Overview of Multiple Sclerosis Care

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Disclosures

I have no relevant financial relationships to disclose.

I will discuss off label use or investigational use in my presentation.

- Rituximab for MS

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Objectives

- Recognize clinical phenotypes and typical clinical symptoms of MS
- Review diagnostic criteria and diagnostic challenges
- Understand the role of disease modifying therapies
- Highlight on health maintenance and wellness in collaborative care

Introduction

- Chronic neurologic disorder involving central nervous system
- Immune mediated demyelinating disease with neurodegenerative mechanisms
- F:M (3:1)
- Onset of symptoms 20-50 years of age
- Clinical phenotypes[1]
  - Relapsing Remitting
  - Secondary Progressive
  - Primary Progressive

Disease Course

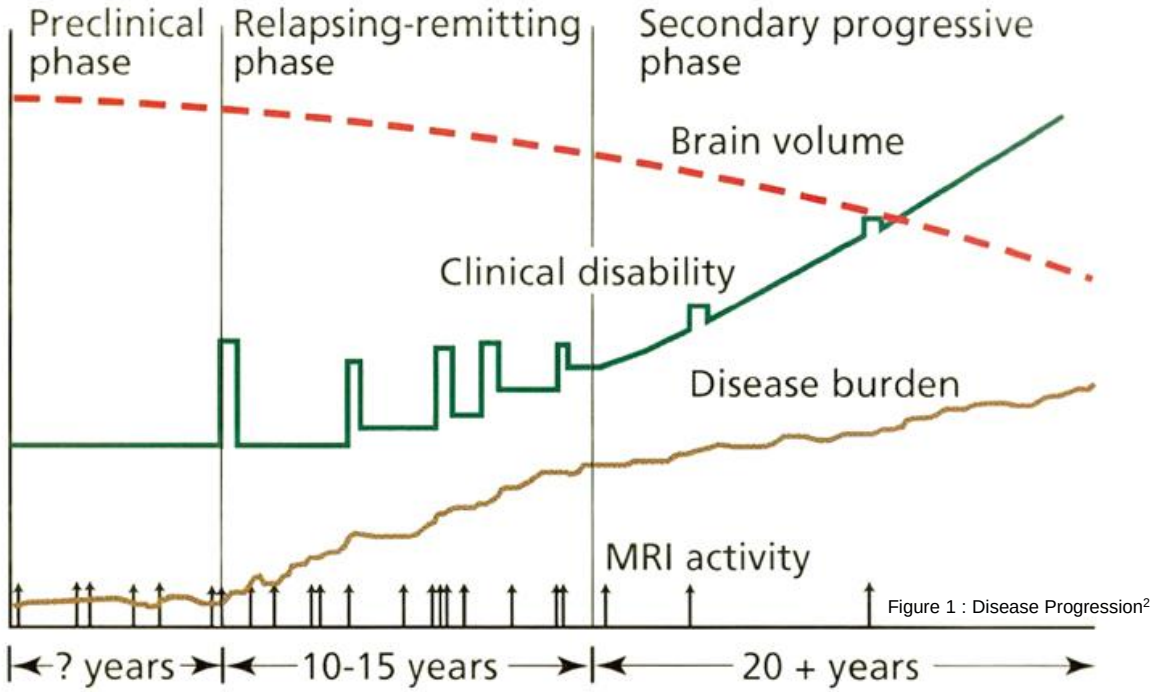

Figure 1 : Disease Progression[2]

Treatment benefit

Symptom management and rehab needs

Health Maintenance and Wellness

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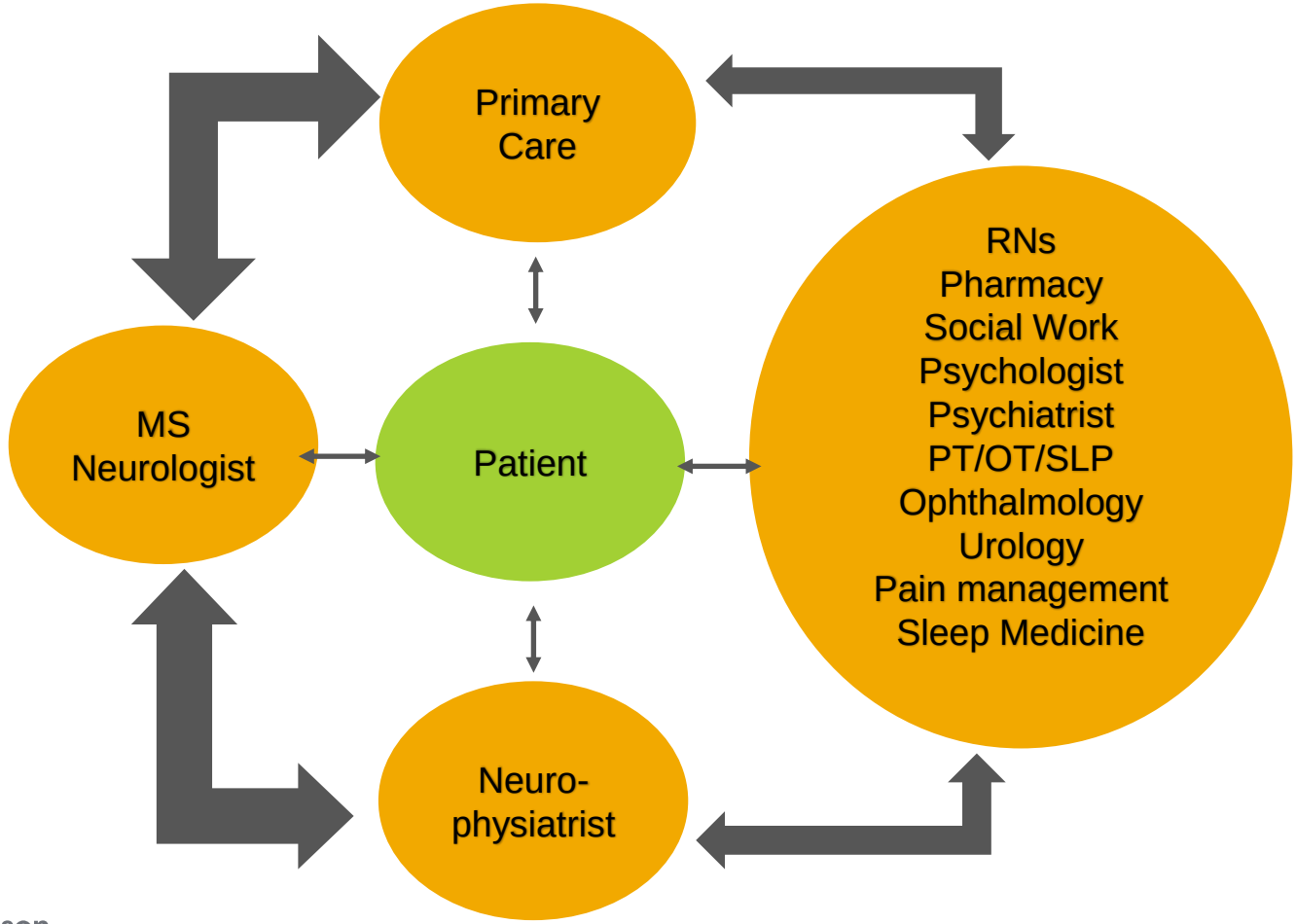

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Typical MS presenting symptoms

- Paresthesias – hemibody and face involvement
- Transverse/partial myelitis – ascending numbness, numbness/weakness in arm/leg on one side
- Optic Neuritis – monocular vision loss, eye pain
- Brainstem - vertigo, ataxia, double vision
- Lhermitte's
- *Slow progressive gait difficulty with weakness

- Non-specific symptoms such fatigue, cognitive dysfunction, blurry vision, headache, diffuse pain, tingling in feet, bladder and bowel changes by themselves are not likely to be MS

Clinical Relapse: subacute onset of focal neurologic symptoms with progression lasting longer than 24 hours

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There is no specific diagnostic biomarker for MS

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Diagnosis

- Combination of clinical + MRI criteria +/- CSF specific OCBs
- “DIT” and “DIS”

TABLE 1. MCDONALD CRITERIA FOR DIAGNOSIS OF MULTIPLE SCLEROSIS

Typical attack or clinically isolated syndrome at onset	≥2 attacks and objective clinical evidence of ≥2 lesions
	≥2 attacks and objective clinical evidence of 1 lesion AND history of prior attack
	≥2 attacks and objective clinical evidence of 1 lesion **AND** history of prior attack implicating different lesion site **OR** ≥1 MS-typical T2-enhancing lesion that is perientricular, juxtacortical, infratentorial, or in spinal cord
	1 attack and objective clinical evidence of ≥2 lesions **AND** history of prior attack implicating different lesion site **OR** simultaneous presence of BOTH enhancing and nonenhancing MS-typical lesions (symptomatic or asymptomatic) **OR** new T2 or enhancing MS-typical lesion compared to previous MRI findings **OR** presence of oligoclonal bands in CSF (not serum)
	1 attack and objective clinical evidence of 1 lesion **AND** history of prior attack implicating different lesion site **OR** ≥1 MS-typical T2-enhancing lesion in ≥2 periventricular, juxtacortical, infratentorial, or spinal cord sites **AND** history of prior attack implicating different lesion site **OR** simultaneous presence of BOTH enhancing and nonenhancing MS-typical lesions (symptomatic or asymptomatic) **OR** new T2 or enhancing MS-typical lesion compared to previous MRI findings **OR** presence of oligoclonal bands in CSF (not serum)
Progression of disability from onset	1 year of disability progression **AND** 2 of the following: **OR** ≥1 MS-typical T2-enhancing lesion in ≥2 periventricular, juxtacortical, infratentorial, or spinal cord sites **OR** ≥2 T2 spinal cord lesions **OR** presence of oligoclonal bands in CSF (not serum)

Abbreviation: CSF, cerebrospinal fluid.

Figure 2. 2017 McDonald’s Criteria[3,4]

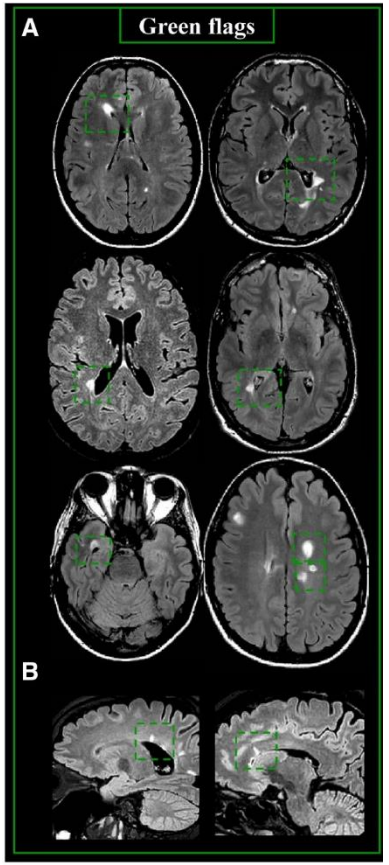

Figure 3. Typical MS MRI lesions.[5]

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Diagnostic challenges

- Patients may not meet full diagnostic criteria at initial onset
- Clinical symptoms that are typical of MS but MRI is not diagnostic
- RIS: incidental MRI lesions suggestive of demyelinating disease w/o clinical symptoms
- Incidental non-specific white matter lesions with diffuse non-specific neurologic symptoms without a clear diagnosis

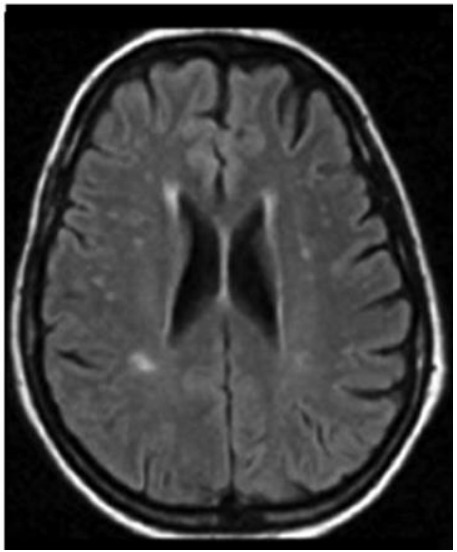

Figure 4. Non-specific white matter disease

Disease modifying therapies are not curative, not restorative, not fully preventive, but are effective at modifying disease course and slowing disability progression

Disease modifying therapies

- > 20 brand name or generic treatments
  - Injectables, orals, infusions
- Primarily target inflammatory activity
  - Decrease clinical relapses
  - Decrease MRI lesions – Gd and T2
- Early treatment is key in preventing disability
- Evidence less robust for progressive disease
  - Ocrelizumab for PPMS[7]
- Discontinuation trials are now underway

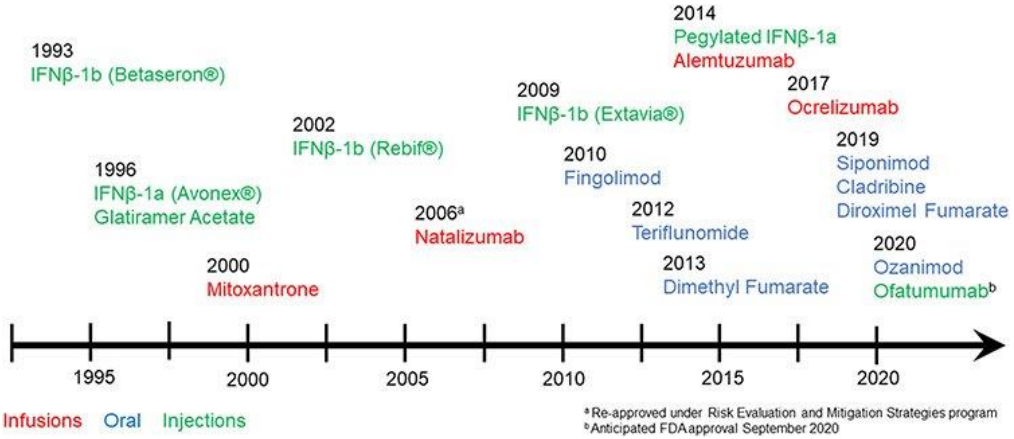

Figure 5: Disease modifying therapies[6]

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Disease modifying therapies: monitoring

- Escalation or change in therapy may be needed
  - Goal = NEDA “No evidence of disease activity”
    - MRI brain +/- spine 1-3 years while on therapy for subclinical disease (local imaging)
    - Monitor clinical relapses (treat as needed)
  - Monitor for Adverse Effects
    - Laboratory data – consolidate with PCP annual labs
    - Monitor for severe infections - re-evaluate risk/benefit
    - Lymphopenia - may or may not represent an increase risk in infections (S1P1 receptor modulators)[7]
- Non-live vaccines are safe in MS patients[8]
  - Ocrelizumab, Ofatumumab, Rituximab; Fingolimod, Siponimod, and Ozanimod have shown decreased vaccine responses[9,10]

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Relapse treatment

- Evaluate for pseudo-relapse first: worsening of usual baseline symptoms
  - Rule out any infection including URI, UTI
- IV methylprednisolone 1000 mg x 3-5 days +/- prednisone taper
- PO bioequivalent 1250 mg prednisone x 3 days[11]
  - Used for new *disabling symptoms* related to a clinical relapse
  - Relapses can naturally get better on their own
  - Decrease duration of symptoms
- Physical Therapy referrals
- Consider MRI Imaging

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Chronic symptoms

- Spasticity and pain
- Impaired gait and mobility
- Mood disorders
- Cognitive disorder
- Visual changes
- Speech, swallowing difficulties
- Sexual Dysfunction
- Neurogenic Bowel
- Neurogenic Bladder
- Fatigue

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Health Maintenance & Wellness

- Smoking cessation counseling
- Optimizing Vitamin D (goal level 40 – 60)
- Regular aerobic exercise
- Attention to cardiovascular risk factors
- Mental health support
- Fall prevention
- Monitor for osteoporosis
- Vaccinations
- Encourage initiation of DMT in hesitant young RRMS pts

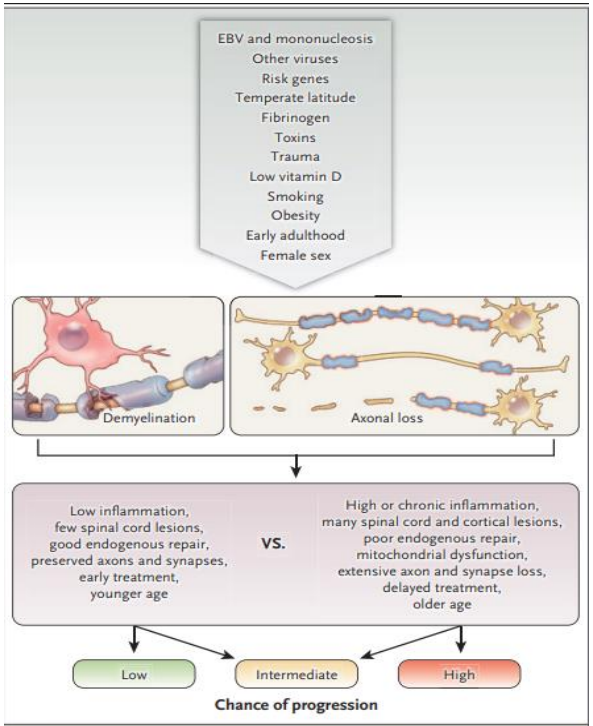

Figure 3. Risk Factors, Triggers, Modifiers, and Disease Courses.
It is unlikely that multiple sclerosis will ultimately be attributed to a single cause. Rather, the genetic and environmental factor or combination of factors that result in a predisposition to multiple sclerosis, initiate the disease, and modify its course are highly diverse from one person to the next. The top portion of the figure shows the funneling of proposed factors, for which varying levels of evidence exist, into the development of inflammatory, demyelinating lesions with heterogeneous axonal loss (middle portion). The bottom portion of the figure lists features of the lesions and their consequences that are generally salutary or deleterious and that modify the risk of progression. EBV denotes Epstein–Barr virus.

Figure 6: MS Risk factors, triggers, modifiers[12]

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Questions?

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