page 14.)
- ▶ **Rebif®**
- ▶ Flu-like symptoms following injection, which lessen over time for many. (See "Managing side effects" below.) Injection site reactions. Less common: liver abnormalities, depression, allergic reactions, and low red or white blood cell counts. (See "Rebif Warnings" on page 16.)

(NMS, 2013)

Fingolimod (Gilenya®)

- ▶ Approved in 2010 for adults with relapsing/remitting MS to reduce the frequency of clinical relapses and delay increase in physical disability.
- ▶ Exclusion criteria: known allergy to fingolimod, pregnancy (category C) or breast feeding, cardiac abnormalities – AV block sick sinus syndrome, CHF or ischemic heart disease
- ▶ Dose is 0.5 mg capsule once a day

(U of M pharmacy, 2013)

Fingolionmod continued

▶ Pre-dose requirements

- EKG
- Liver function tests
- Complete blood cell count
- BUN/creatinine
- Pregnancy test
- Pulmonary function test
- Ophthalmology consult
- Dermatology consult
- VCZ antibody status

▶ Monitoring 1st dose

- EKG prior to 1st dose and 6 hours post dose
- Hourly vital signs

Fingolimod continued

▶ Post dose monitoring

- Ophthalmology evaluation 3–4 months after first dose
- Monitor liver enzymes , ALT & AST, approximately 3 and 6 months

▶ Gilenya Support Program

- (877)408-4974

Fingolimod continued

- ▶ Side effects
 - Headache
 - Diarrhea
 - Back pain
 - Cough
 - Hypertension
 - Alopecia, eczema, pruritus
 - Fetal risk lasts 2 months after medication is discontinued

(Package insert)

Fingolimod continued

- ▶ Adverse Reactions:
 - Ketoconazole
 - QT prolonging medications
 - Vaccines
 - Citalopram(Celexa)

(package insert)

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(package insert)

Teriflunomide (Aubagio®)

- ▶ Approved in 2012 for treatment of relapsing/remitting MS
- ▶ Shown to reduce rate of relapses and MRI disease activity
- ▶ Dose is 7 mg or 14 mg once a day
- ▶ Pregnancy X
 - Accelerated elimination protocol
 - Pregnancy deferred until blood test 0.02 micrograms per milliliter of teriflunomide

(CMSC, 2013)

Teriflunomide (Aubagio®)

- ▶ Pre dose:
 - Pregnancy test
 - Liver enzymes
 - Complete blood cell count
 - Screen for latent tuberculosis
 - Baseline blood pressure
 - No current infections
- ▶ During therapy:
 - Liver functions tests
 - Complete blood cell count
 - Confirm use of reliable contraception

(U of M Pharmacy, 2013)

Common Side effects of Teriflunomide

- ▶ Diarrhea
- ▶ Nausea
- ▶ Dyspepsia
- ▶ Increased liver enzymes
- ▶ Alopecia
- ▶ Skin rashes
- ▶ Infections
- ▶ Neutropenia
- ▶ Paresthesia
- ▶ Hypertension

(CMSC, 2013)

Dimethyl fumarate (Tecfidera®)

- ▶ Approved in 2013
- ▶ Dose titrated 120mg capsule by mouth twice a day for 7 days then 240 mg capsule by mouth twice a day
- ▶ Called BG12

(CMSC, 2013)

Dimethyl fumarate (Tecfidera®)

- ▶ Exact mode of action is unknown.
- ▶ Thought to inhibit immune cells and molecules
- ▶ May have anti-oxidant properties, could be protective against damage to spinal cord and brain

(NMSS, 2013)

Dimethyl fumarate (Tecfidera®)

- ▶ Side Effects:
 - Flushing (40%)
 - GI side effects
 - Pain (18%)
 - Diarrhea (14%)
 - Nausea (12%)
 - Vomiting (9%)
 - Dyspepsia (5%)
 - Itching

(CMSC, 2013)

Dimethyl fumarate (Tecfidera®)

- ▶ Can be taken without food but taking with food may reduce risk of flushing
- ▶ Reduced blood lymphocyte (WBC) No significant or severe infections
- ▶ Liver enzymes elevated No reports of significant liver injury or liver failure
- ▶ Patient Support Program– MS ActiveSource
 - (800)–456–2255

(NMSS, 2013)

Dalfampridine (Ampyra®)

- ▶ Extended Release Tablets, 10 mg
- ▶ Potassium channel blocker indicated as a treatment to improve walking in patients with MS. This was demonstrated by an increase in walking speed.

Ampyra® (dalfampridine) prescribing information.

Dalfampridine (cont)

- ▶ Dalfampridine improved walking speed in significantly more individuals than placebo (sugar pill) in 2 clinical studies (34.8% vs. 8.3% and 42.9% vs. 9.3%)
- ▶ Do not take dalfampridine if you've ever had a seizure
- ▶ Do not take dalfampridine if you have decreased kidney function as this may increase your risk of seizure
 - Tell your healthcare provider if you have or believe you may have kidney problems

Ampyra® (dalfampridine) prescribing information.

What Are Some of the Potential Issues With Compounded 4-Aminopyridine (4-AP)?

- ▶ Not FDA regulated
- ▶ May require frequent dosing
- ▶ Overdose resulting from pharmacy errors

(CMSC, 2013)

IV therapy

- ▶ Tysabri
- ▶ Novantrone
- ▶ Cytoxan
- ▶ Rituximab

