THE 13TH ANNUAL LINDA MORGANTE

Multiple Sclerosis Nurse Leadership Program

2022

WELCOME

Provided by Academy for Continued Healthcare Learning and Annenberg Center for Health Sciences at Eisenhower

ACHL
ACADEMY for CONTINUED HEALTHCARE LEARNING

ANNENBERG CENTER FOR HEALTH SCIENCES AT EISENHOWER

The program is supported through educational grants from Biogen, Bristol-Myers Squibb, Inc., and Novartis Pharmaceuticals Corporation.

Activity Overview

Target Audience
This activity is intended for nurses and advanced practice clinicians who manage patients with multiple sclerosis (MS).

Learning Objectives
Upon completion of this activity, participants will be able to:

- Apply evidence-based diagnostic and assessment approaches for evaluating disease activity in the brain and spinal cord to develop individualized treatment plans in patients with MS
- Improve patient outcomes and adherence to therapy by identifying, assessing, and managing emerging MS-related symptoms and disease modifying therapy (DMT)-related adverse events.
- Employ treat-to-target strategies and precision medicine to improve patient long-term outcomes

Support
Supported by educational grants from Biogen, Bristol-Myers Squibb, and Novartis Pharmaceuticals Corporation.

Faculty

Colleen Harris, MN, NP (Co-Chair)
Nurse Practitioner
University of Calgary MS Clinic
Calgary, Alberta, Canada

Amy Perrin Ross, MSN, APN (Co-Chair)
Neuroscience Program Coordinator
Loyola University Chicago Medical Center
Maywood, Illinois

Faculty

Stephanie Agrella, PhD, APN-BC, MSCN
Director of Clinical Services
MS Clinic of Central Texas Neurology
Round Rock, TX

Aliza Ben-Zacharia, PhD, DNP, ANP-BC, FAAN, MSCN
Assistant Professor
Co-Director of the Research, EBP and QI Fellowship
Phillip School of Nursing, Mount Sinai and Hunter College Assistant Professor
New York, New York

Constance Easterling, MSN, ARNP
Advanced Practice Registered Nurse
Research Consultant
MS Care Center
Neurological Services of Orlando
Orlando, Florida

June Halper, MSN, APN-C, MSCN, FAAN
Chief Executive Officer
Consortium of Multiple Sclerosis Centers and International Organization of Multiple Sclerosis Nurses
Hackensack, New Jersey

Michelle Keating, RN, MSCN
MS Nurse Consultant
President of MS Bright Spots of Hope
St. Louis, Missouri

Beverly Layton, RN, BSN
MS Nurse Consultant
Birmingham, Alabama

Lynn McEwan, NP, MScN
Nurse Practitioner MS Clinic
London, Ontario Canada

Marie Namey APRN, MSCN
Independent MS Nurse Consultant
Cleveland, Ohio

Accreditation and Credit Designation

Annenberg Center for Health Sciences is accredited as a provider of continuing nursing education by the American Nurses Credentialing Center’s Commission on Accreditation.

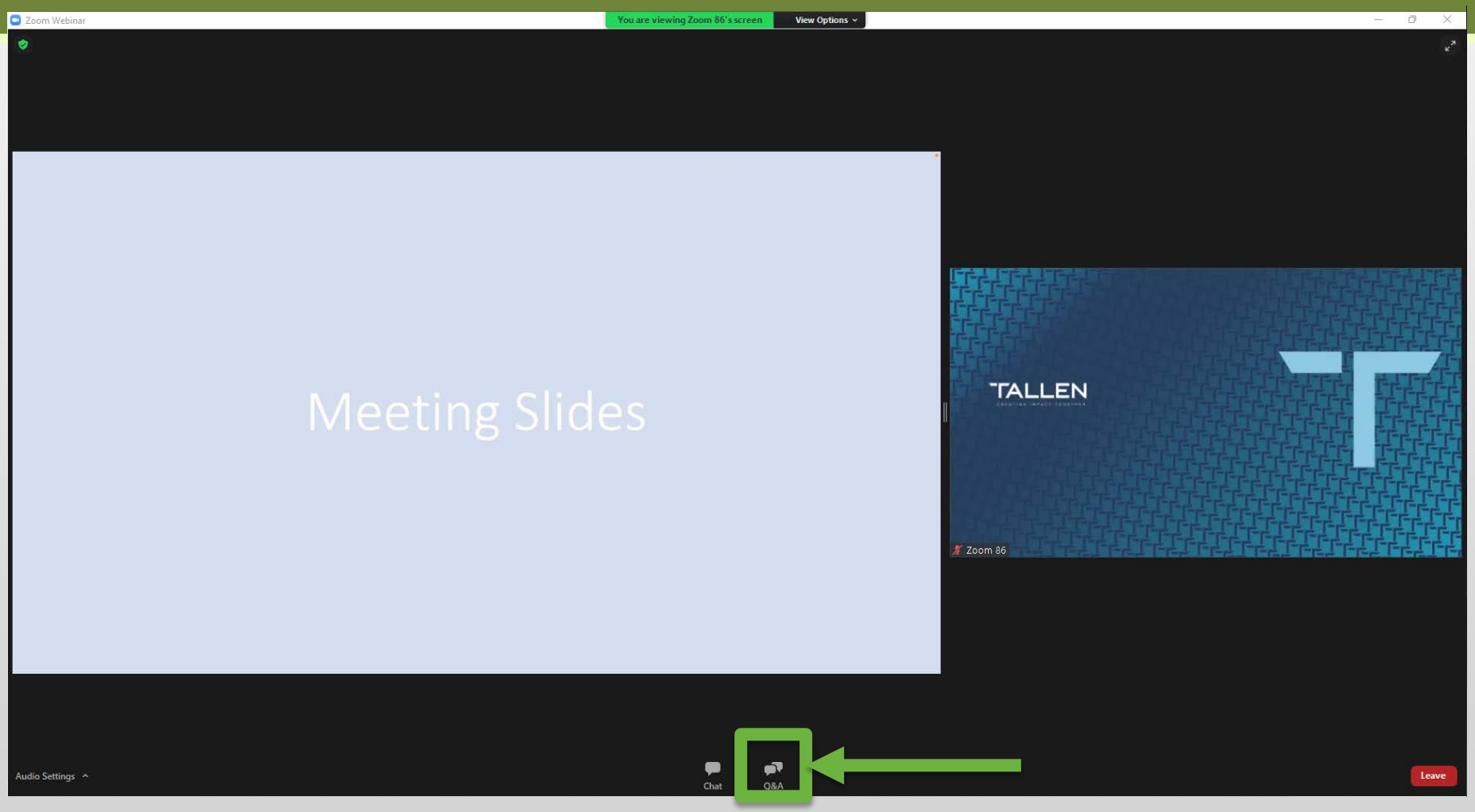
A maximum of 5.5 contact hours, which includes 1.25 pharmacology hours, may be earned for successful completion of this activity.

How to Receive Credit

1. Complete the pretest
2. Participate in the live virtual activity
3. Complete the posttest and evaluation
4. Certificate will be emailed to you within 2 weeks

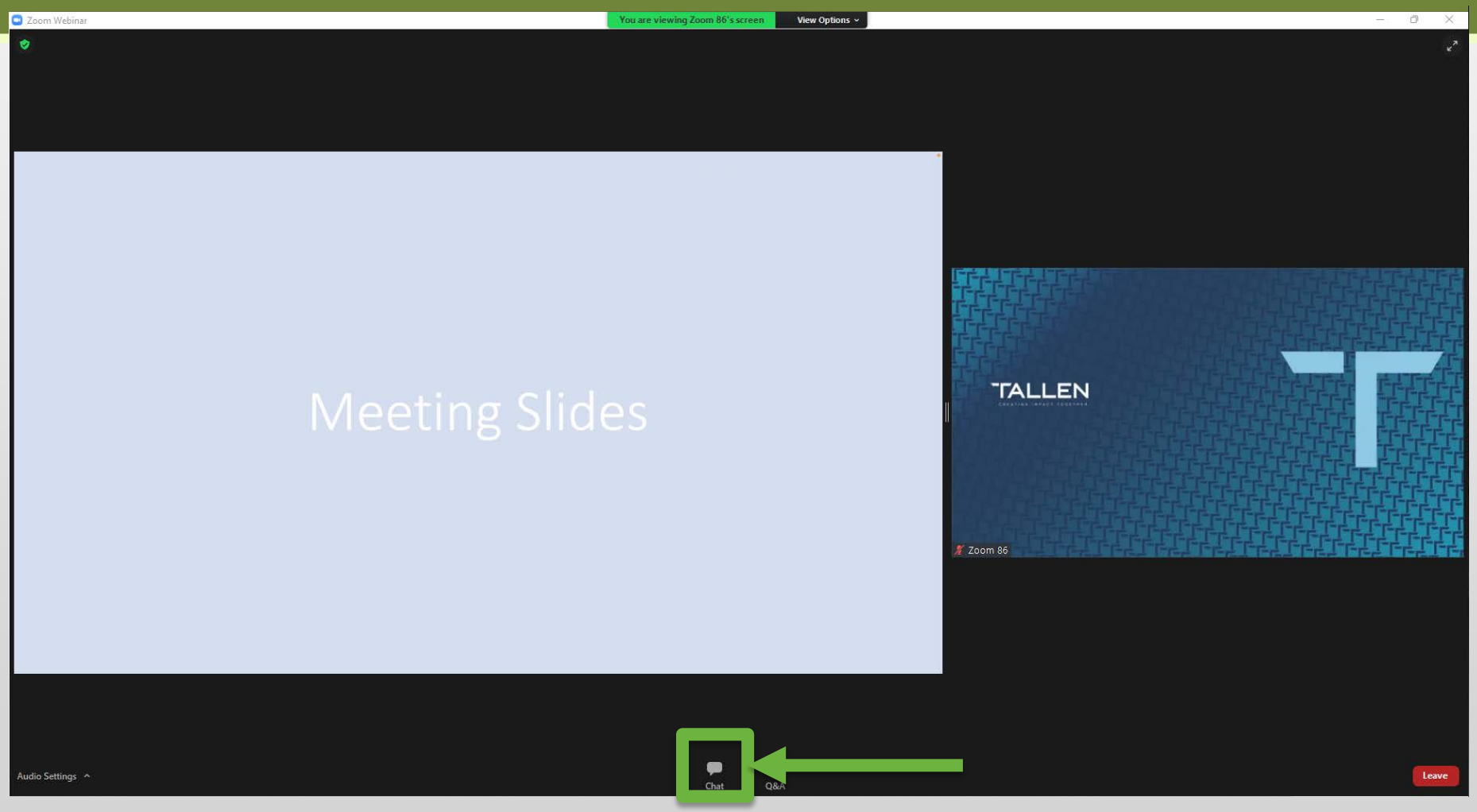
For questions, contact Katie Hacias at khacias@achlcme.org

Zoom Webinar Q&A



- Click on the Q&A Button
- This will open the Q&A box

Zoom Webinar Chat



- Click on the Chat Button.
- This will open the Chat box.

Linda Morgante:
A Nursing Hero

“Her persona was her beautiful self, her soft voice, her sensitivity to others, her tenderness and skills as a nurse, her great dignity and intelligence.”

June Halper

March 26, 2007

THE 13TH ANNUAL LINDA MORGANTE MS Nurse Leadership Program

About Linda

- Linda was an Advanced Practice MS Nurse
- She worked at Maimonides Medical Center in Brooklyn for over 20 years, then moved to the Corinne Goldsmith Dickinson Center at Mount Sinai Hospital in New York City
- She completed her career at St. Joseph’s College in Brooklyn, New York, as an Assistant Professor of Nursing

Linda: To Her Colleagues

Role model

Teacher

Mentor

Writer

Compassionate friend

Linda: To Her Patients From “Losing Someone Twice”

- “Just the sound of her voice put me at ease.”
- “She was not only the resource of wealth and information, but she could also listen like no one I know in the world of medicine.”
- “She sympathized without being dramatic or condescending.”
- “She was my first guide, companion, confidant, friend, and teacher in this life with MS.”
- “I told her when she left to teach that the only reason I was letting her go without a fight was to make more nurses like her.”

http://mslol.wordpress.com/losing-someone-twice. Accessed May 27, 2021.

Linda and Hope

- Linda was known for her studies of hope, and she inspired it in others
- In Linda's words…

"Hope is an essential element of life—it embodies our vision of the future, our opinion of ourselves and others, and our sense of control over the events and direction of our lives. The presence of hope for someone experiencing an illness can provide the energy necessary to promote health and enhance well being."

Linda Morgante…

Images courtesy of Colleen Harris, MN, NP, and Amy Perrin Ross, APN, MSN, CNRN, MSCN

…and Friends

Images courtesy of Colleen Harris, MN, NP, and Amy Perrin Ross, APN, MSN, CNRN, MSCN

THE 13TH ANNUAL LINDA MORGANTE

Multiple Sclerosis Nurse Leadership Program

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MULTIPLE SCLEROSIS OVERVIEW AND DIAGNOSIS

Aliza Ben-Zacharia, PhD, DNP, ANP-BC, FAAN
Private NP Multiple Sclerosis Practice
Assistant Professor, Co-Director Research/EBP, Mount Sinai
Assistant Professor, Hunter Bellevue School of Nursing

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MS Overview and Diagnosis

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Epidemiology

Multiple Sclerosis (MS)

- Immune-mediated disease of the CNS
- Affects an estimated 900,000 people in the US
- Leading cause of nontraumatic disability in young adults
- Mean age of onset: 20-30 years
- Female:male ratio → 3:1
- Leads to physical disability, cognitive impairment, and decreased quality of life
- Reduces life expectancy by 7 to 14 years

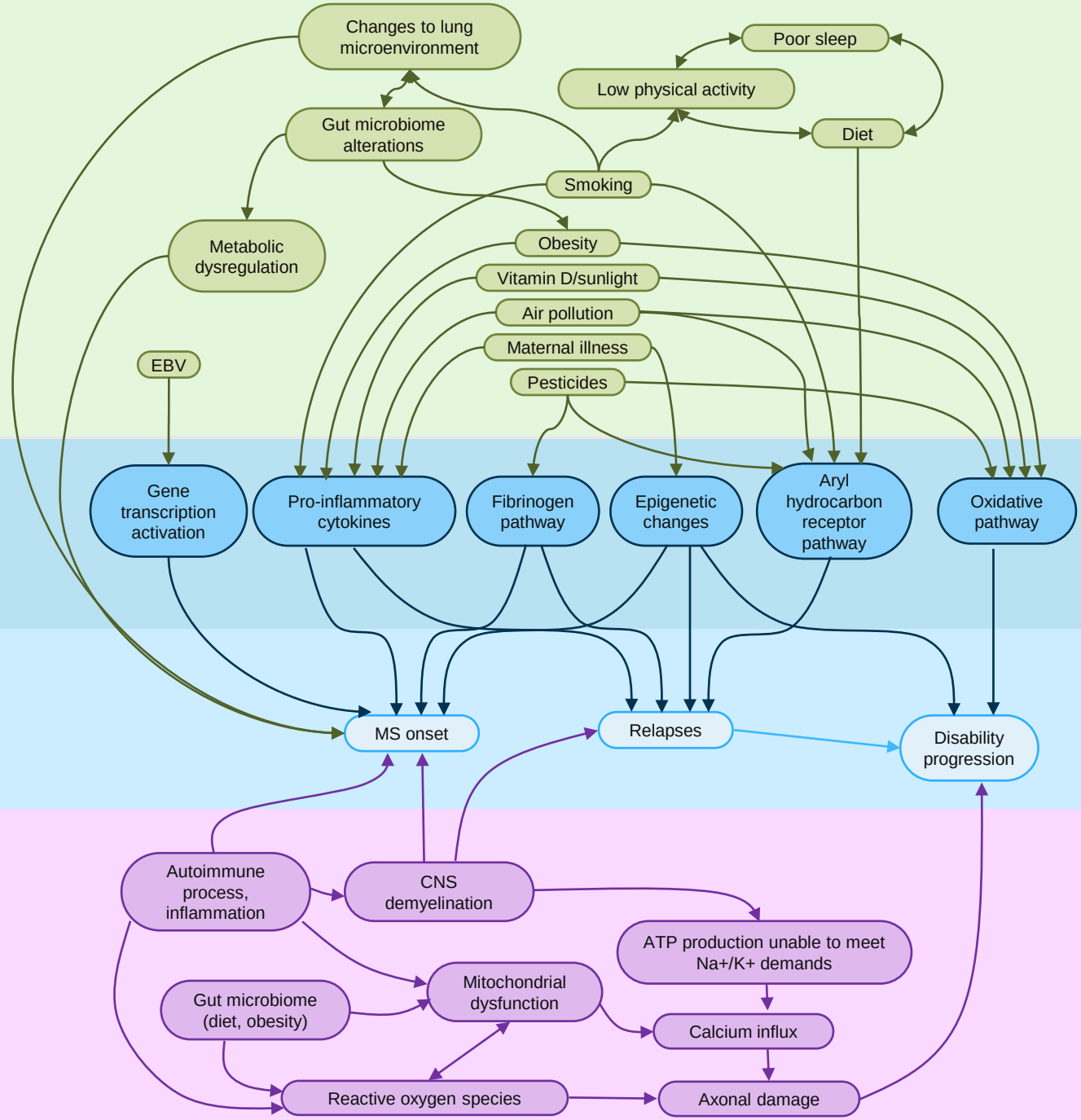
CNS = central nervous system

Magyari M et al. *Curr Opin Neurol*. 2019;32(3):320-6. Vaughn CB et al. *Nat Rev Neurol*. 2019;15(6):329-42.

Etiology

Environmental and Genetic Factors

- Around 20% of the heritability risk is attributable to HLA variant
  - HLA DRB15:01 haplotype (odds ratio [OR] ~3)
- Smoking
- Obesity
- Low sun exposure
  - Vitamin D deficiency
  - Latitude
- Infections
  - Epstein-Barr virus (EBV)



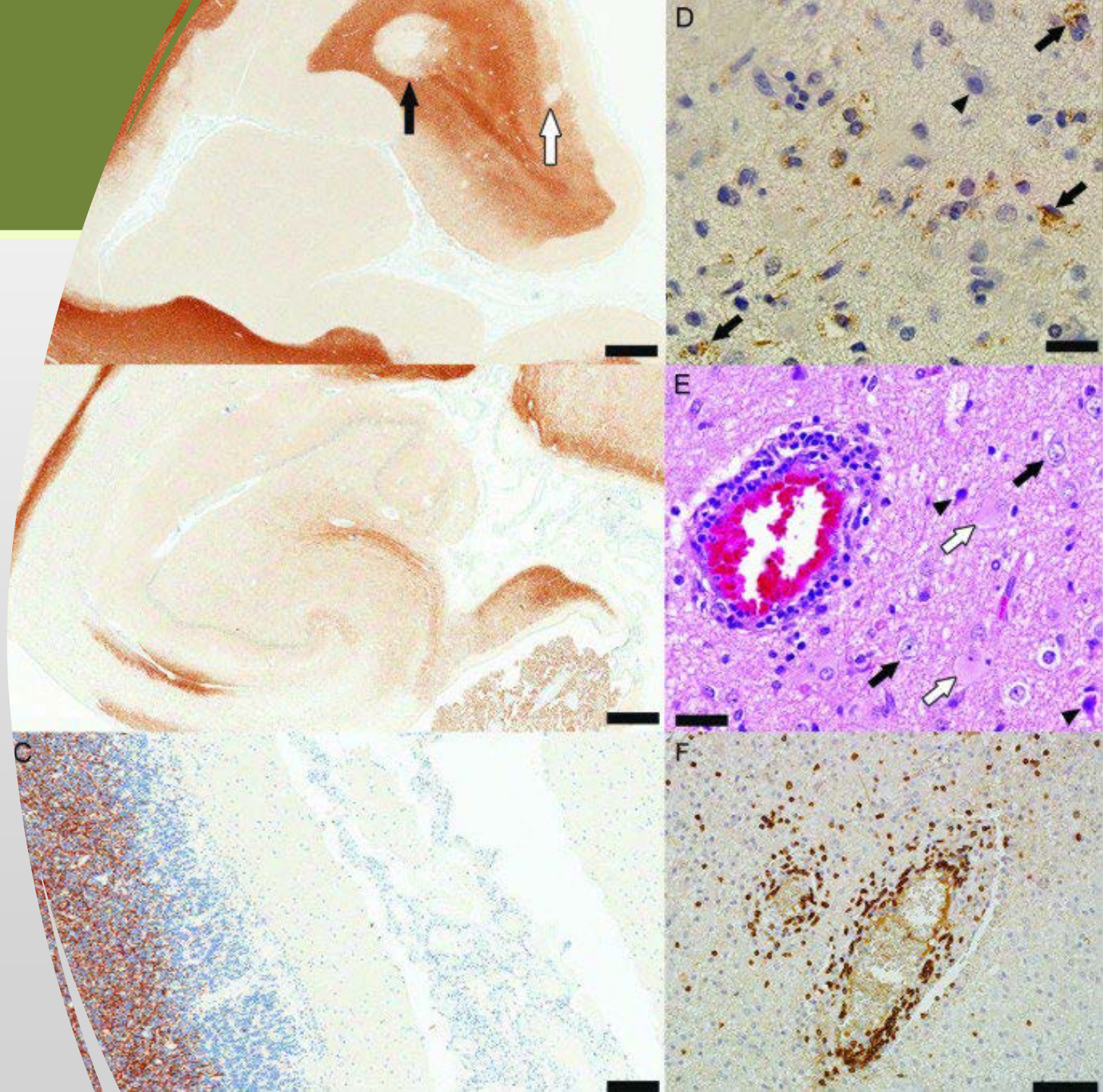
ATP = adenosine triphosphate; HLA human leukocyte antigen

Waubant E et al. *Ann Clin Transl Neurol*. 2019;6(9):1905-22.

Pathophysiology

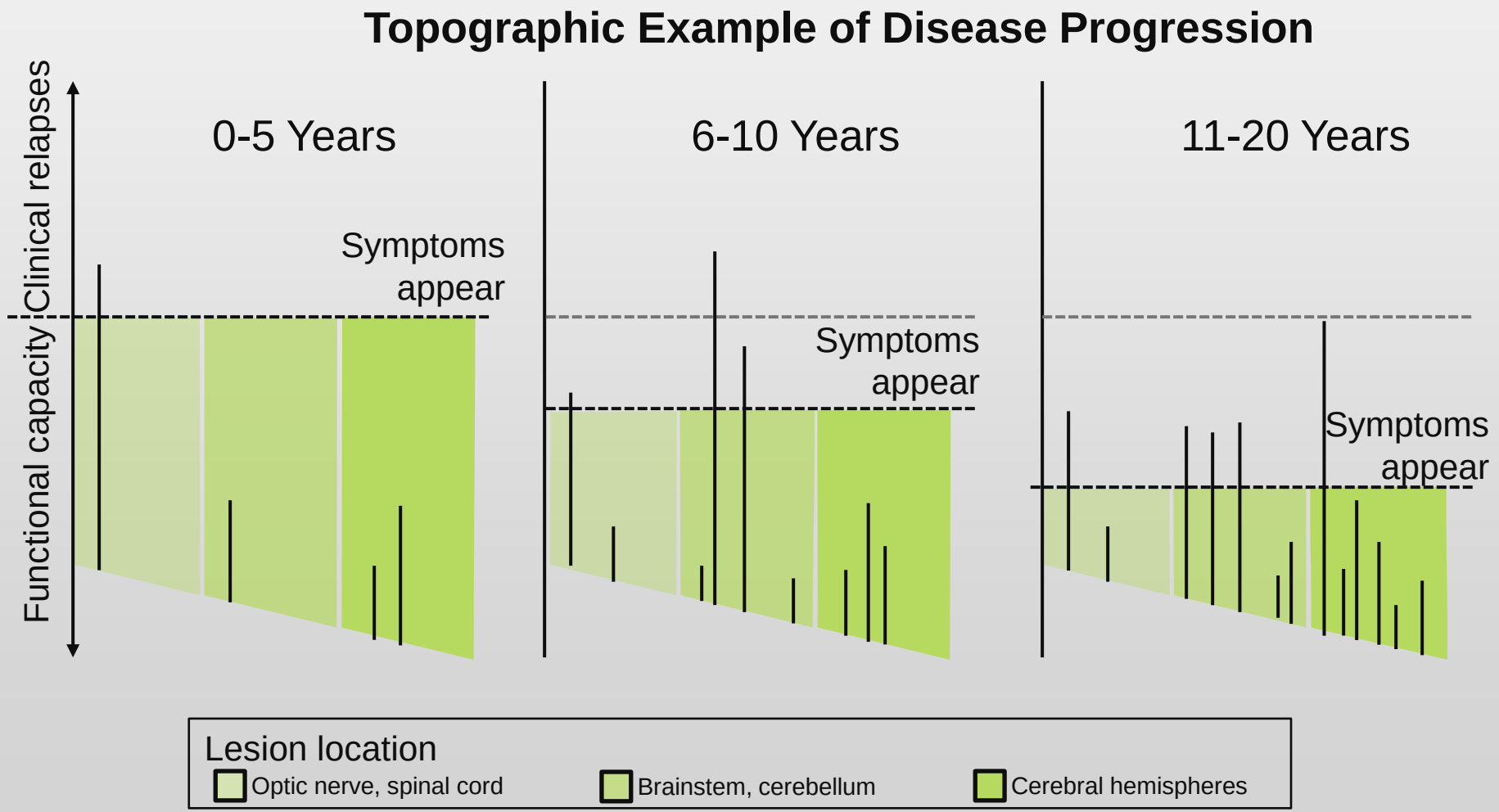
Multiple Sclerosis

- Inflammation with demyelination
- Astroglial proliferation (gliosis) and neurodegeneration
- Meningeal and cortical grey matter pathology in multiple sclerosis



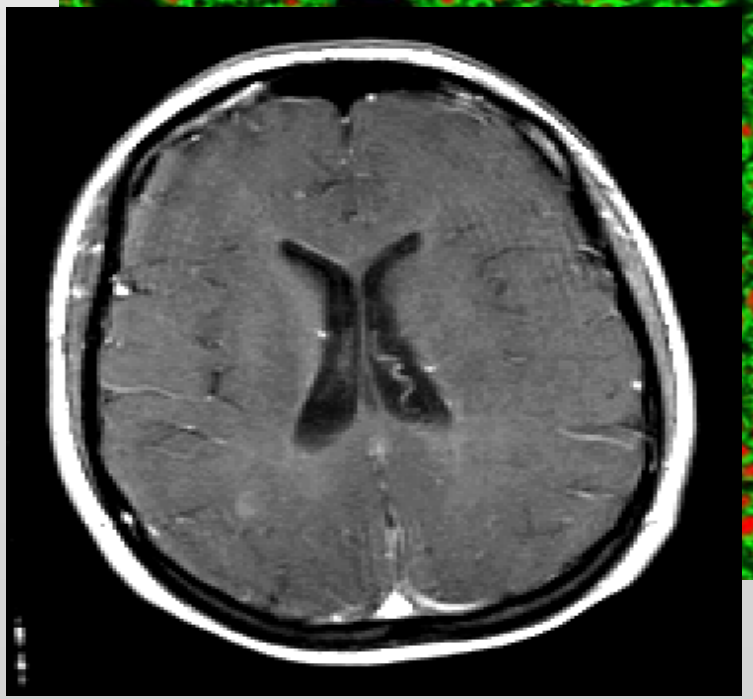
Popescu BFG et al. *BMC Neurology*. 2012;12:11.

MS as a Silent Disease: Topographic Model



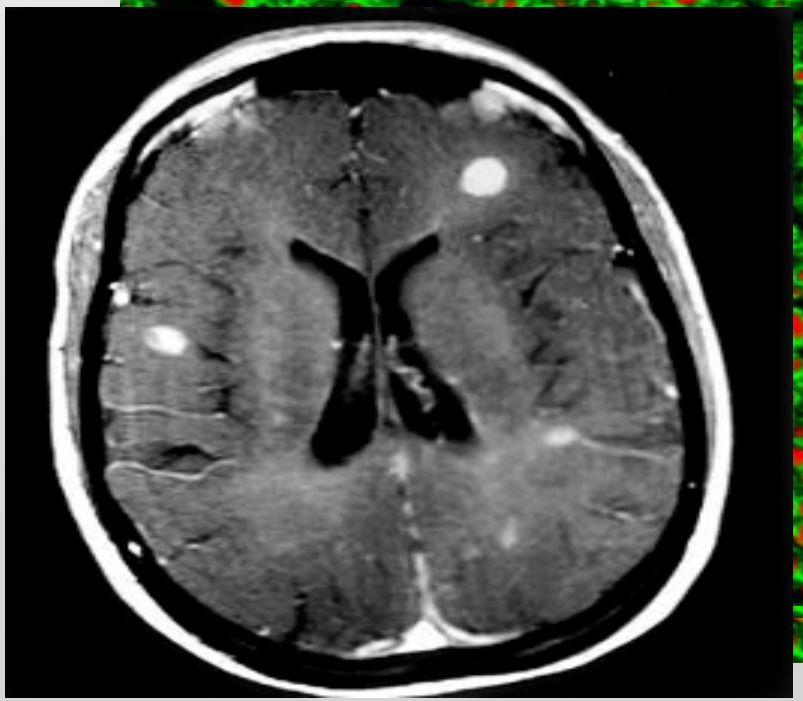
Krieger SC. 2015 CMSC; Poster DX47.

Normal White Matter



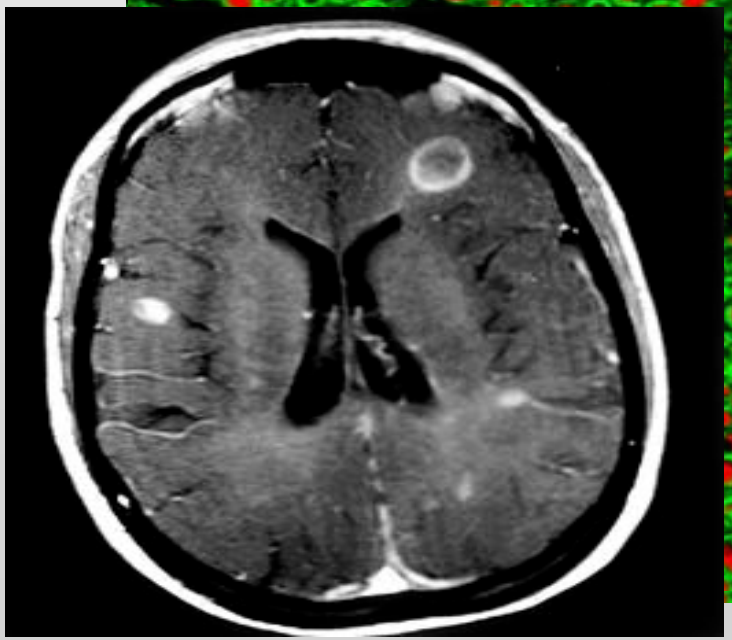
Images courtesy of Bruce D. Trapp

Active Lesion



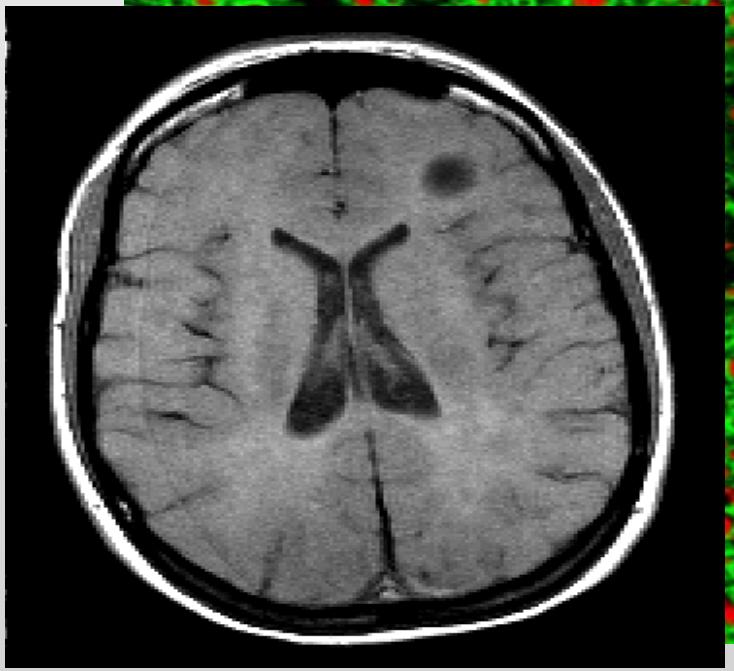
Images courtesy of Bruce D. Trapp

Chronic Active Lesion



Images courtesy of Bruce D. Trapp

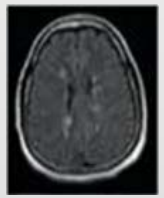
Chronic Inactive Lesion

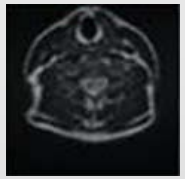


Images courtesy of Bruce D. Trapp

Prodromal Phase and Natural History

Prodromal MS





Genetic Factors

Environmental Exposures

Disease Initiation

RIS

Prodromal Period

CIS

MS Diagnosis

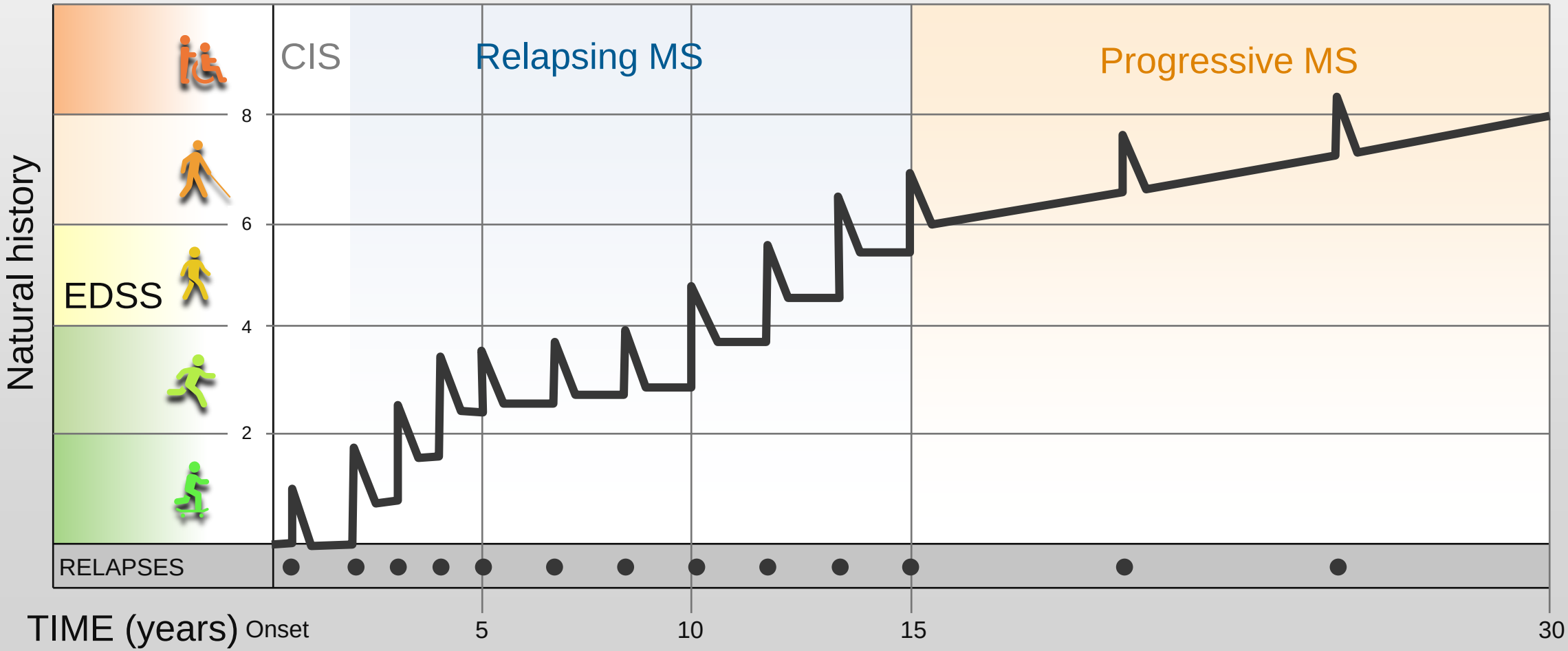
Risk factors for MS

Prodrome
fatigue, pain, headache, low mood, anxiety, bladder issues, infections

CIS = clinically isolated syndrome; RIS = radiologically isolated syndrome

Adapted from Tremlett H et al. *Mult Scler*. 2021;27(1):6-12.

Natural History of MS Pretreatment Era



EDSS = Expanded Disability Status Scale

Hauser SL et al. *Am J Med*. 2020;133(12):1380-90.

Diagnosis

MS Diagnosis

MS is diagnosed based on clinical findings and supporting evidence from ancillary tests

Magnetic resonance imaging (MRI)	Evoked potentials	Lumbar puncture
• The imaging procedure of choice for confirming MS and monitoring disease progression in the CNS	• Used to identify subclinical lesions; results are not specific for MS	• May be useful to support DIT; CSF is evaluated for oligoclonal bands and intrathecal immunoglobulin (Ig)G production

CSF = cerebrospinal fluid; DIT = dissemination in time

https://cdn.ymaws.com/mscare.site-ym.com/resource/collection/9C5F19B9-3489-48B0-A54B-623A1ECEE07B/2018MRIGuidelines_booklet_with_final_changes_0522.pdf. Accessed August 16, 2021.

Difficulty in Diagnosing MS

- There is no single pathognomonic clinical feature or diagnostic test for MS
- Other conditions can mimic MS in:
  - MRI appearance
  - Clinical presentation
  - Clinical course
  - CSF findings
- Increased risk for more than 1 autoimmune condition
- Great variability in MS
  - Age of onset
  - Clinical course
  - Symptoms and signs
  - Paraclinical evidence
- Misdiagnosis of MS remains a problem in clinical practice

Gaitán MI et al. *Front Neurol*. 2019;10:466.

Typical Presenting Syndromes of MS

Optic Neuritis	Myelitis	Brainstem/ Cerebrum	Cerebellum
• Unilateral • Retrobulbar pain and/or with movement • Recovery expected • No retinal exudates or disc hemorrhages	• Partial sensory or motor • Bowel and bladder dysfunction • Thoracic band-like sensation • L'hermitte's sign	• Ocular motor syndromes • Hemisensory, crossed sensory • Hemiparesis • Trigeminal neuralgia • Hemifacial spasms	• Cerebellar tremor • Acute ataxia

Frohman EM et al. *Neurology*. 2003;61(5):602-11. Solomon AJ et al. *Neurology*. 2019;92(1):26-33. Brownlee WJ et al. *Mult Scler*. 2021;27(6):805-6.

Atypical Presenting Syndromes of MS

- Isolated 4th CN palsy
- Complete 3rd CN palsy
- Hearing loss
- Homonymous hemianopsia
- Aphasia
- Seizures
- Depressed LOC
- Progressive motor deficit
- Extrapyramidal features
- Loss of reflexes

CN = cranial nerve; LOC = locus of control

Solomon AJ et al. *Neurology*. 2019;92(1):26-33. Brownlee WJ et al. *Mult Scler*. 2021;27(6):805-6.

Disorders That Can Mimic MS

Vascular	• Migraine; CNS vasculitis; antiphospholipid syndrome; CADASIL (cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy)
Inflammatory autoimmune diseases	• Systemic lupus erythematosus (SLE); neuro-Behçet disease; Sjögren syndrome; sarcoidosis; Susac's syndrome
Inflammatory demyelinating disorders	• Neuromyelitis optica spectrum disorders (NMOSDs); anti-MOG; acute disseminated encephalomyelitis (ADEM); tumefactive MS
Infectious disorders	• Neuroborreliosis (Lyme disease); syphilis; West Nile virus; progressive multifocal leukoencephalopathy (PML); cysticercosis; HTLVI/II; HIV, or herpes encephalitis

HIV = human immunodeficiency virus; HTLVI/II = human T-lymphotropic virus type I/II; MOG = myelin oligodendrocyte glycoprotein

https://www.nationalmssociety.org/Symptoms-Diagnosis/Other-Conditions-to-Rule-Out. Accessed August 16, 2022.

Disorders That Can Mimic MS (cont)

Metabolic disorders	• Mitochondrial disorders (MELAS, MERRF, LHON); B_{12} deficiency; Wilson's disease
Leukodystrophies	• Adrenoleukodystrophy • Metachromatic leukodystrophy
Multifocal CNS neoplasms	• Lymphoma; gliomatosis cerebri • Metastases
Other	• Spinal stenosis; central pontine myelinolysis; radiation therapy • Medication: adalimumab

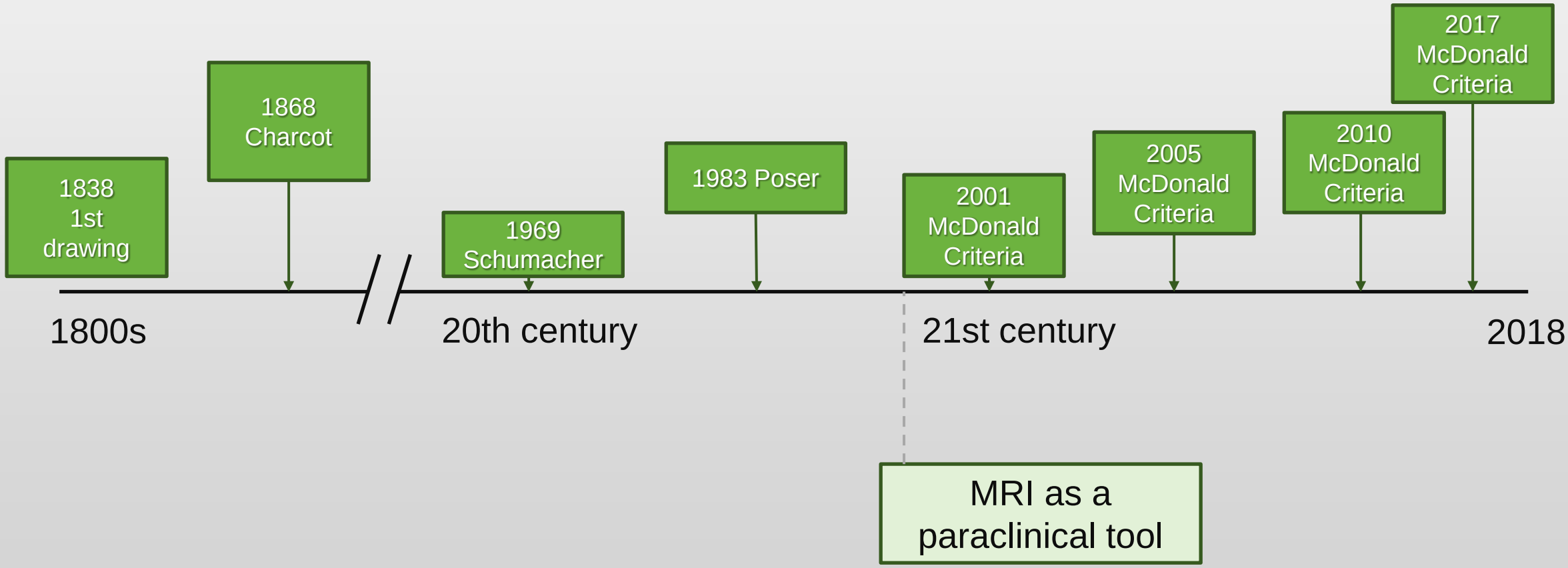
LHON = Leber hereditary optic neuropathy; MELAS = mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes; MERRF = myoclonus epilepsy with ragged-red fibers

https://www.nationalmssociety.org/Symptoms-Diagnosis/Other-Conditions-to-Rule-Out. Accessed August 16, 2022.

MRI Diagnostic Criteria

MRI = magnetic resonance imaging

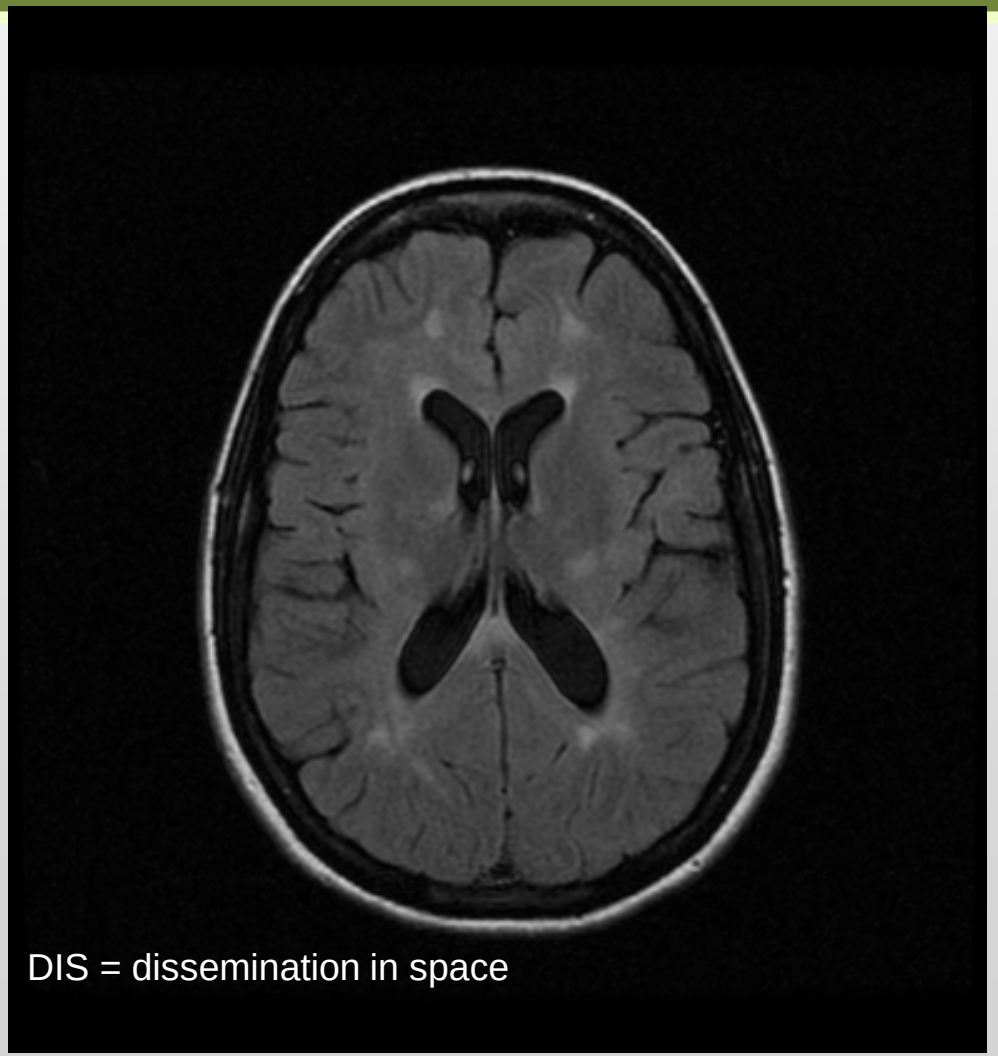
MS Criteria



Thompson AJ. *Lancet*. 2018;391(10130):1622-36. Partucco L. *Mult Scler J Exp Transl Clin*. 2017;3(3):2055217317721943.

2017 McDonald Criteria for Diagnosis of MS

No. of Clinical Attacks	No. of MRI Lesions With Objective Clinical Evidence	Additional Data Needed for Diagnosis of MS
Relapsing-remitting multiple sclerosis (RRMS)		
≥2	≥2	None
≥2	1 and evidence of prior attack different location	None
≥2	1	DIS demonstrated by an additional clinical attack implicating a different CNS site or by MRI
1	≥2	DIT demonstrated by additional clinical attack, MRI, or CSF-specific oligoclonal bands
1	1	DIS demonstrated by additional clinical attack implicating a different CNS site or by MRI *and* DIT demonstrated by an additional clinical attack or by MRI or demonstration of CSF-specific oligoclonal bands
Primary progressive multiple sclerosis (PPMS)		
Required: 1 year of disability progression (retrospectively or prospectively determined) independent of clinical relapse Plus 2 of the following: 1 or more T2-hyperintense lesions characteristic of MS in 1 or more of the following brain regions: periventricular cortical or juxtacortical, or infratentorial; 2 or more T2-hyperintense lesions in the spinal cord; presence of CSF-specific oligoclonal bands		



DIS = dissemination in space

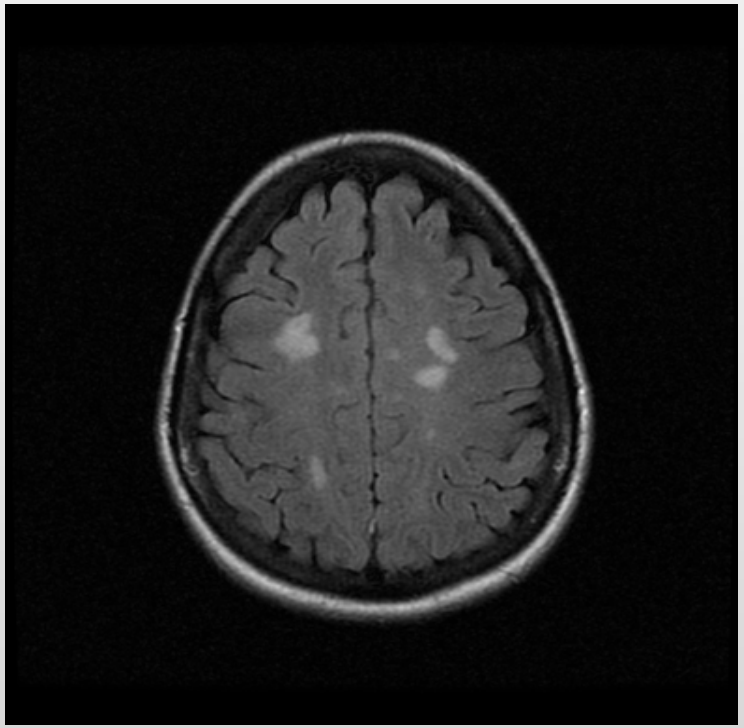
Thompson AJ et al. *Lancet Neurol*. 2018;17(2):162-73. Image courtesy of Aliza Ben-Zacharia, PhD, DNP, ANP-BC, FAAN

Key Changes Made to McDonald Criteria in 2017

- Brain stem and cord lesions can now be counted among the 2 lesions disseminated in space and time
- CSF oligoclonal bands can now be used to substitute for demonstration of dissemination in time in some settings
- Asymptomatic and now symptomatic MRI lesions can be considered in determining DIS (optic nerve lesions are still excluded)
- Cortical lesions have been added to juxtacortical lesions as determinant for DIS

Thompson AJ et al. *Lancet Neurol*. 2018;17(2):162-73.

MS Lesion Checklist



https://practicalneurology.com/articles/2018-july-aug/the-multiple-sclerosis-lesion-checklist. Accessed August 16, 2022. Image courtesy of Aliza Ben-Zacharia, PhD, DNP, ANP-BC, FAAN

FLAIR = fluid-attenuated inversion recovery

Description of Lesion Types	Present = yes Absent = no (Circle)	Note Number of Lesions
Nerve root entry zone. The lesions that track along nerve roots, especially the trigeminal nerve root, favor an inflammatory over vascular etiology. In an active MS lesion, enhancement may extend from parenchyma into nerve proper.	**Yes No**	
Middle cerebellar peduncle. Middle cerebellar peduncle (MCP) involvement in MS is seen frequently, but less than in the body of the pons.	**Yes No**	
Medial longitudinal fasciculus. This tract is commonly affected in MS clinically (internuclear ophthalmoplegia [INO]) and on MRI; however, vascular etiology is more common. Bilateral internuclear ophthalmoplegia may be somewhat more common in MS compared to stroke but is seen in many conditions.	**Yes No**	
Other brainstem lesions adjacent to CSF border. "With remarkable regularity the brainstem lesions [are] contiguous with the inner and outer CSF borders."	**Yes No**	
Cerebellar hemisphere. Demyelinating cerebellar lesions are not contiguous with the CSF border but appear within the deep cerebellar white matter. The cerebellum is often spared in vascular disease, but is commonly affected in MS, especially when the brainstem is involved.	**Yes No**	
Inferior temporal lobe. Another area of white matter that is preferentially affected in MS compared to vascular disease.	**Yes No**	
Lesions adjacent to lateral ventricle—*Dawson's fingers*. "Wedge-shaped areas with broad base to the [lateral] ventricle, and extensions into adjoining tissue in the form of finger-like processes or ampullae, in each of which a central vessel could usually be found." Frontal caps and bands along ventricular surface are normal signs of aging and should not be confused with periventricular demyelinating lesions.	**Yes No**	
Corpus callosum. Demyelination at the callosal-septal interface may take the form of discrete lesions or more diffuse lumpy-bumpy appearance (ie, dot-dash sign), which is seen on multiple sagittal FLAIR images, in contrast to the smooth appearance of the subcallosal vein that is usually only seen on a single sagittal image.	**Yes No**	
U-fibers (arcuate fibers). U-fiber lesions that track along arcuate fibers are particularly characteristic of demyelination and are not seen in normal aging or vascular disease.	**Yes No**	
Other cortical/juxtacortical lesions. Plaques in cortex and at junction of cortex and white matter are very common in MS. A recent study recommended combining cortical and juxtacortical lesions for purposes of MS diagnosis. Cortical lesions may be better appreciated on double inversion recovery (DIR) sequence, which is not routinely available.	**Yes No**	

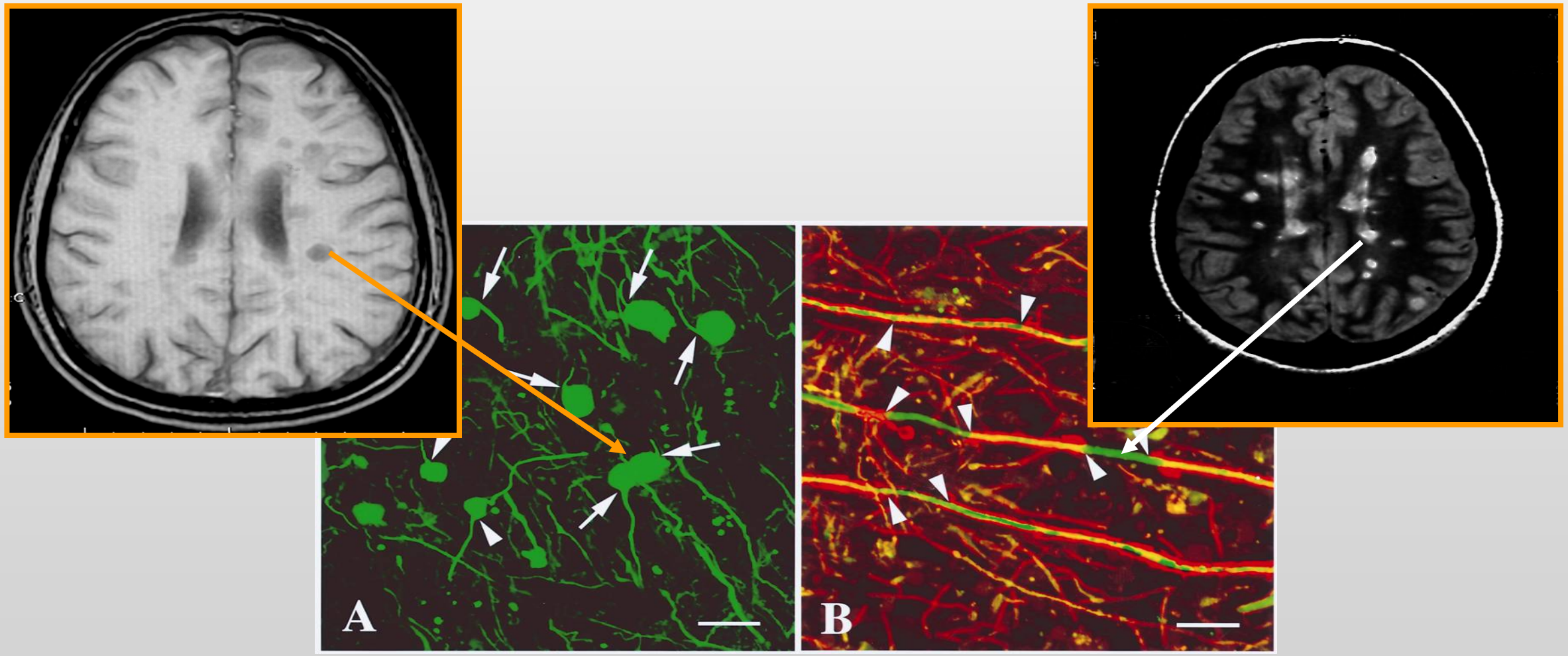
Typical MS Lesions

- Key locations
  - Periventricular
  - Corpus callosum
  - Cortical juxtacortical
  - Cerebellar peduncle
  - Cervical spine
- Shape
  - Oval/ovoid/>3-5 mm
  - Dawson’s fingers
- Well demarcated
- No mass effect/tumefactive

- Spinal cord lesions
  - <3 vertebral segments
  - Only part of cross-section of the cord
  - No extensive cord swelling
- Gadolinium (Gad) enhancement
  - Initially nodular
  - Can evolve to a ring or arc
    - T1 hypointense center
    - Opening of ring points toward cortex

Neema M et al. *Neurotherapeutics.* 2007;4(4):602-17.

Demyelination and Axonal Transection on MRI



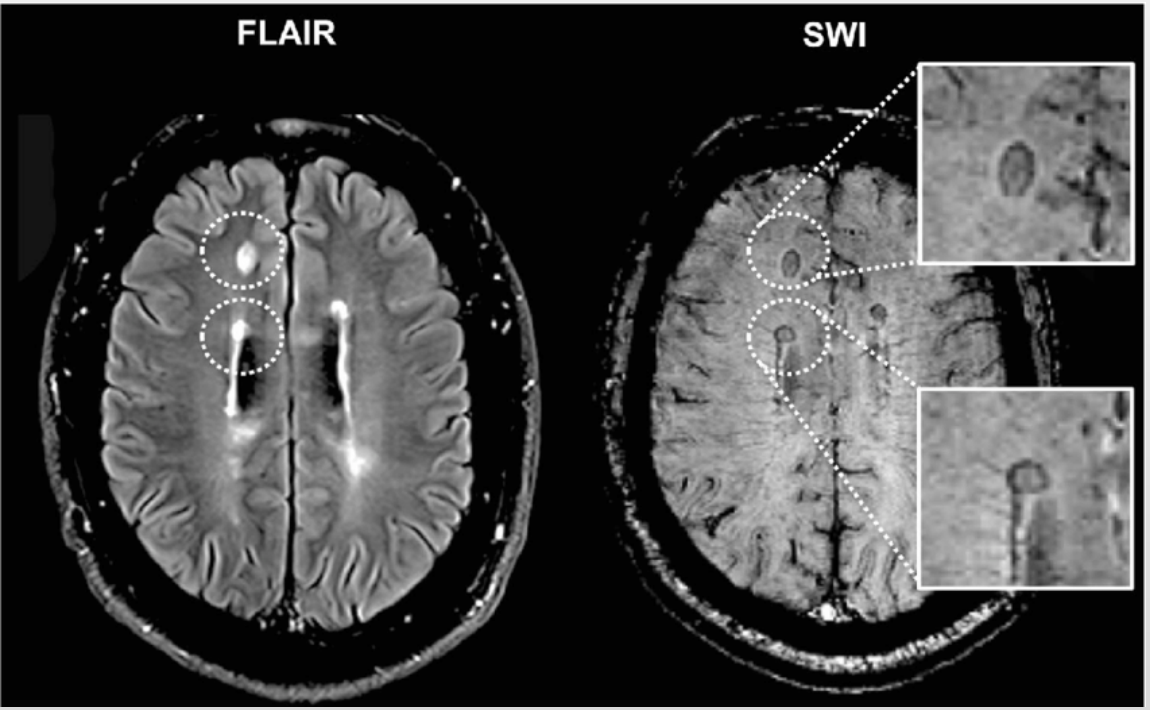
Images courtesy of Bruce D. Trapp

Central Vein Sign (CVS) and Iron Rim Lesions (IRLs)

- CVS and IRLs are biomarkers for MS
- Threshold of 40% of lesions with CVS distinguish MS from non-MS patients but not the different phenotypes
- IRLs reflect chronic active lesions, develop in RRMS patients, and persist in progressive MS
- Presence of at least 4 iron rim lesions is associated with earlier clinical disability, higher prevalence of clinically progressive MS, and more severe brain atrophy

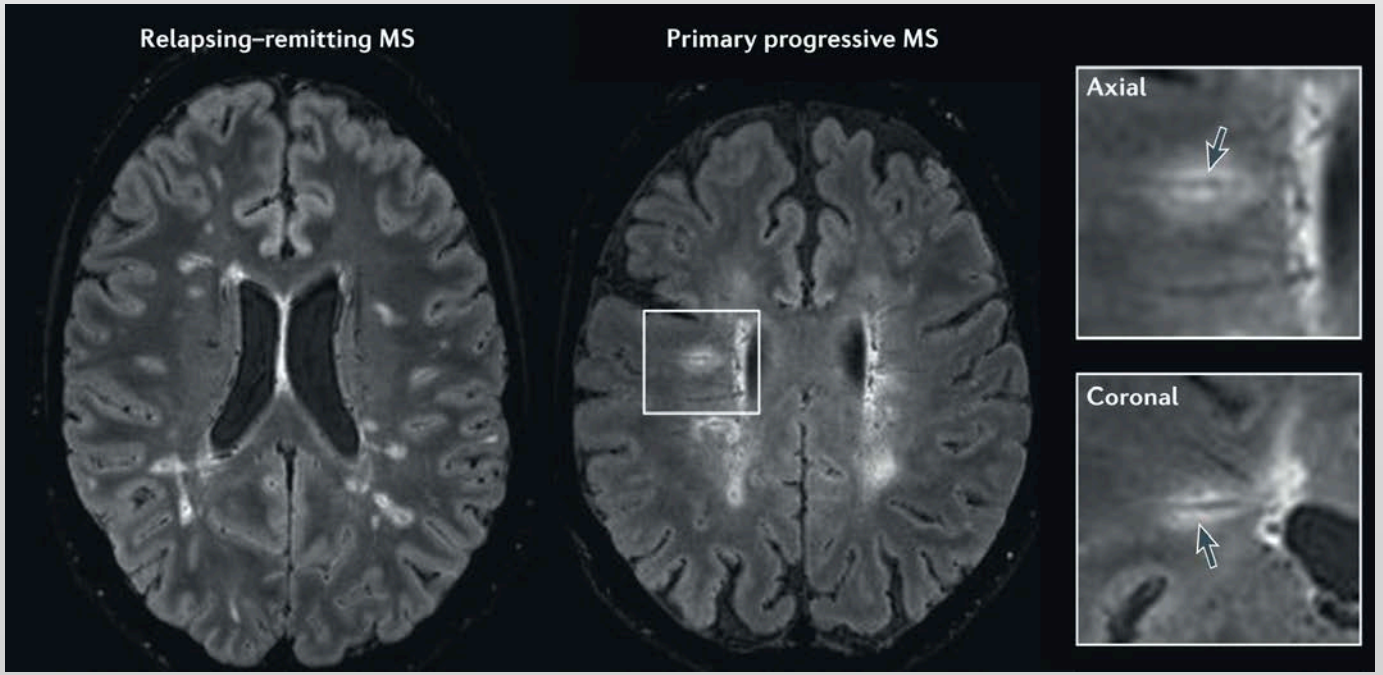
Sati P et al. *Nat Rev Neurol*. 2016;12(12):714-22. Preziosa P et al. *Curr Opin Neurol*. 2021;34(4):505-13.

IRLs and CVS in MS



SWI

- An MRI sequence that is particularly sensitive to compounds that distort the local magnetic field and as such make it useful in detecting blood products, calcium, iron, etc



SWI = susceptibility weight imaging

Sati P et al. *Nat Rev Neurol*. 2016;12(12):714-22.

Blood, CSF, and EVP Biomarkers

EVP = extracellular vesicle and particle

Oligoclonal Bands in CSF

- Presence is independent predictor of CIS to RRMS and RIS to CIS or disability accumulation (HR 2.0, 95% CI 1.2-3.6) in CIS
- Patients with CIS who had 8-12 oligoclonal bands had a 2.5-fold greater risk of conversion to CD MS than patients with fewer oligoclonal bands

CD = clinically definite; CI = confidence interval; HR = hazard ratio

Deisenhammer F et al. *Front Immunol*. 2019;10:726.

Neurofilament Light: Blood and CSF

- NfL CSF and blood concentration are increased in MS and CIS
- Biomarker of axonal damage and potential prognostic factor
- Lack of disease specificity and anatomical characterization of NfL measurement cannot replace MRI in diagnosis of MS and CIS, and in exclusion of MS disease mimics
- NfL measurement is useful for predicting disease prognosis
- Clinical meaningfulness needs to be established pre-use
- Quanterix

NfL = neurofilament

Gaetani L et al. *J Neurol Neurosurg Psychiatry*. 2019;90(8):870-81. Kuhle J et al. *Neurology*. 2019;92(10):e1007-15.

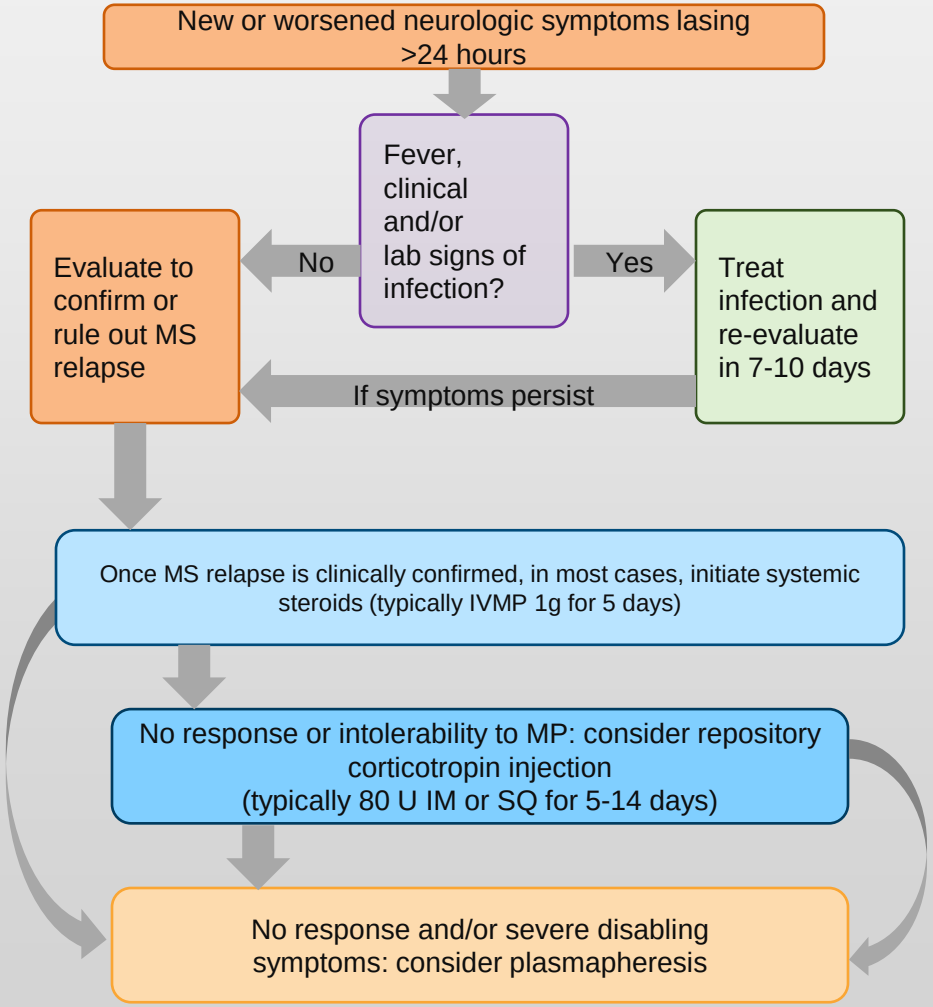
Evoked Potentials (EPs) in MS

- EPs characterize signal conduction in selected tracts of the CNS in a quantifiable way
- Alteration of signal conduction is the main mechanism of symptoms and signs in MS
  - EP may serve as a measure of functional impairment in MS
- EPs have been shown to be predictive for disease course
- EPs can detect deterioration, as well as improvement of impulse propagation, independently from the mechanism causing the change

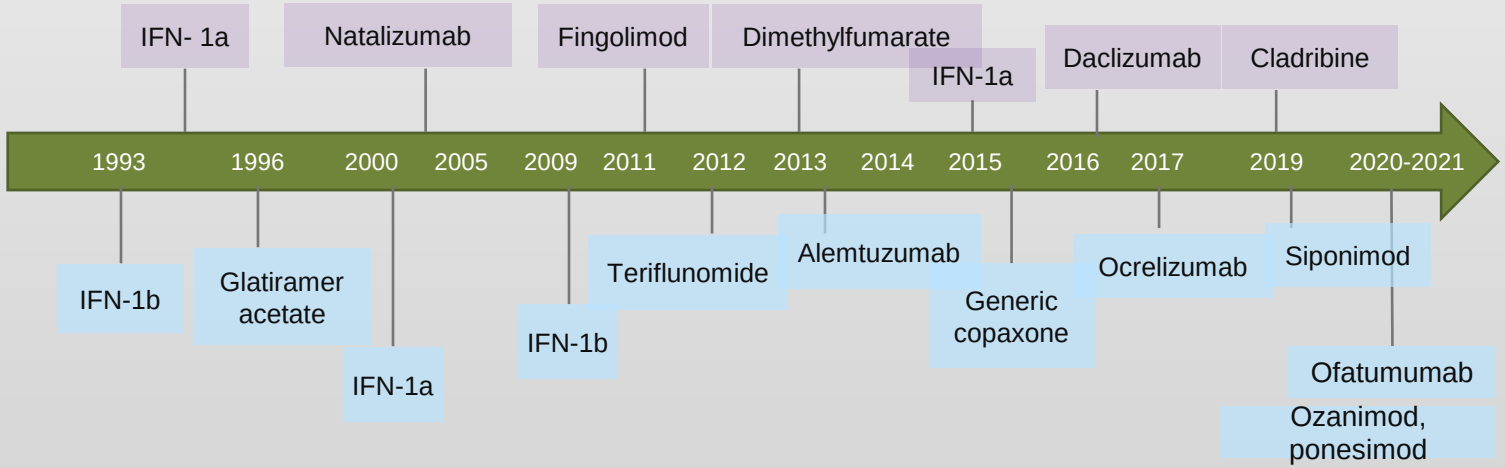
Hardmeier M et al. *Mult Scler J*. 2017;23(10):1309-19.

Confirmed Diagnosis and Treatment

Confirmed MS Diagnosis



Initiate DMT

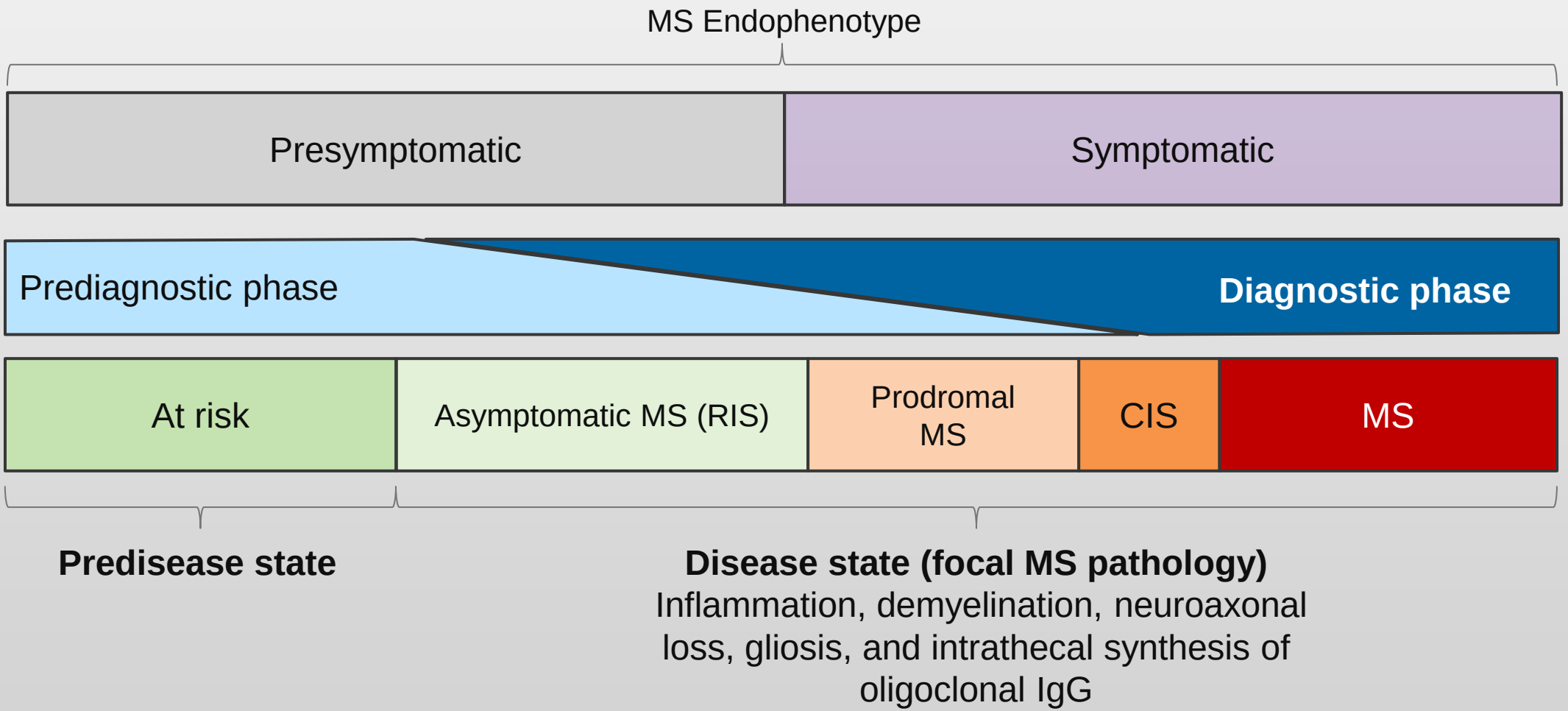


DMT = disease-modifying therapy; IFN = interferon; IM = intramuscular; IVMP = IV methylprednisolone; MP = methylprednisolone; SQ = subcutaneous

https://cdn.ymaws.com/mscare.site-ym.com/resource/collection/9C5F19B9-3489-48B0-A54B-623A1ECEE07B/2018MRIGuidelines_booklet_with_final_changes_0522.pdf. Accessed August 16, 2022.

Endophenotypes and Phenotypes

MS Endophenotypes



Giovannoni G. *Lancet Neurol*. 2017;16(6):413-4.

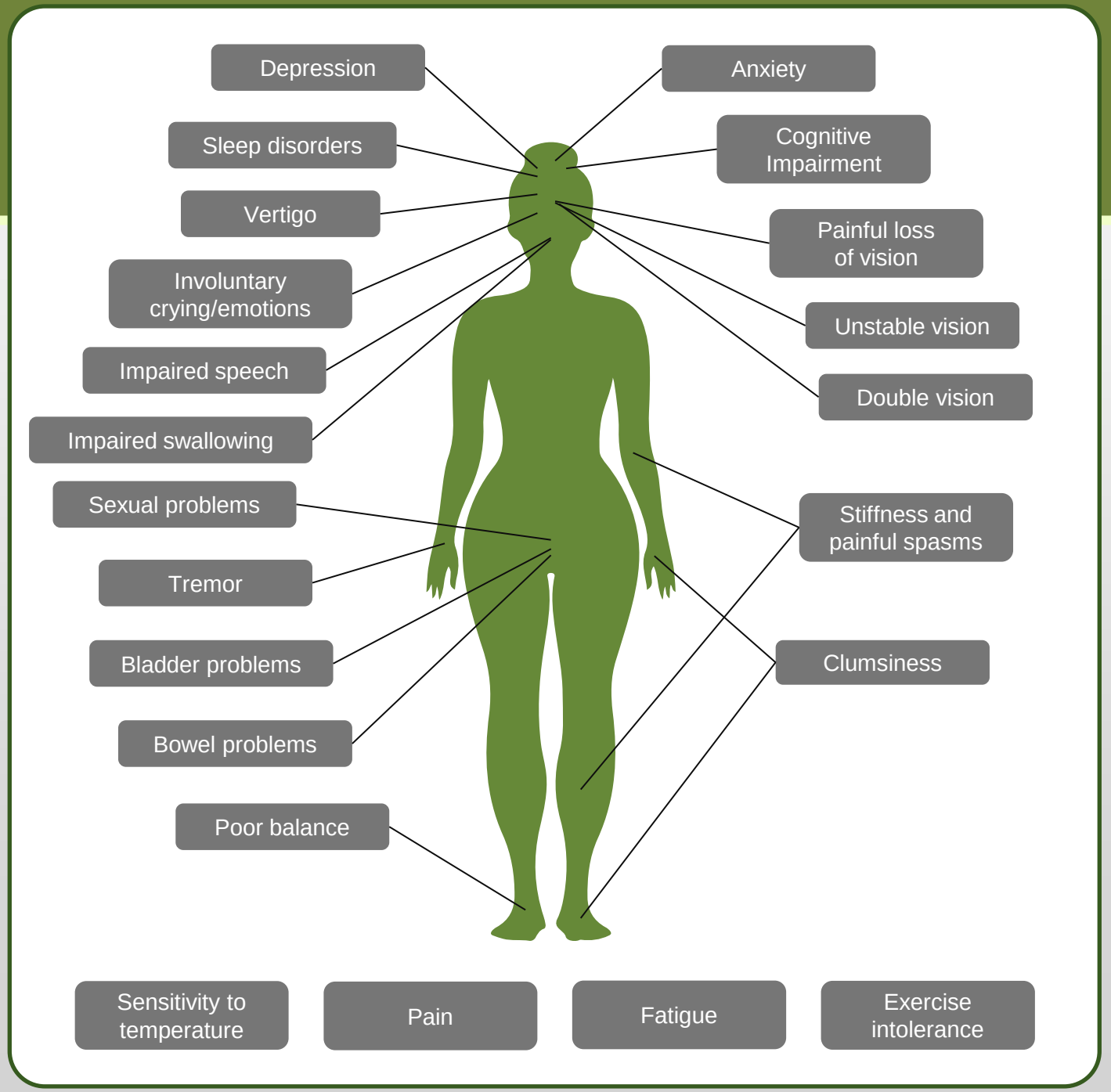
Relapse vs Pseudorelapse

Characteristic	Relapse	Pseudorelapse
Nature	New or worsened symptoms, which are due to new inflammatory MS activity in the brain or spinal cord	Worsened neurologic symptoms; the underlying cause of the worsening is not from new immune system activity or inflammation
Timing	New symptoms manifest over a few hours or days and then plateau over a few days to weeks and then slowly improve over weeks to months	Worsened symptoms fluctuate; especially if they resolve completely and then return
Recurrence	MS does not often result in repeated inflammation in the exact same part of the brain	Recurrence of old symptoms is more common in a pseudorelapse
Localization	Symptoms that can be explained by a new active MS lesion in the CNS	No place that a lesion in the CNS causes the symptoms; Caused by another process: infection, medication, stress
Type of symptoms	Vision loss, numbness, and weakness are typical symptoms of a relapse	Sudden worsening of spasticity and pain are rarely due to an acute relapse

https://mymsaa.org/publications/ms-relapse-toolkit/pseudoexacerbation/. Accessed August 16, 2022.

Signs and Symptoms of MS

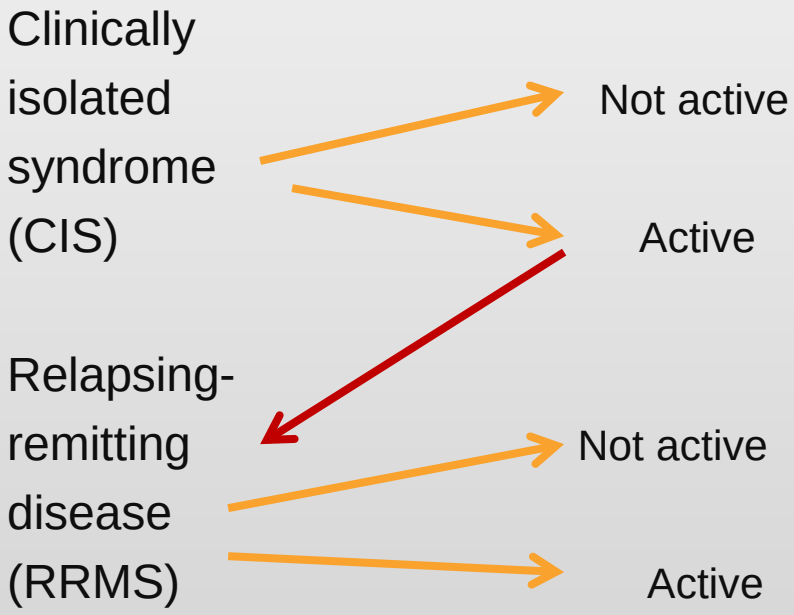
A common misconception is that any attack of CNS demyelination means a diagnosis of acute MS



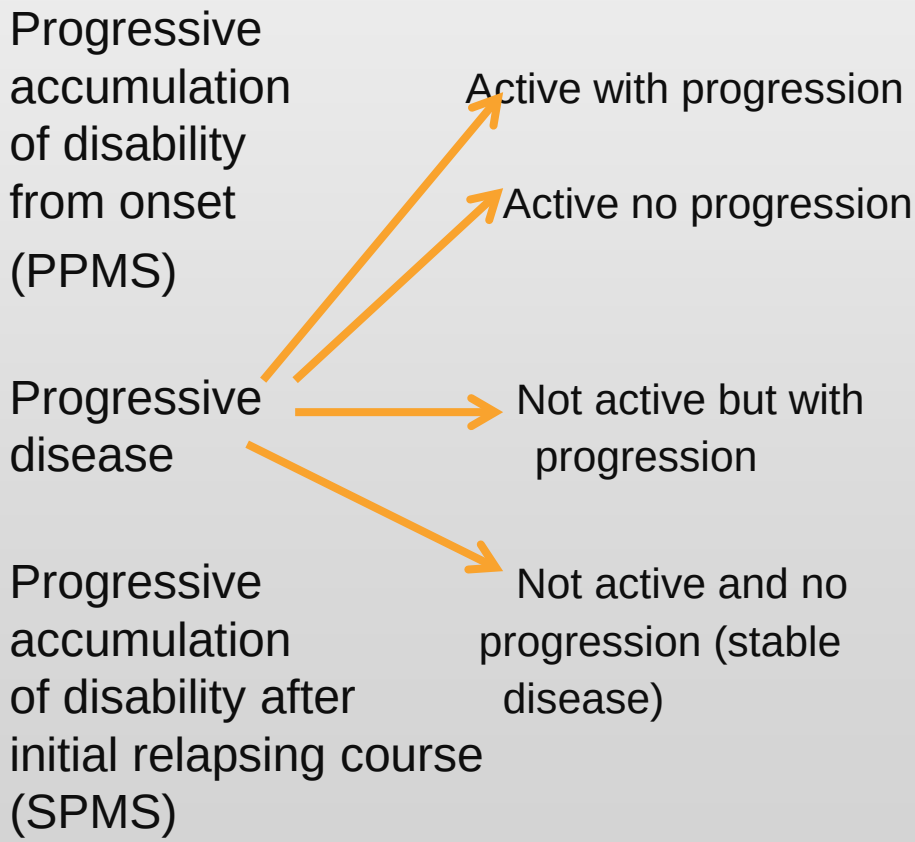
https://www.nationalmssociety.org/Symptoms-Diagnosis/MS-Symptoms. Accessed August 16, 2022.

Revised Clinical Phenotypes

Relapsing-Remitting Disease



Progressive Disease



SPMS = secondary progressive MS

Adapted from Lublin F et al. *Neurology*. 2014;83(3):278-86.

Polling Question

Which of the following is the most common MS phenotype that you encounter in your practice?

A. CIS

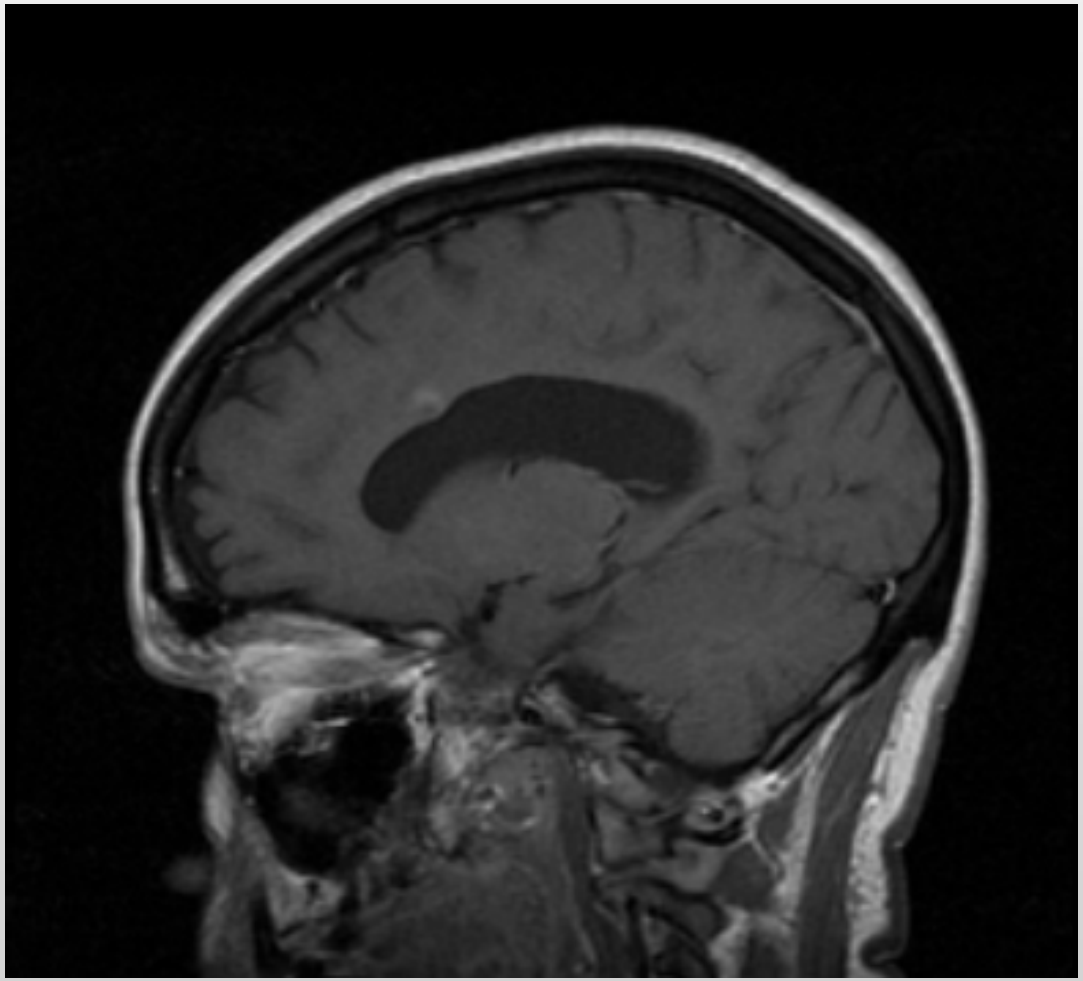
B. RRMS, active disease

C. PPMS, active disease

D. SPMS, active disease

Radiologically Isolated Syndrome (RIS)

- Diagnosis of RIS occurs during diagnosis of another unrelated condition, such as migraine headaches or trauma to the area
- Typical MRI MS lesions without clinical presentation
- 2-year period, one-third of patients with RIS develop a neurologic event and are diagnosed with MS, one-third develop a new finding on MRI without any symptoms, and one-third show no change



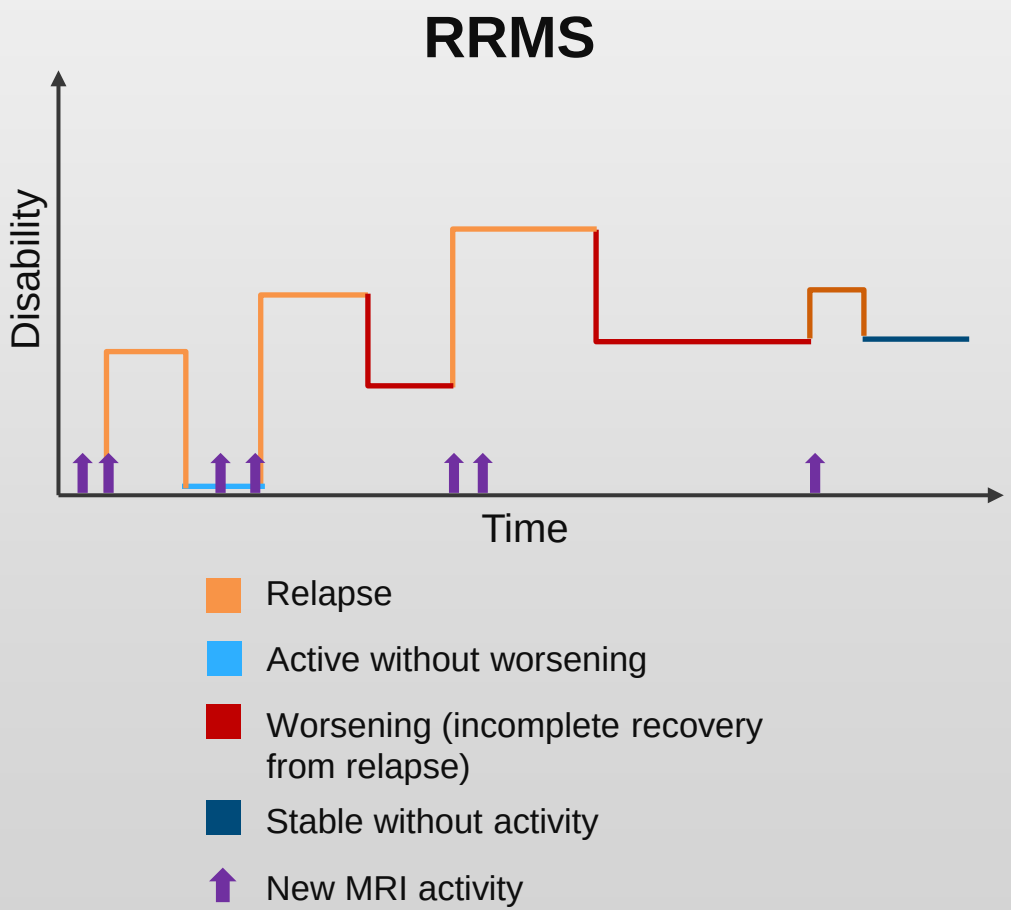
Okuda DT et al. *PloS One*. 2014;9(3):e905. Image courtesy of Aliza Ben-Zacharia, PhD, DNP, ANP-BC, FAAN

Clinically Isolated Syndrome (CIS)

- CIS is a 1st episode of neurologic symptoms caused by inflammation and demyelination in the CNS
- The episode must last for at least 24 hours, is characteristic of MS, but does not yet meet criteria for an MS diagnosis because people who experience a CIS may or may not go on to develop MS
- 2017 McDonald criteria make it possible to diagnose MS in a person with CIS who also has specific findings on brain MRI

https://www.nationalmssociety.org/What-is-MS/Types-of-MS/Clinically-Isolated-Syndrome-(CIS). Accessed August 16, 2022.

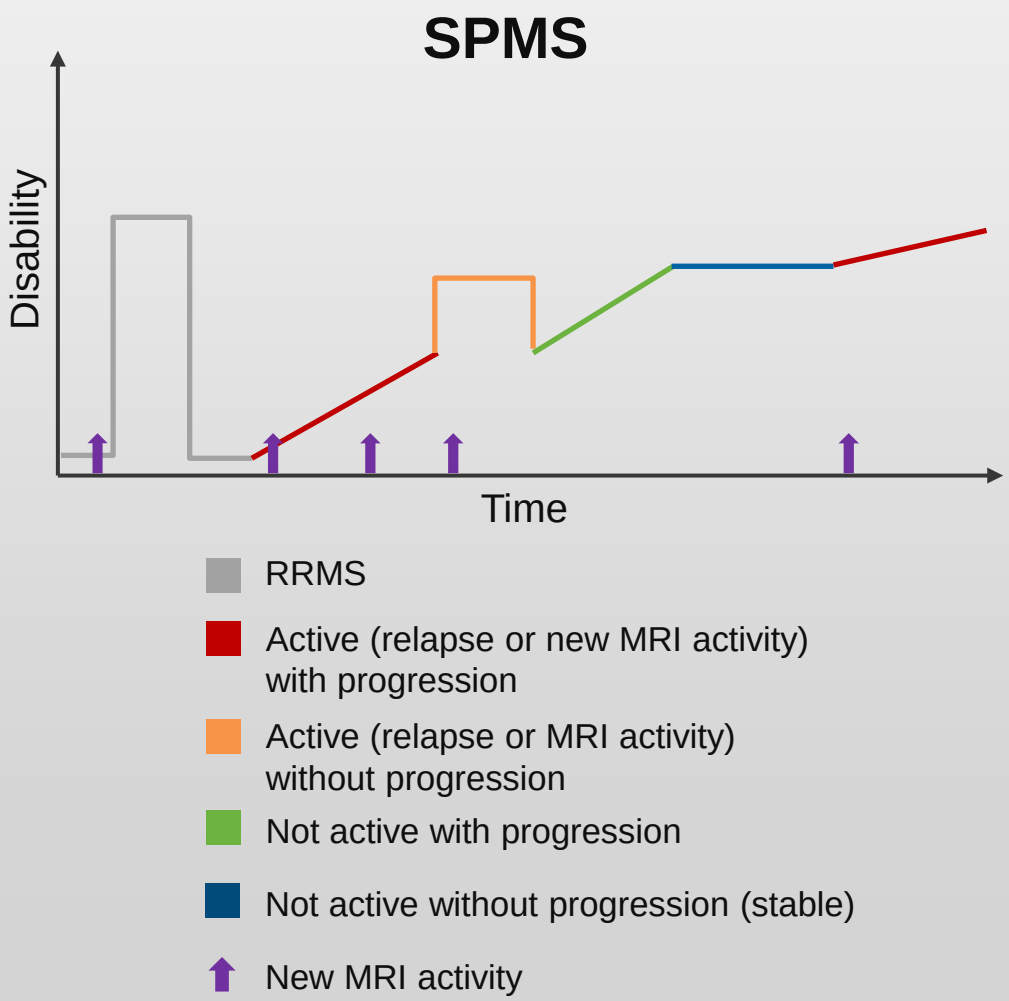
Relapsing-Remitting Multiple Sclerosis (RRMS)



- Relapses and remissions
- Transforms into SPMS
- Attacks of new or increasing neurologic symptoms
- Relapses lead to disability accumulation/EDSS
- RRMS active (with relapses and/or evidence of new MRI activity)
- RRMS not active, worsening (a confirmed increase in disability following a relapse) or not worsening

https://www.nationalmssociety.org/What-is-MS/Types-of-MS/Relapsing-remitting-MS. Accessed August 16, 2022.

Secondary Progressive MS (SPMS)

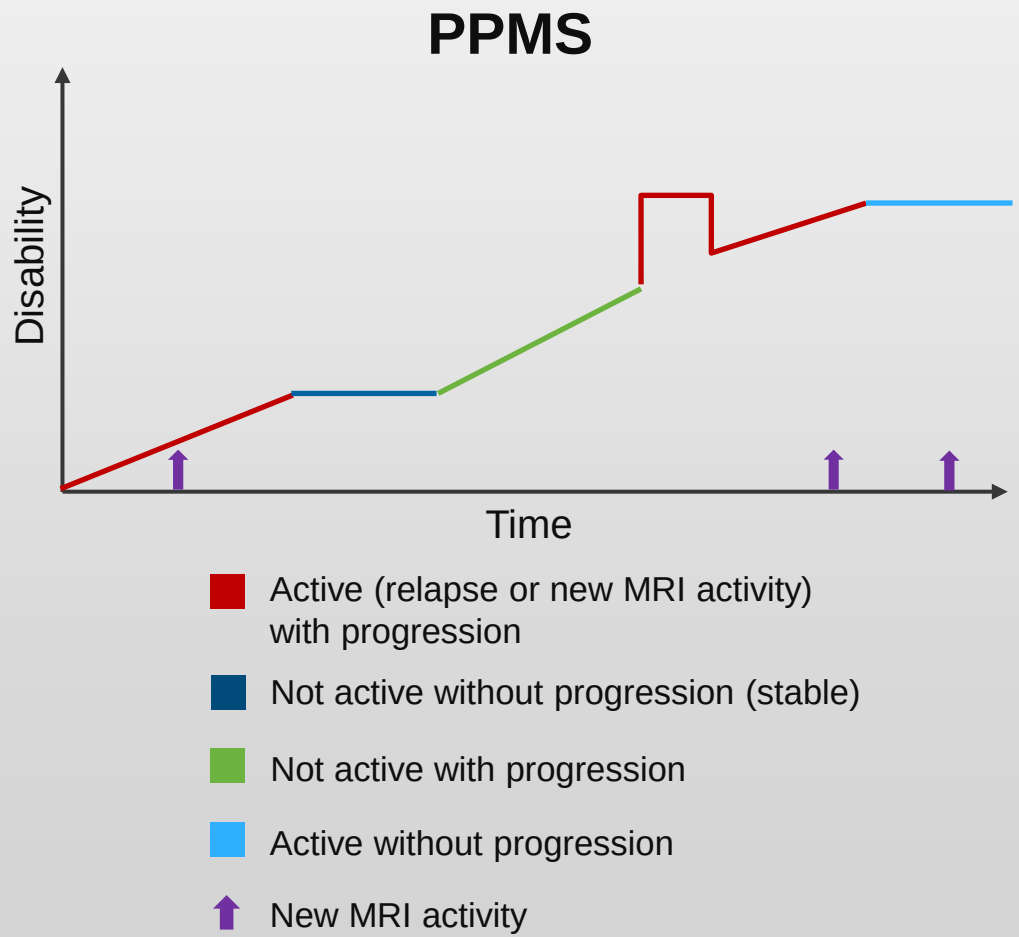


- SPMS follows an initial RRMS
- SPMS, a progressive worsening of neurologic function (accumulation of disability) over time
- SPMS active with relapses and/or evidence of new MRI activity
- SPMS not active, with progression (evidence of disability accumulation over time, with or without relapses or new MRI activity) or without progression

https://www.nationalmssociety.org/What-is-MS/Types-of-MS/Secondary-progressive-MS. Accessed August 16, 2022.

Primary Progressive MS (PPMS)

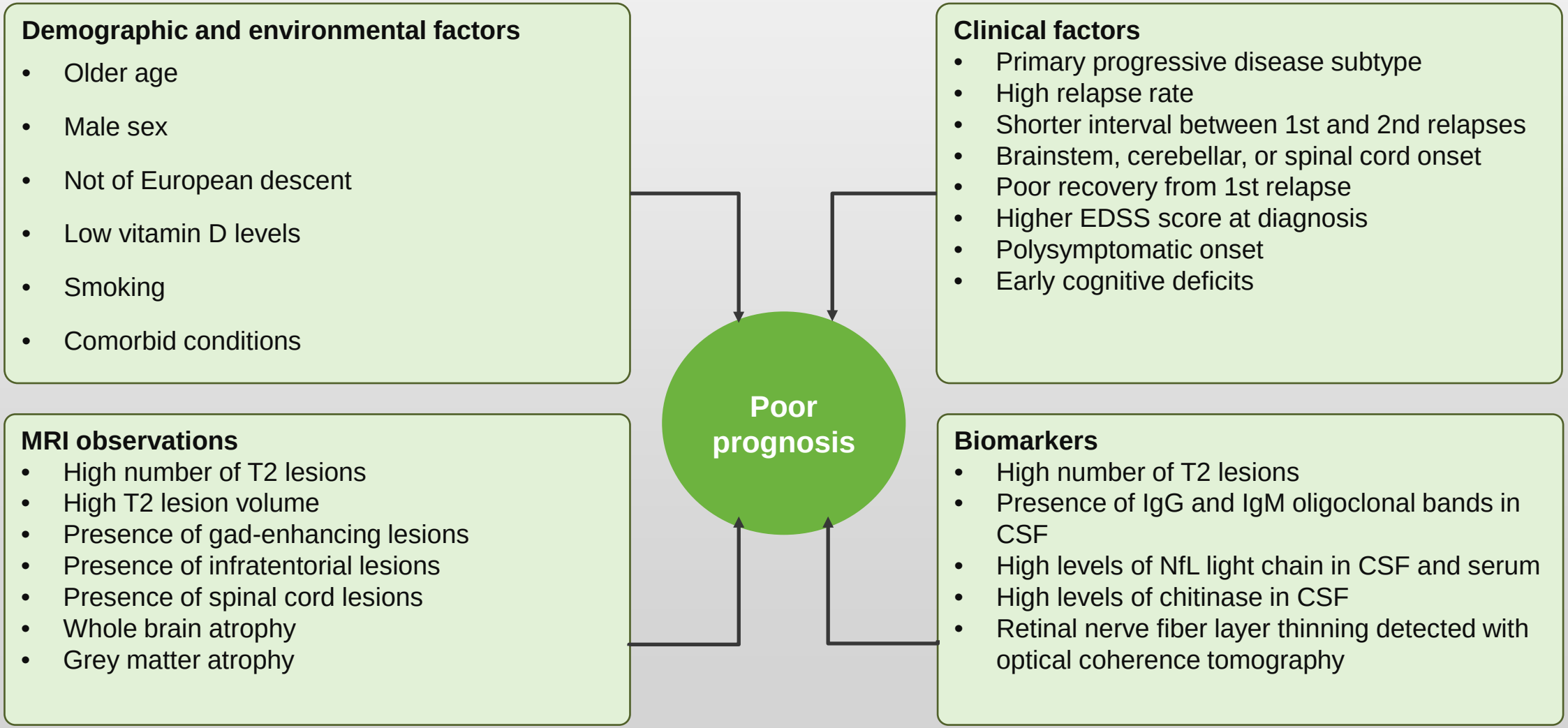
- PPMS: worsening neurologic function (accumulation of disability) from onset of symptoms, without early relapses or remissions
- PPMS active (with an occasional relapse and/or evidence of new MRI activity over a specified period of time)
- PPMS not active, with progression (evidence of disability accumulation over time, with or without relapse or new MRI activity) or without progression



https://www.nationalmssociety.org/What-is-MS/Types-of-MS/Primary-progressive-MS. Accessed August 16, 2022.

Prognosis

MS Prognosis

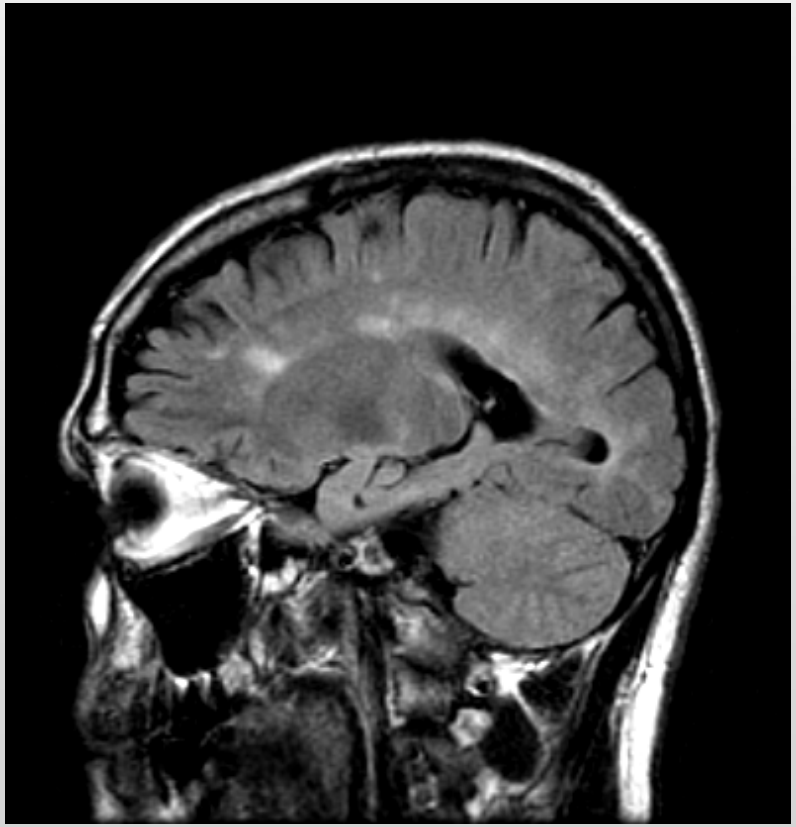


Rotstein D et al. *Nat Rev Neurol*. 2019;15(5):287-300.

Case Studies

THE 13TH ANNUAL LINDA MORGANTE MS Nurse Leadership Program

Clinical Case #1

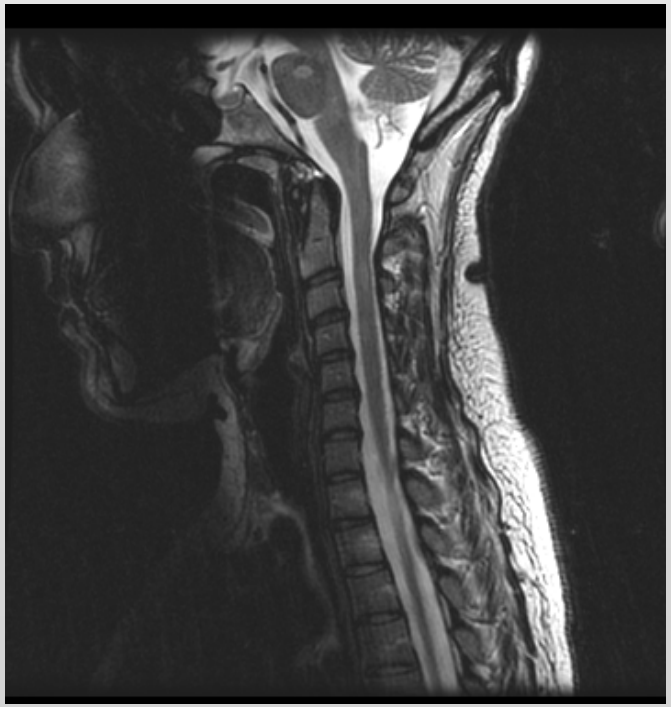


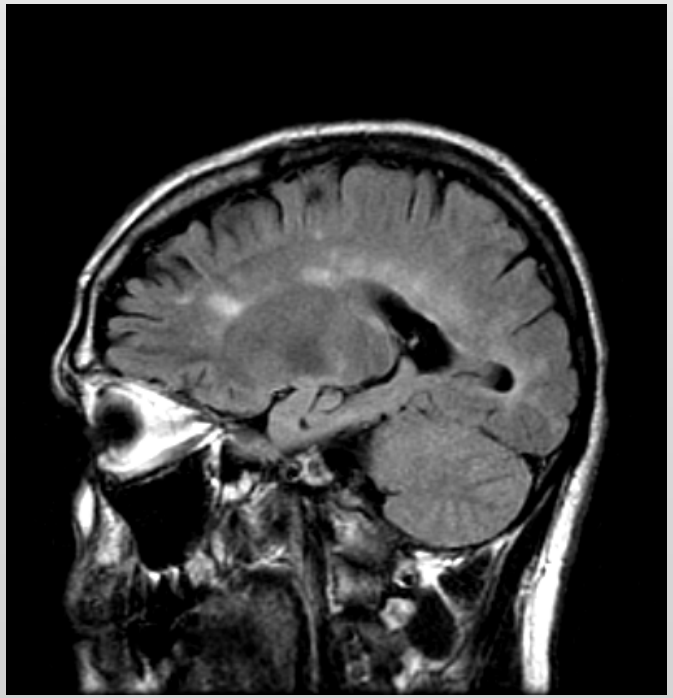
- 25-year-old Hispanic female
- New onset: weakness of left arm, numbness
- Medical history: optic neuritis 3 years ago, depression, smoker
- Current medication: Vitamin D, partially adherent
- Cultural considerations: her mother has never heard of the disease
- Brain MRI 3 years ago

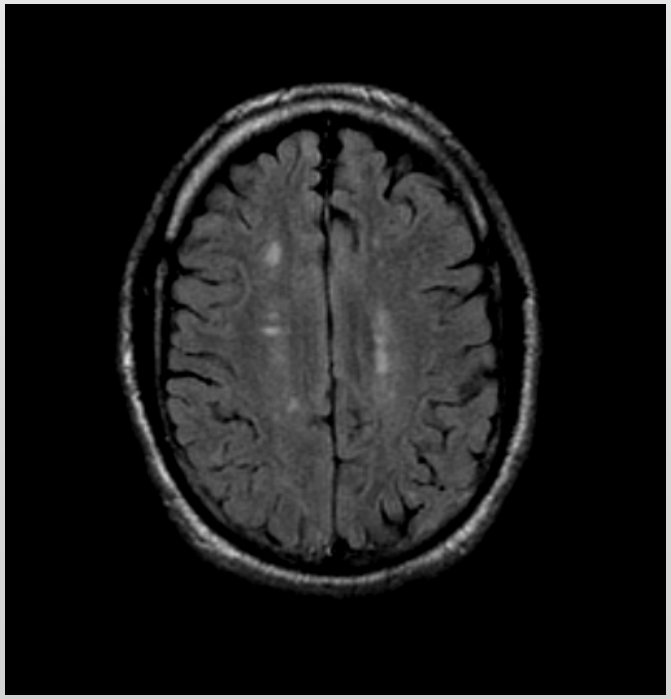
Image courtesy of Aliza Ben-Zacharia, PhD, DNP, ANP-BC, FAAN

Meet Criteria?

No. of Clinical Attacks	No. of MRI Lesions With Objective Clinical Evidence	Additional Data Needed for Diagnosis of MS
RRMS		
≥2	≥2	None



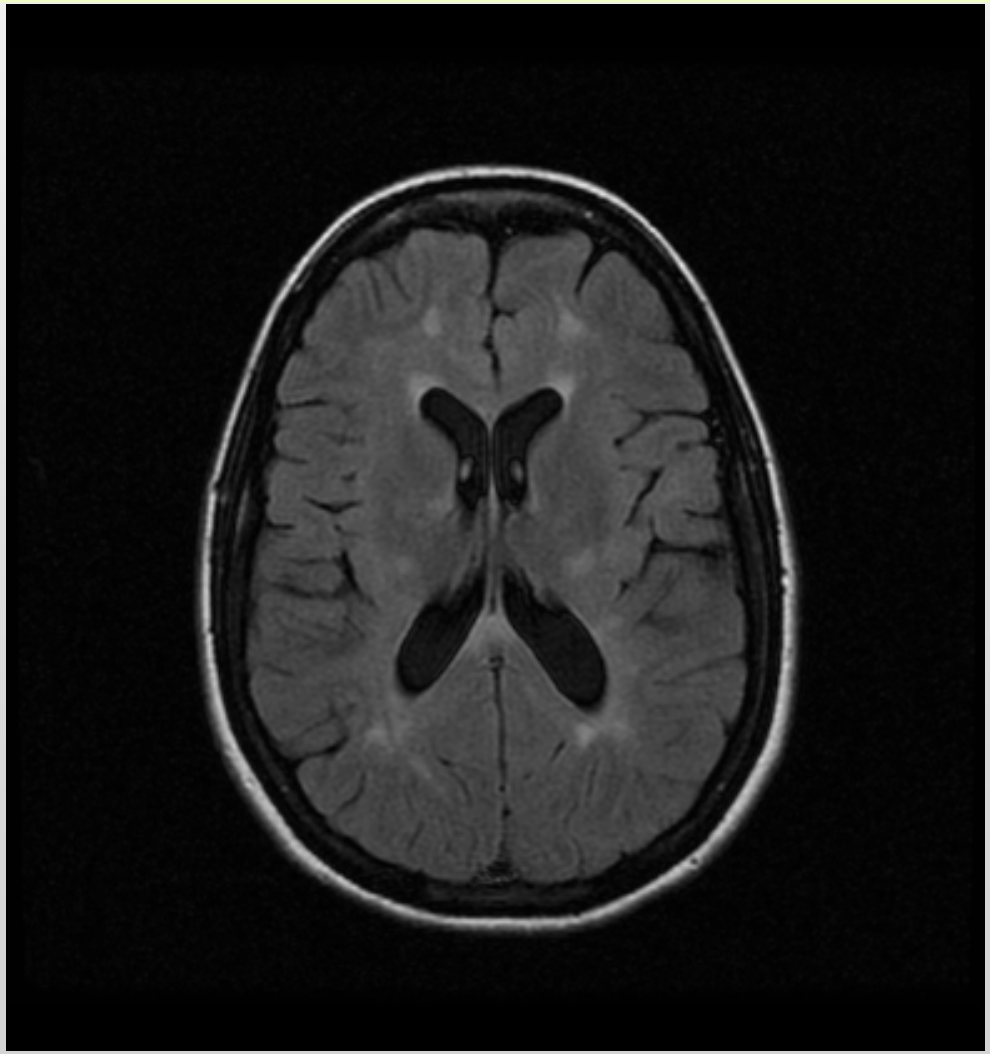




Images courtesy of Aliza Ben-Zacharia, PhD, DNP, ANP-BC, FAAN

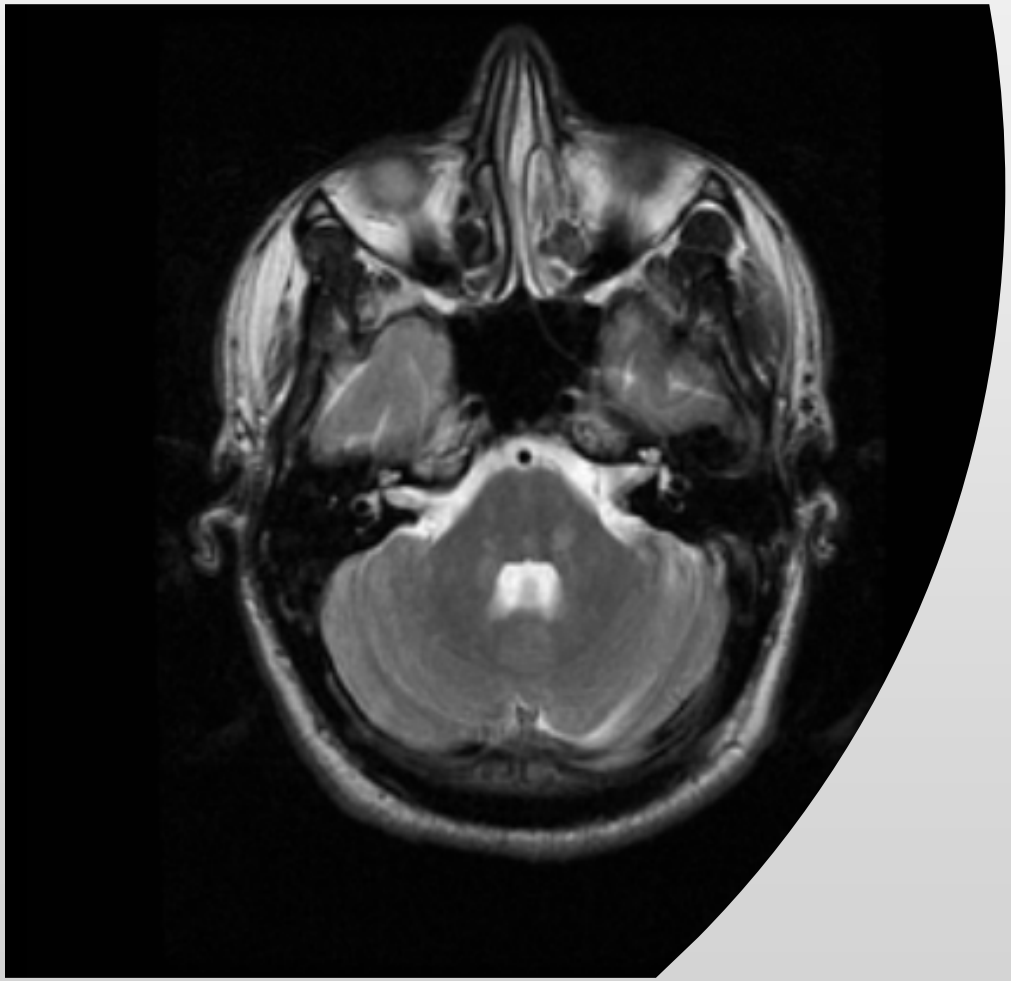
2017 McDonald Criteria for Diagnosis of MS

No. of Clinical Attacks	No. of MRI Lesions With Objective Clinical Evidence	Additional Data Needed for Diagnosis of MS
RRMS		
≥2	≥2	None
≥2	1 and evidence of prior attack, different location	None
≥2	1	DIS demonstrated by an additional clinical attack implicating a different CNS Site or by MRI
1	≥2	DIT demonstrated by additional clinical attack, MRI, or CSF-specific oligoclonal bands
1	1	DIS demonstrated by additional clinical attack implicating a different CNS site or by MRI *and* DIT demonstrated by an additional clinical attack or by MRI or demonstration of CSF-specific oligoclonal bands
PPMS		
Required: 1 year of disability progression (retrospectively or prospectively determined) independent of clinical relapse Plus 2 of the following: 1 or more T2-hyperintense lesions characteristic of MS in 1 or more of the following brain regions: periventricular cortical or juxtacortical, or infratentorial; 2 or more T2-hyperintense lesions in the spinal cord; presence of CSF-specific oligoclonal bands		



Thompson AJ et al. *Lancet Neurol*. 2018;17(2):162-73. Image courtesy of Aliza Ben-Zacharia, PhD, DNP, ANP-BC, FAAN

Clinical Case #2



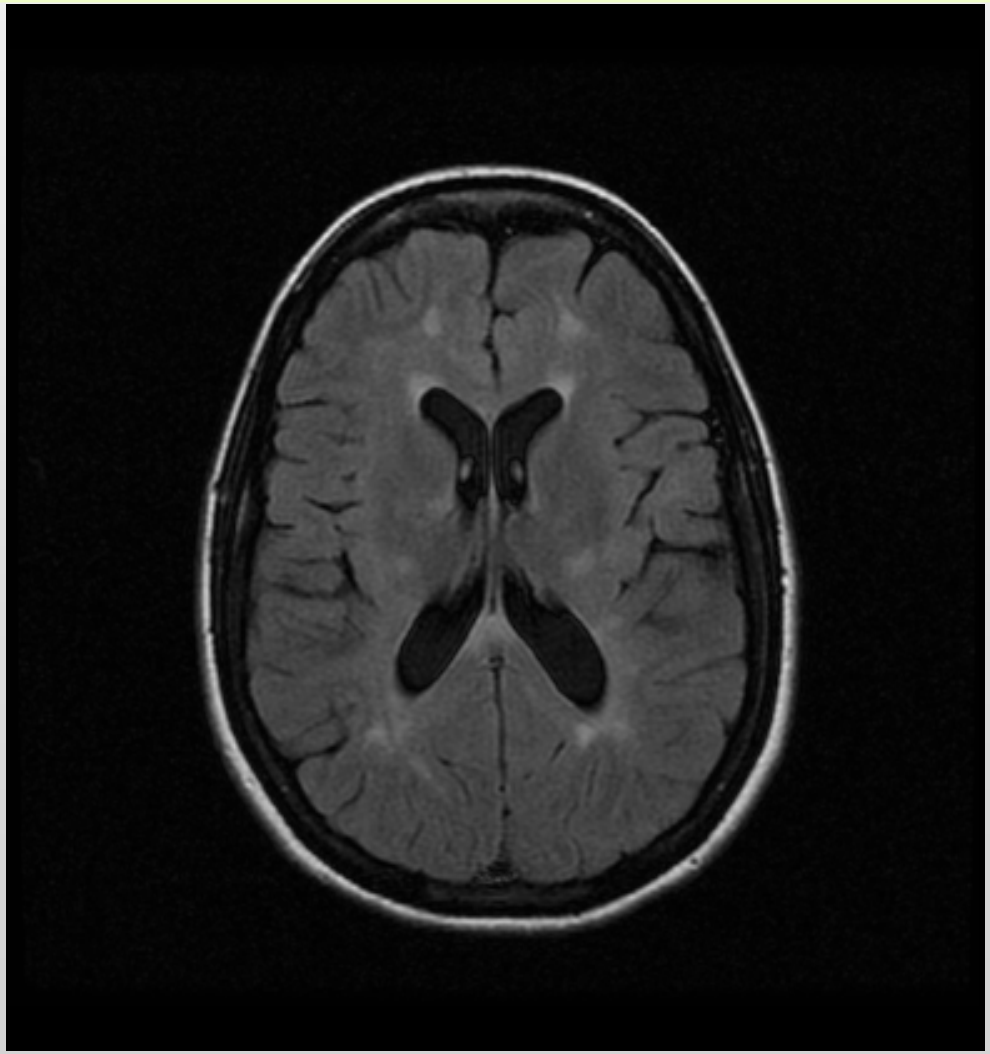
- 35-year-old African-American male
- New onset: OS optic neuritis
- Medical history: HTN, smoker
- Current medications: antihypertensive meds
- Cultural considerations: family eats salty food
- Brain MRI: + periventricular lesions + brainstem lesion + gad-enhancing lesions
- Cervical spine MRI: 1 lesion at C4

HTN = hypertension; OS = left eye

Image courtesy of Aliza Ben-Zacharia, PhD, DNP, ANP-BC, FAAN

2017 McDonald Criteria for Diagnosis of MS

No. of Clinical Attacks	No. of MRI Lesions With Objective Clinical Evidence	Additional Data Needed for Diagnosis of MS
RRMS		
≥2	≥2	None
≥2	1 and evidence of prior attack, different location	None
≥2	1	DIS demonstrated by an additional clinical attack implicating a different CNS site or by MRI
1	≥2	DIT demonstrated by additional clinical attack, MRI, or CSF-specific oligoclonal bands
1	1	DIS demonstrated by additional clinical attack implicating a different CNS site or by MRI *and* DIT demonstrated by an additional clinical attack or by MRI or demonstration of CSF-specific oligoclonal bands
PPMS		
Required: 1 year of disability progression (retrospectively or prospectively determined) independent of clinical relapse Plus 2 of the following: 1 or more T2-hyperintense lesions characteristic of MS in 1 or more of the following brain regions: periventricular cortical or juxtacortical, or infratentorial; 2 or more T2-hyperintense lesions in the spinal cord; presence of CSF-specific oligoclonal bands		



Thompson AJ et al. *Lancet Neurol*. 2018;17(2):162-73. Image courtesy of Aliza Ben-Zacharia, PhD, DNP, ANP-BC, FAAN

Conclusion

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Conclusion

- MS is a complex disease with multiple endophenotypes
- High-risk RIS and prodrome may become a part of the MS spectrum in the next version of the McDonald criteria
- Many patients previously labelled as CIS now receive the diagnosis of MS, making the prognosis of both CIS and RRMS milder
- Important to diagnose early and treat early
- Once MS is diagnosed, it is important to assess poor prognostic indicators and symptoms and begin to treat exacerbations, start DMT, and manage comorbidities

THE 13TH ANNUAL LINDA MORGANTE

Multiple Sclerosis Nurse Leadership Program

2022

EXPERT DISCUSSION #1

Provided by Academy for Continued Healthcare Learning and Annenberg Center for Health Sciences at Eisenhower

ACHL ACADEMY for CONTINUED HEALTHCARE LEARNING

ANNENBERG CENTER FOR HEALTH SCIENCES AT EISENHOWER

The program is supported through educational grants from Biogen, Bristol-Myers Squibb, Inc., and Novartis Pharmaceuticals Corporation.

Expert Discussion Questions

- What obstacles do you continue to face related to timely and appropriate diagnosis of MS?
- Which MS phenotypes do you most commonly see in your practice?
- What additional questions do you have related to MS diagnosis?

MS = multiple sclerosis

THE 13TH ANNUAL LINDA MORGANTE

Multiple Sclerosis Nurse Leadership Program

2022

TREATMENT OVERVIEW: DISEASE-MODIFYING THERAPIES AND RELAPSE MANAGEMENT

Marie A. Namey, APRN, MSCN-e
Independent MS Nurse Consultant

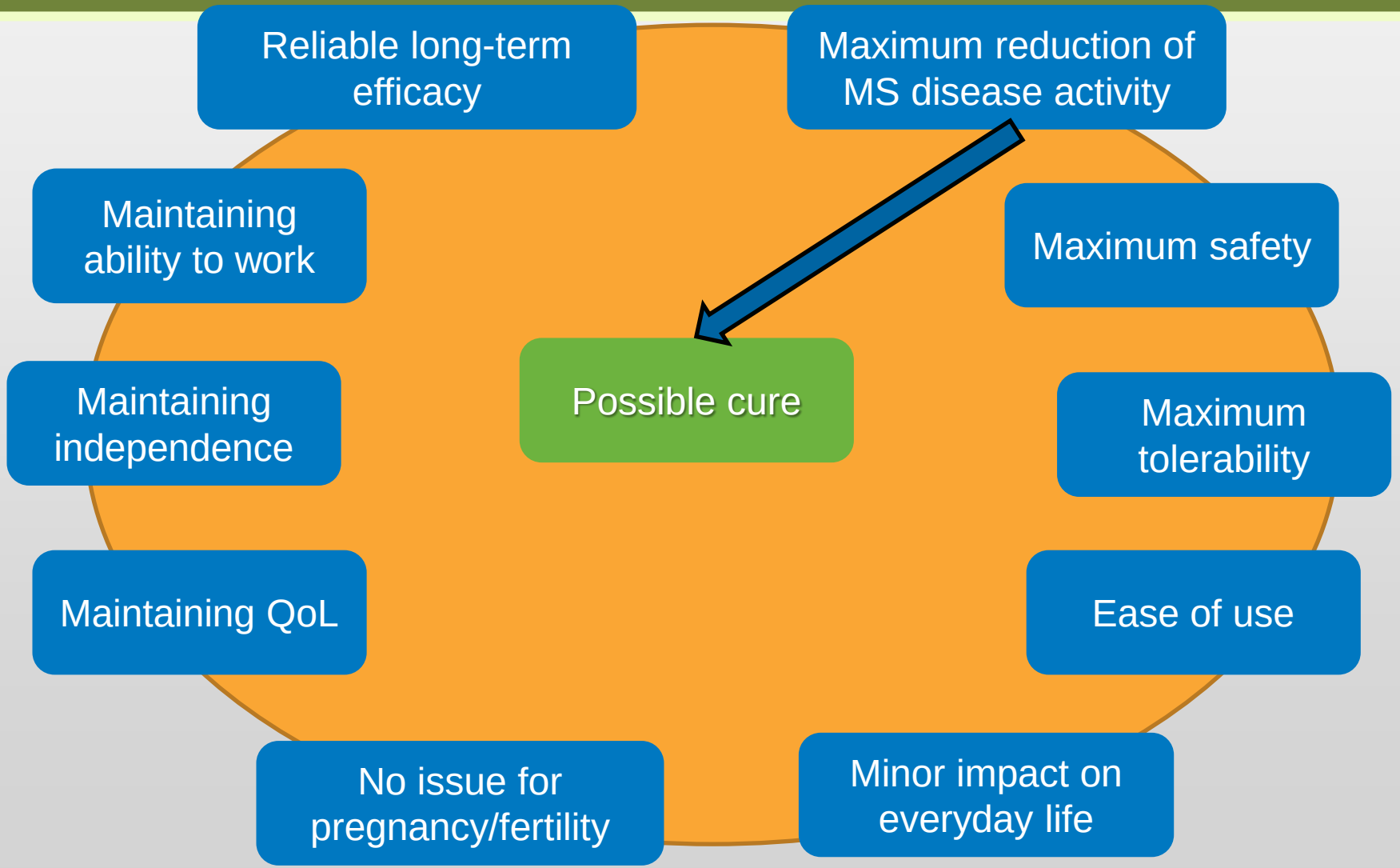
Provided by Academy for Continued Healthcare Learning and Annenberg Center for Health Sciences at Eisenhower

ACHL ACADEMY for CONTINUED HEALTHCARE LEARNING

ANNENBERG CENTER FOR HEALTH SCIENCES AT EISENHOWER

The program is supported through educational grants from Biogen, Bristol-Myers Squibb, Inc., and Novartis Pharmaceuticals Corporation.

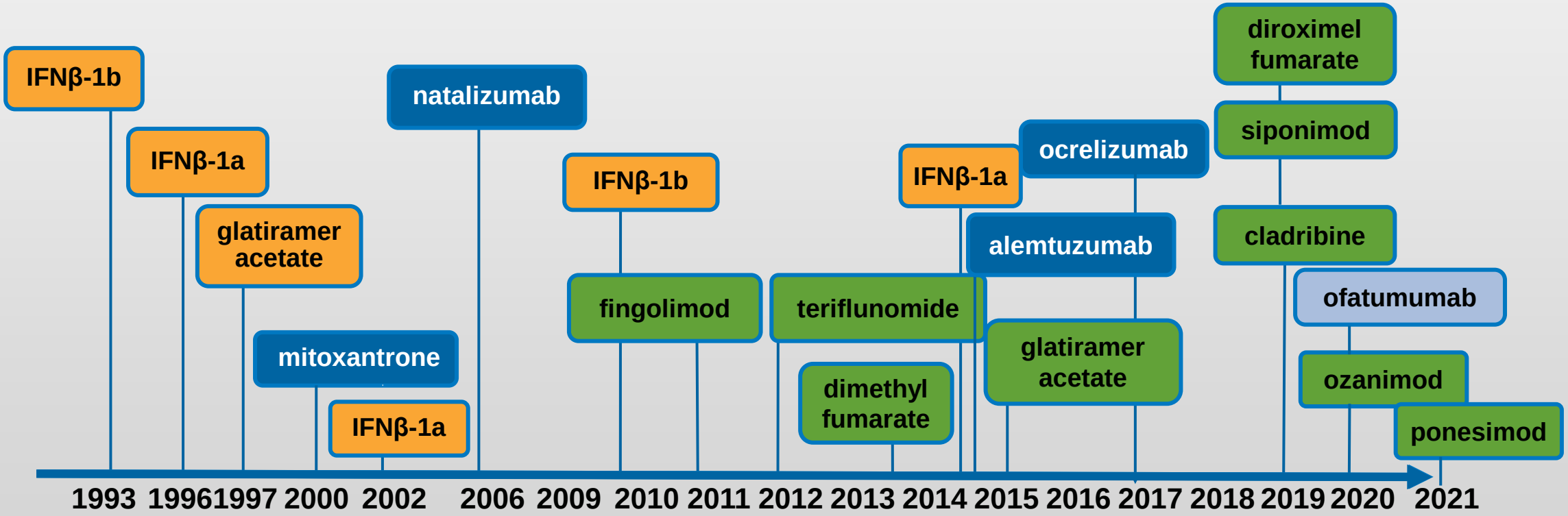
Ideal MS Therapy



https://www.aan.com/Guidelines/home/GuidelineDetail/898. Accessed August 10, 2022.

MS = multiple sclerosis; QoL = quality of life

FDA-Approved MS Therapies in 2022



IFN = interferon

https://www.nationalmssociety.org/Treating-MS/Medications. Accessed August 11, 2022.

MS 2022

Current DMT Landscape

- >20 distinct MS DMTs (includes generics)
- 10 different MoAs
- All approved for relapsing forms of MS
  - 1 approved for PPMS
- Timely initiation is emphasized
- 3 administration categories
  - Injectable (IM, SQ)
  - Oral
  - Infusion
- Set realistic expectations

Goals of Treatment

Modify or reduce relapses and delay disability progression

Decrease new MRI activity

Facilitate acceptable QoL

DMT = disease-modifying therapy; IM = intramuscular; MoA = mechanism of action; MRI = magnetic resonance imaging; PPMS = primary progressive MS; SQ = subcutaneous

Bross M et al. *Int J Mol Sci*. 2020;21(12):4312.

General Immunotherapeutic Mechanisms of MS Therapies

Immunomodulation/ alteration of cell function

IFNß (SQ/IM)
Glatiramer acetate (SQ)
Dimethyl fumarate (oral)
Monomethyl fumarate (oral)
Diroximel fumarate (oral)
Teriflunomide (oral)

Cell trafficking/migration

Natalizumab (IV)
Fingolimod (oral)
Ozanimod (oral)
Siponimod (oral)
Ponesimod (oral)

Immunosuppressive

Mitoxantrone (IV)

Cell depletion

Alemtuzumab (IV)
Cladribine (oral)
Ocrelizumab (IV)
Ofatumumab (SQ)

IV = intravenous

Bruck W et al. *JAMA Neurol*. 2013,70(10):1315-24. Freedman MS et al. *Can J Neurol Sci*. 2020;47(4):437-55. https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/213498s000lbl.pdf. Accessed August 10, 2022.

DMT Armamentarium: 2 Perspectives

MS practitioners should consider the entire armamentarium of DMTs as well as all DMT choices for all patients

OR

MS practitioners should move towards precision medicine, personalizing DMTs to target the individual's disease characteristics

https://www.aan.com/Guidelines/home/ByTopic?topicId=18. Accessed August 10, 2022.

General Considerations When Selecting DMTs

Factors to consider when selecting DMTs	• Lifestyle, availability of care partner, acceptability of injection, availability of infusion services, mental health concerns, pregnancy planning, comorbidities
DMT considerations	• Medication efficacy, safety factors, MoAs, adverse effects, schedule of treatment, ease and route of administration, previous use of DMTs
Severity of disease	• More aggressive treatment may not be appropriate in patients with multiple risk factors
Cost considerations	• Many 2nd- and 3rd-line medications may not be covered until 1st-line treatment is tried
Insurance considerations	• Insurance companies want to know that patients are receiving benefit from costly medications

https://www.aan.com/Guidelines/home/ByTopic?topicId=18. Accessed August 10, 2022.

Escalation vs Induction

Escalation Therapy	Induction Therapy

• Escalation paradigm may minimize medication risks and long-term disability in MS
• Treatment side effects should be proportional to disease state
• 1st-line therapy continues for at least 6 months to assess treatment response
  • If patient experiences relapse or breakthrough disease activity, consider another treatment option (if patient has been adherent to treatment)
• Immunocompromised persons are at increased risk of infections
  • Can sometimes have fatal consequences
	• Consider high-efficacy agents as initial therapy for an informed patient who has high level of disease activity
	• Start with a highly effective agent, considering efficacy over safety
	• Initiate treatment of aggressive immunosuppressant drugs to slow or prevent progression
	• Consider course of B-cell depleting therapy to start induction paradigm

https://www.aan.com/Guidelines/home/ByTopic?topicId=18. Accessed August 10, 2022.

Trading Efficacy for Safety

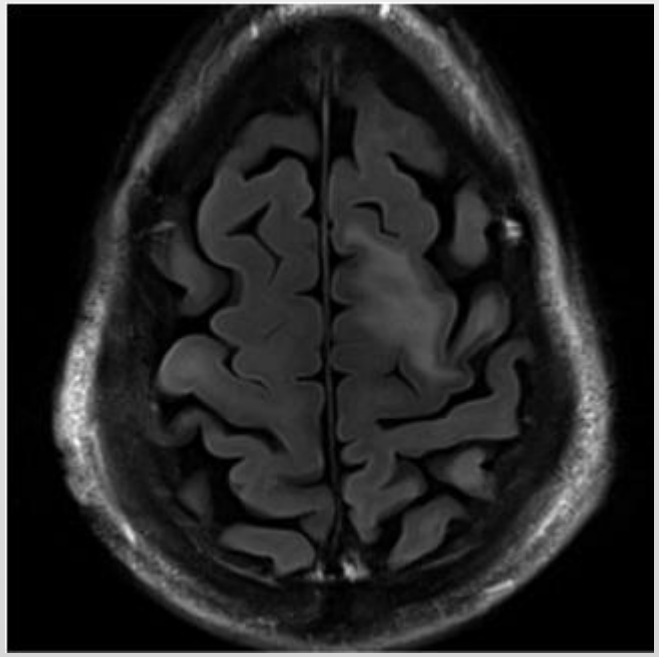
Manageable Safety Concerns	Serious Safety Concerns
• Liver function abnormalities • Bradycardia • Reactive airway disease • Proinflammatory • Blood pressure elevations • GI disturbance • Hair thinning • Infusion reactions	• Immune surveillance • Infections • Malignancies • Long-lasting and irreversible effects • Autoimmunity • Teratogenicity • PML • The unknown

Zadeh AR et al. *Int J Physiol Pathophysiol Pharmacol*. 2019;11(4):105-14.

GI = gastrointestinal;
PML = progressive multifocal leukoencephalopathy

Progressive Multifocal Leukoencephalopathy (PML)

Risk factors	• Previous immunosuppression, exposure to natalizumab >2 years • JC virus positivity
Clinical symptoms	• Motor function abnormalities, hemiparesis, ataxia • Cognitive impairment, behavioral changes, language disorders, visual problems • Headache, sensory loss, seizures
Radiologic	• T2 FLAIR multifocal lesions, coalescence of new lesions • Involves subcortical and juxtacortical white matter • T1 hypointense • Mass effect absent • Enhancement present in ~9% of patients



JC = John Cunningham

Chalkey JJ et al. *Curr Neurol Neurosci Rep*. 2013;13(12):408. https://my.clevelandclinic.org/departments/neurological/depts/multiple-sclerosis/ms-approaches/pml-diagnosis-management. Accessed August 10, 2022.

IMMUNOMODULATION/ALTERATION OF CELL FUNCTION

Interferons/Glatiramer acetate

Fumarates

Teriflunomide

Immunomodulation/Alteration of Cell Function

Interferons

MoA	Promotes shift from Th1→Th2, inhibits antigen presentation, enhances apoptosis of autoreactive T cells
Side Effects	Flu-like symptoms, injection-site reactions, increased LFTs, decreased WBCs
Dosing	IM or SQ injection

Glatiramer acetate (GA)

MoA	Promotes differentiation to Th2 and T reg cells leading to bystander suppression in CNS, deletion of myelin reactive T cells
Side Effects	Injection-site reactions, postinjection reaction, lipoatrophy
Dosing	Daily or 3x/wk SQ injection

Graber JJ et al. *Clin Neurol Neurosurg*. 2010;12(7):583-91.

CNS = central nervous system; LFT = liver function test; WBC = white blood cell; wk = week

Interferons and GA

- Approved for relapsing MS (RMS), active secondary progressive MS (SPMS), and clinically isolated syndrome (CIS)
- Slowly shrinking market

Advantages	Disadvantages
• Long-term safety and efficacy data • No surprises, well known side-effect profile/tolerability • Low risk	• Inconvenience of injectables • Lower efficacy • Concerns with adherence • Flu-like side effects with interferons • Possible immediate postinjection reaction with GA • Lipoatrophy with GA

Marrie RA et al. *Nat Clin Pract Neurol*. 2006;2:34-44. https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/020622s102lbl.pdf. Accessed August 10, 2022.

Fumarates (Dimethyl Fumarate, Monomethyl Fumarate, Diroximel Fumarate)

MoA	Esterase conversion to monomethyl fumarate (MMF); exact MoA not clear, MMF activates Nrf2 pathway, Nrf2 pathway involved in cellular response to oxidative stress, anti-inflammatory, cytoprotective, immunomodulating properties
Side Effects	• Flushing (~40%) • GI (abdominal pain, diarrhea, nausea, vomiting) • Pruritis • Lymphopenia • LFT elevation • PML (10 cases/>500,000 patients, all over age 50 years, with chronic persistent lymphopenia)
Dosing	• Dose titration • Temporary dose reductions/extend titration period if necessary
Elimination	• Terminal half-life of fumarates approximately 1 hour; accumulation of MMF does not occur with multiple doses

Nrf2 = nuclear factor erythroid 2–related factor 2

Gold R et al. *N Engl J Med*. 2012;367(12):1098-107.

Teriflunomide

MoA	• Noncompetitive/selective/reversible inhibitor of dihydroorotate dehydrogenase (DHODH)
	  • DHODH enzyme necessary for proliferating T/B cells; other cells untouched
	  • Active metabolite of leflunomide

Side Effects	• Hepatic metabolism → hepatotoxicity • Teratogenicity • Hair thinning • Paresthesia • Clear contraindications for teriflunomide include pregnancy, significant liver dysfunction, and concomitant use of leflunomide
Dosing	• 7 or 14 mg/d
Elimination	• Effect of drug may stay in the blood for 8 months to 2 years • 11-day accelerated elimination procedure with cholestyramine, oral activated charcoal powder

O'Connor P et al. *N Engl J Med*. 2011;365(14):1293-303.

CELL TRAFFICKING

Natalizumab

S1P Receptor Modulators

Natalizumab

MoA	• Selective mAb directed at α4β-1 integrin, blocks attachment of activated lymphocytes to VCAM-1 on endothelial cells and subsequent migration into CNS • Immune selective blockade
Side Effect Considerations	• TOUCH REMS program Adverse events • Headache, fatigue, UTI, URI, gastroenteritis, joint pain, diarrhea • Infections, hepatotoxicity, thrombocytopenia • PML
Dosing	• 300 mg administered q28d via infusion
Elimination	• Pharmacokinetic studies showed that natalizumab can be effectively removed from the blood compartment using plasmapheresis • Mean half-life 11 days

mAb = monoclonal antibody; q28d = every 28 days; REMS = Risk Evaluation and Mitigation Strategies; URI = upper respiratory tract infection; UTI = urinary tract infection; VCAM-1 = vascular cell adhesion molecule 1

Miller DH et al. *N Engl J Med*. 2003;348(1):15-23.

Sphingosine-1-Phosphate (S1P) Receptor Modulators

MoA	Adverse Effects
• Immune selective blockade • Binds with high affinity to S1P receptors • Blocks lymphocytes' ability to egress from lymph nodes, therefore reducing number of lymphocytes in peripheral blood • Precise mechanism by which S1P receptor modulators exert therapeutic effects in MS is unknown but may involve reduction of lymphocyte migration into CNS	• Bradycardia and atrioventricular (AV) conduction delays • Risk of infections • Herpes viral infections • Cryptococcal infections • Respiratory effects • Liver injury • Macular edema • Posterior reversible encephalopathy (PRES) • Immune system effects after stopping • Potential risk of rebound

Chaudhry B et al. *Neurotherapeutics*. 2017;14(4):859-73.

S1P Agents

Fingolimod: Receptor Targets 1, 3-5

Evidence	2 studies • Fingolimod vs placebo • Fingolimod vs IFNß-1a IM weekly
Dosing	Requires 6-hour 1st-dose observation (FDO) • Adults: 0.5 mg/d • Pediatric patients >10 years: 0.25 mg
Elimination	Pharmacologic effect can last up to 2 months after stopping medication

Siponimod: Receptor Targets 1,5

Evidence	Pivotal trial was the largest controlled clinical study of SPMS patients
Dosing	• Dose requires brief upward titration to mitigate decreased heart rate associated with initial dosing. Titration and maintenance dose regimens are determined by CYP2C9 genotype • Dosing: Initiate with 5-day titration, then 1 or 2 mg on Day 6 and maintenance
Elimination	7 days

Cohen JA et al. *N Engl J Med*. 2010;362(5):402-15. Kappos L et al. *Lancet*. 2018;391(10127):1263-73.

Selective S1P Agents

Ozanimod: Receptor Targets 1,5

Evidence	Compared to IFNß-1a IM in studies
Dosing	• 0.92-mg dose • 7-day starter pack to slowly increase dose over 1st week • No requirement for genotyping before initiation; no required FDO
Elimination	Approximately 11 days

Ponesimod: Receptor Targets 1

Evidence	• Most recently approved S1P modulator (March 2021) • Ponesimod proved superior to teriflunomide for improving annualized relapse rate, fatigue, MRI activity, brain volume loss, and disease activity status in patients with RMS
Dosing	• 20-mg dose • 14-day starter pack • No FDO requirement
Elimination	1 week

Cohen JA et al. *Lancet Neurol*. 2019;18(11):1021-33.
Kappos L et al. *JAMA Neurol*. 2021;78(5):558-567.

IMMUNOSUPPRESSIVE AGENTS

Mitoxantrone

Mitoxantrone

MoA	Disrupts DNA synthesis and repair; inhibits B cell, T cell, and macrophage proliferation; impairs antigen presentation as well as secretion of interferon γ, TNF, and IL-2
Indications	Worsening RRMS, PRMS, SPMS
Dosing	12 mg/m^2 every 3 months
Adverse Events	Temporary blue discoloration of sclera and urine, nausea, alopecia, menstrual disorders including amenorrhea and infertility, infections (URI, UTI, stomatitis), and cardiac toxicity (arrhythmia, abnormal EKG, CHF)
WARNINGS	Severe tissue damage if extravasation from IV site, cardiotoxicity, acute myelogenous leukemia, myelosuppression

CHF = congestive heart failure; EKG = electrocardiogram; IL = interleukin; PRMS = progressive relapsing MS; RRMS = relapsing-remitting MS; TNF = tumor necrosis factor

https://www.accessdata.fda.gov/drugsatfda_docs/label/2009/019297s030s031lbl.pdf. Accessed August 10, 2022.

CELL-DEPLETION THERAPIES

Cladribine

Alemtuzumab

Ocrelizumab

Ofatumumab

Cladribine

MoA	Not fully elucidated but thought to involve cytotoxic effects on B and T lymphocytes through impairment of DNA synthesis, resulting in depletion of lymphocytes. Causes a dose-dependent reduction in lymphocyte counts followed by recovery • Prolonged effect on T cells, transient effect on B cells
Indications	RRMS and active SPMS not CIS • Recommended for patients who have had an inadequate response to, or are unable to tolerate, alternate drug indicated for treatment of MS
Dosing	Short course of oral treatment • 3.5 mg/kg body weight over 2 years, administered as 1 treatment course of 1.75 mg/kg/y, each consisting of 2 treatment weeks • Median time to recovery from lymphocyte counts <500 cells/µL to at least 800 cells/µL was approximately 28 weeks
Adverse Events	>20% compared to placebo • URI, headache, lymphopenia, hematologic toxicity, liver Injury, tuberculosis, complications with blood transfusions
WARNINGS	Malignancies and risk of teratogenicity • Long-term monitoring for malignancies

Grieb P et al. *Lancet*. 1994;344(8921):538.

Alemtuzumab

MoA	Directed against CD52 antigen found on T and B lymphocytes and monocytes (induction strategy)
Dosing	12 mg IV daily on 5 consecutive days at Month 0 then 3 consecutive days at Month 12

Adverse Event Considerations	FDA-mandated REMS program
	• Adverse events
	  • Infusion reactions (cytokine release syndrome, premedicate (IVMP, acetaminophen, diphenhydramine)
	  • Antibody-mediated autoimmunity (thyroid disease 34% of patients), immune thrombocytopenia, glomerular nephropathies, miscellaneous autoimmune conditions
	  • Infection due to prolonged CD4+ T-cell depletion (herpes virus, human papilloma virus [HPV], tuberculosis, fungal infections, Listeria meningitis)
	  • Malignancy (thyroid cancer, melanoma, lymphoproliferative disorders)
	  • Pneumonitis
	• Requires monthly lab draws x 5 years → risk of loss for follow-up

Elimination	Approximately 2 weeks after IV infusion

Coles AJ et al. *Lancet*. 2012;380(9856):1829-39. Coles AJ et al. *J Neurol*. 2006;253(1):98-108.

IVMP = intravenous methylprednisolone

Ocrelizumab

MoA	Anti-CD20 B-cell mAb, humanized immunoglobulin (Ig)G1
Indications	RMS and PPMS
Dosing	600 mg administered IV q6mo • Starting dose: two 300 mg infusions given 2 weeks apart • Premedications: IVMP, acetaminophen, diphenhydramine

Adverse Event Considerations	No REMS program
	• Side effects
	  • Infusion reactions, infections
	• Less common adverse events
	  • Hepatitis B reactivation, decreased IgG/IgM, malignancies
	Contraindications
	• Hepatitis B infection

Elimination	Terminal elimination half-life = 26 days

q6mo = every 6 months

Kappos L et al. *Lancet*. 2011;378(9805):1779-87.

Ofatumumab

MoA	Anti-CD20 mAb
Evidence	Compared to teriflunomide in study
Dosing	Administered via SQ injection • 20 mg SQ at Weeks 0, 1, 2, 4, then monthly • Stored in refrigerator
Adverse Events	Common side effects • Injection-related reactions, low immunoglobulins, URI, headache Serious adverse events • Infections, reactivation of hepatitis B, decreased immunoglobulins Contraindications • Active hepatitis B virus infection
Elimination	Half-life = approximately 14 days (range: 2-61 days)

https://www.accessdata.fda.gov/drugsatfda_docs/label/2014/125326s060lbl.pdf. Accessed May 18, 2021.

BTK Inhibitors in Late-Stage Development for MS

- Small molecules that selectively block activity of BTK (enzyme important for the activation of B cells and microglia)
- Selectively targets B cells
  - Evobrutinib
  - Fenebrutinib
  - Remibrutinib
  - Tolebrutinib

BTK = Bruton's tyrosine kinase

ClinicalTrials.gov. Accessed August 10, 2022.

Additional Agents in Late-Stage Development for MS

CD20-directed mAb

- Ublituximab

Immunomodulators

- Glatiramer acetate depot (IM injection)

Dihydroorotate dehydrogenase inhibitor

- Vidofludimus calcium

Gold nanocrystal suspension

- CNM-Au8

Immunomodulatory vaccines

- T cell receptor peptide vaccine

Agents being developed for MS spasticity

- Arbaclofen
  - Selective GABA type B receptor agonist
- Nabiximols
  - Cannabis extract

ClinicalTrials.gov. Accessed August 10, 2022.

GABA = gamma-aminobutyric acid

Patient and Family Education/Learning Needs

- Active participation in care
- Ability to make informed choices
- Ability to engage in self care with confidence and competence
- Assess ability to learn
- Level of education
- Cognition
- Readiness to learn
- Cultural literacy/cultural health beliefs
- Healthcare literacy
- Role of family/family support
- Coping mechanisms

https://practicalneurology.com/articles/2017-apr/shared-decision-making-in-multiple-sclerosis-management. Accessed August 10, 2021.

MS RELAPSE

MS Relapse

- Episode of focal neurologic disturbance lasting >24 hours without alternate explanation and with preceding period of clinical stability lasting at least 30 days
- Onset of neurologic symptoms that evolve over days or weeks
- Plateaus within 1-2 weeks
- Recovery time varies
- Depends on severity of relapse
- Some symptoms become permanent
- Relapse rate and degree of recovery after relapses predict long-term disability
- Relapse is usually not a medical emergency

Goodin DS et al. *Mult Scler Relat Disord*. 2016;6:10-20.

Management of Relapse

- Assess if acute relapse, pseudo-relapse, or disease progression
- Treatment options
  - Corticosteroids
  - IVMP 1-2 g/d for 3-5 days
  - High-dose oral MP 500mg-1g for 3-5 days
  - Oral prednisone 1250 mg/d for 3-5 days
  - Oral dexamethasone 96-160 mg PO for 3-5 days
- Repository corticotropin injection 40-80 U IM or SQ once daily for 2-3 weeks
- Plasmapheresis (used as 2nd-line therapy after systemic corticosteroids)
- Assess for adherence to treatment
- Consider escalating DMT treatment

PO = by mouth

Ontaneda D et al. *Ann Indian Acad Neurol*. 2009;12(4):264-72. Weiner H et al. *Neurology*. 1989;39(9):1143-9.

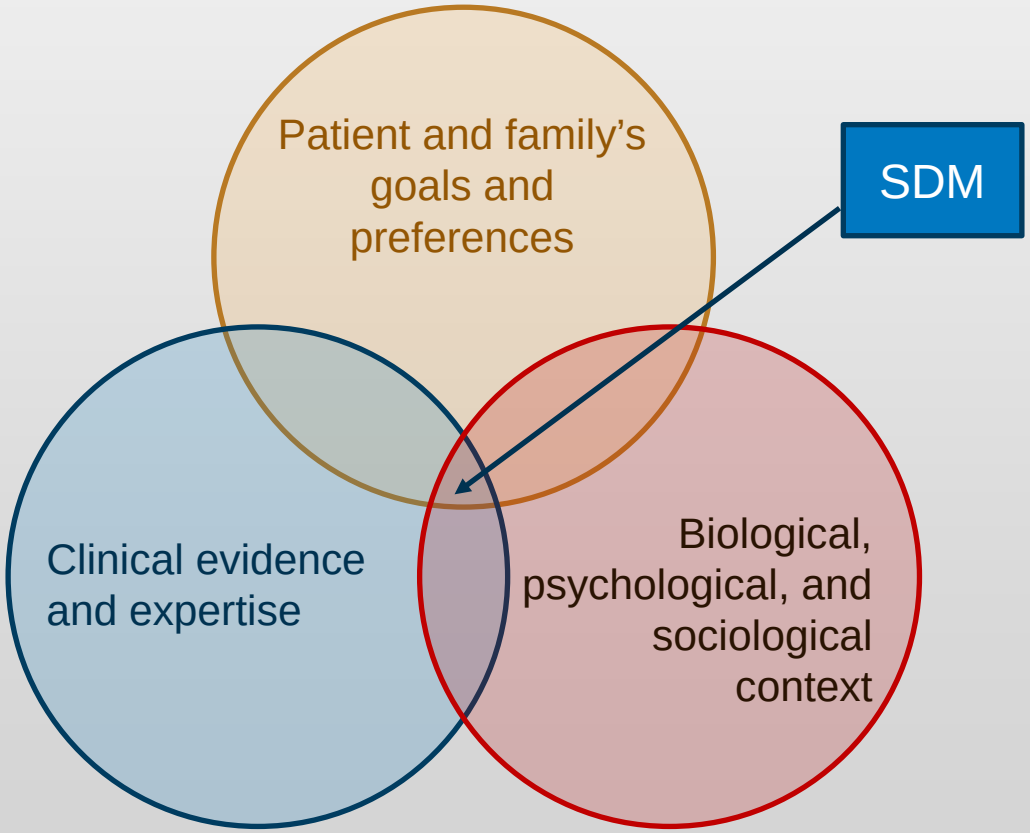
Management of Relapse: Nonpharmacologic

- Maximize recovery
- Refer to rehabilitation therapy
  - Physical therapy
  - Occupational therapy
  - Speech therapy
- Refer to psychology or social work

https://emedicine.medscape.com/article/1146199-treatment#showall. Accessed May 18, 2021.

Shared Decision-Making (SDM)

Decision-making process



https://www.cincinnatichildrens.org/

- Patient-centered care
- Collaborative relationship between clinicians and patients
- Incorporates patient preferences and values
- Patient education
- 2-way communication
- Positive impact on patient adherence

https://practicalneurology.com/articles/2017-apr/shared-decision-making-in-multiple-sclerosis-management. Accessed August 11, 2022.

Summary

- MS treatment landscape is increasingly complex and crowded
- We have entered a new era of complex choices that challenges the professional community with the need to keep current and constantly updated
- Abundance of choice for RRMS
- Acute and long-term management of relapses as well as the disease itself require nursing knowledge, vigilance, and patient and family education
- Multiple considerations
  - Risk factors for disease course and progression
  - Sequencing of DMTs
  - Patient factors
  - Shared decision-making
- PML is rare, but can be associated with significant disability

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2022

EVOLUTION OF PRECISION MEDICINE: TREAT-TO-TARGET APPROACHES

Stephanie Agrella, PhD, ANP-B.C., MSCN
Director of Clinical Services
MS Clinic of Central Texas Neurology
Round Rock, TX

Provided by Academy for Continued Healthcare Learning and Annenberg Center for Health Sciences at Eisenhower

ACHL ACADEMY for CONTINUED HEALTHCARE LEARNING

ANNENBERG CENTER FOR HEALTH SCIENCES AT EISENHOWER

The program is supported through educational grants from Biogen, Bristol-Myers Squibb, Inc., and Novartis Pharmaceuticals Corporation.

What We Know

- MS: autoimmune demyelinating disease of CNS
- Most common nontraumatic disability of young adults
- Most patients have RRMS
- Approximately one-half of RRMS patients → SPMS
  (↑ disability and ↓ or ⃠ relapses)
- Early treatment = delayed onset of disability

CNS = central nervous system; MS = multiple sclerosis: RRMS = relapsing-remitting MS; SPMS = secondary progressive MS

Treatment Paradigms in MS

American Academy of Neurology (AAN)

- PRACTICE GUIDELINE RECOMMENDATIONS SUMMARY: *Disease-Modifying Therapies for Adults With Multiple Sclerosis*
- Guideline detail as published in April 2018
- https://www.aan.com/Guidelines/home/GuidelineDetail/898

Therapeutic targets for multiple sclerosis: current treatment goals and future directions

- Smith AL et al. *Neurotherapeutics*. 2017;14(4):952-60.
- American Academy of Neurology (AAN)

Most Common Treat-to-Target Approaches in MS

Rio score

Disease-free survival

No evidence of disease activity (NEDA)

Smith AL et al. *Neurotherapeutics*. 2017;14(4):952-60.

Treat-to-Target Approaches: Rio Score and Modified Rio Score

Rio Score	Modified Rio Score
• Developed in 2008 by Rio J et al to score treatment response • 0-3 score • MRI lesions ≥3, relapse ≥1, EDSS ≥1 sustained 6 months • Patients with score of ≥2 at 12 months = greater chance of disease progression or relapse	• Modified in 2012 • 0-3 score • MRI lesions: ≥6 = 1, relapse ≥1 = 1, then relapse ≥2/y = 2 • Score 0 = responder, 1 = indeterminate (re-evaluate at 6 months), ≥3 = nonresponder • EDSS was removed due to poor intra- and interreliability • ≥2 = 60% chance of worsening at 3 years and probably benefit Δ DMTs

DMT = disease-modifying therapy; EDSS = Expanded Disability Status Scale; MRI = magnetic resonance imaging

Hyun JW et al. *PLoS One*. 2015;10(5):e0129243.

Treat-to-Target Approaches: Disease-Free Survival

- From oncology literature
- Applied only to autologous hematopoietic stem cell transplant
- HALT-MS trial: high-dose immunosuppression
- 78.4% were event-free at 3 years
- Not widely adopted in clinical trials

Smith AL et al. *Neurotherapeutics*. 2017;14(4):952-60.

Treat-to-Target Approaches: NEDA

NEDA 3	NEDA 4

• Absence of relapses, CDW with EDSS, no Gad-enhancing lesions, and no new enlarging T2 lesions
• Stronger focus on inflammatory aspects of MS
• Limitations
  • EDSS: primarily walking disability and no cognitive measurement
  • Not sensitive to capture subtle changes in inflammation or neurodegeneration, which underlie disability
	• BVL >0.4% is predictor of disability and cognitive dysfunction
	• Limitation
	  • Routine BVL measurement is not consistent

BVL =

Guevara C et al. *Front Neurol*. 2019;10:788.

Assessing Response to Therapy

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New Treatment Paradigms in MS: Assessing Response to Therapy

Utilize treat to target to evaluate response to DMT

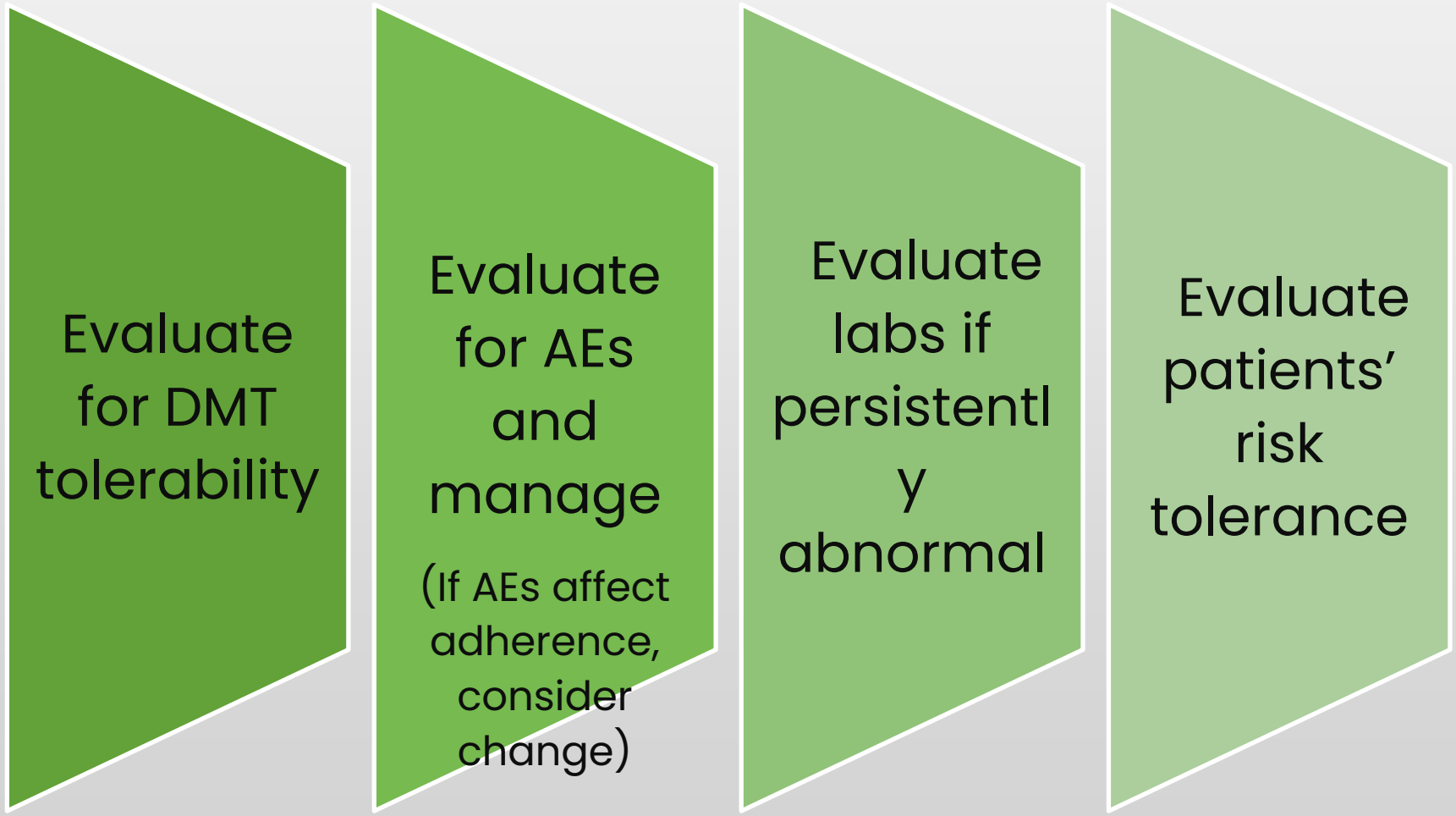
Understand mechanism of action (MoA)

New Treatment Paradigms: Consideration for Switching Therapy

- 1 or more relapses, 2 or more new MRI lesions (Gad or new T2), or increased disability over past 12 months
- Monitor MRI and relapses and understand when DMTs become most effective (eg, how long have they been on DMT?)
- Evaluate degree of disease activity, adherence, adverse event (AE) profiles, and MoA

https://www.aan.com/Guidelines/home/GuidelineDetail/898. Accessed August 15, 2022.

New Treatment Paradigms: Consideration for Switching Therapy (cont)



https://www.aan.com/Guidelines/home/GuidelineDetail/898. Accessed August 15, 2022.

New Treatment Paradigms: Consideration for Switching Therapy (cont)

- Understand long-term safety data (eg, risk of malignancy and infections)
- Be aware of suggested monitoring for each DMT
- Counsel patients (eg, stopping DMT potential risk of significant relapses/ rebound)
- In general, discontinue DMT in context of pregnancy

New Treatment Paradigms

PRECISION MEDICINE IN MS

Precision Medicine Approach: Challenges

Precision diagnosis

Predicting treatment response

Personalized monitoring to progressively update this prediction

Gafson A et al. *Mult Scler J*. 2017;23(3):362-9.

Precision Medicine: Biomarkers

- Brain MRI: key in diagnosis, prognosis, and early treatment response
- Lesion counts (T2), active inflammation with Gad (T1)
- Brain volume: ↑ evidence of its usefulness in monitoring
- CSF CHI3L1 and NfL are promising prognostic and biomarkers in CIS
  - Can show disability development in MS
- CD62L and IgM oligoclonal bands: may play a role in risk of PMS with natalizumab patients

CIS = clinically isolated syndrome; CSF = cerebrospinal fluid; Ig = immunoglobulin; PMS = progressive MS

Comabella M et al. *Curr Opin Neurol*. 2016;29(3):254-62.

Precision Medicine: What Needs to Be Done?

- Large representative datasets
- Agreement on outcomes meaningful to patients
- Validated models predictive of behavior of individual patients
- Decision criteria agreed on by all stakeholders
- Wide access to tools and approaches for personalization

Gafson A et al. *Mult Scler J*. 2017;23(3):362-9.

New Treatment Paradigms in MS: Conclusion

Treat to Target

- Evaluate DMT's efficacy using primarily NEDA 3

Switching Therapies

- With 18+ therapies, it is more important to routinely evaluate response to DMTs
- Not only disease mechanisms, pathogenesis, and MoA, but when to

Precision Medicine

- Right patient, right drug, and right time
- Will require coordinated effort in MS community

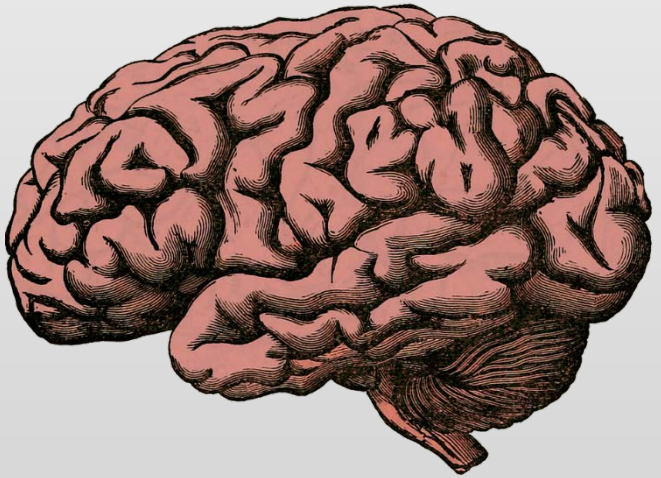
Why Do We Treat Early?

TIME

IS

BRAIN

=



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Multiple Sclerosis Nurse Leadership Program

2022

PATIENT CASE PRESENTATION

Lynn McEwan, NP, MScN, CNNC, MSCN
London Health Sciences Centre-MS Clinic
London, Ontario, Canada

Provided by Academy for Continued Healthcare Learning and
Annenberg Center for Health Sciences at Eisenhower

ACHL
ACADEMY for CONTINUED HEALTHCARE LEARNING

ANNENBERG CENTER FOR HEALTH SCIENCES AT EISENHOWER

The program is supported through educational grants from Biogen, Bristol-Myers Squibb, Inc., and Novartis Pharmaceuticals Corporation.

Case of Newly Diagnosed MS

- In June 2018, presented to urgent ophthalmology clinic with left visual blurring and ocular pain
  - Diagnosed with optic neuritis and referred to MS clinic as possible MS vs NMOSD
- In July 2018, vision improved
- Additional health history
  - 28-year-old Caucasian female, born in Canada, recently married with a 15-month-old and employed full-time
  - March 2018: right arm and leg paresthesia x 2 weeks; walking balance off; notes blurring of vision after a shower
  - Reports significant fatigue, poor sleep, and forgetfulness; feeling very anxious about the diagnosis as she has an aunt with disabling MS; father passed away earlier in the year
  - Smokes 10 cigarettes per day, poor diet: eats sporadically and usually “junk food”
- EDSS 2.0 (visual 1.0 and sensory 2.0)

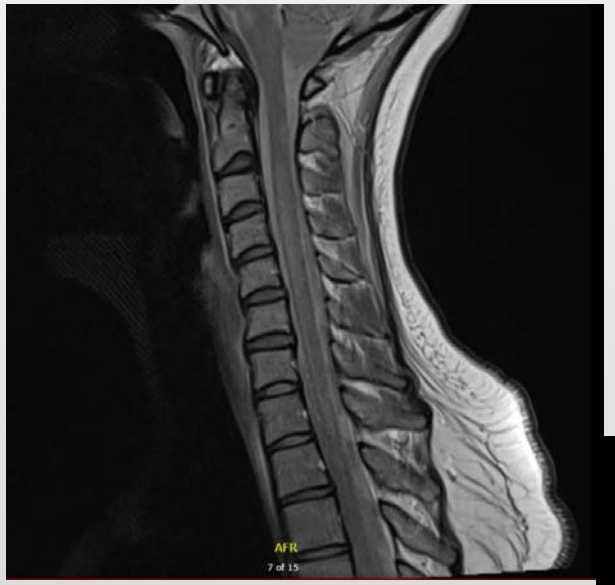
EDSS = expanded disability status scale; MS = multiple sclerosis; NMOSD = neuromyelitis optica spectrum disorder

Investigation: MRI

- MRI with gadolinium
  - Multiple supra and infratentorial lesions
    - Periventricular, subcortical, several have a perpendicular orientation to the lateral ventricle, lesions in the right middle cerebellar peduncle and hemisphere, and upper medulla
    - Several lesions enhance in keeping with active demyelination
  - Left optic nerve with swelling and mild enhancement of the orbital and canalicular portion of the nerve
    - Periependymal signal around anterior aqueduct of the 4th ventricle
    - Longitudinal extensive cervical myelitis, extending from C2-3 to C6 with enhancement

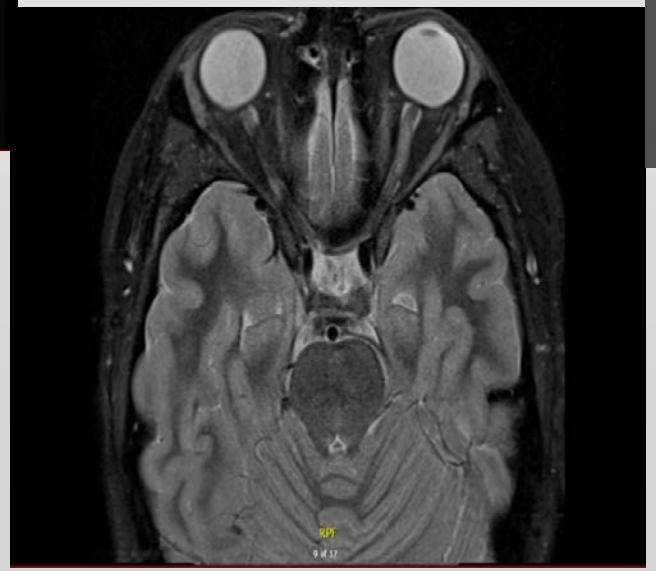
MRI = magnetic resonance imaging

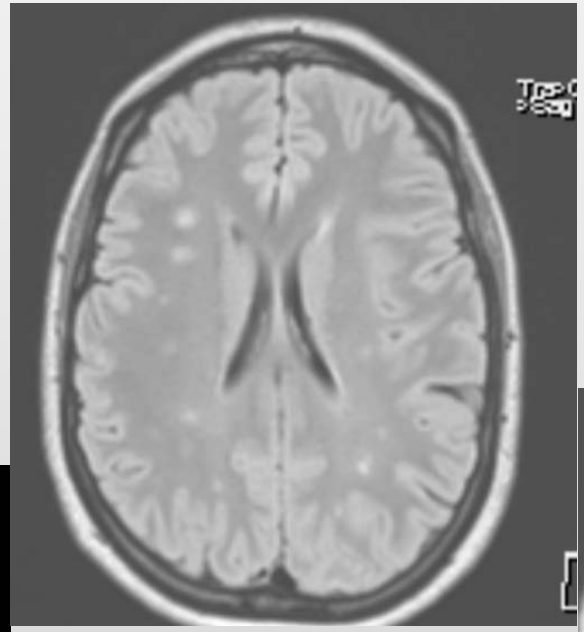
MRI Images



Longitudinal Cord lesion

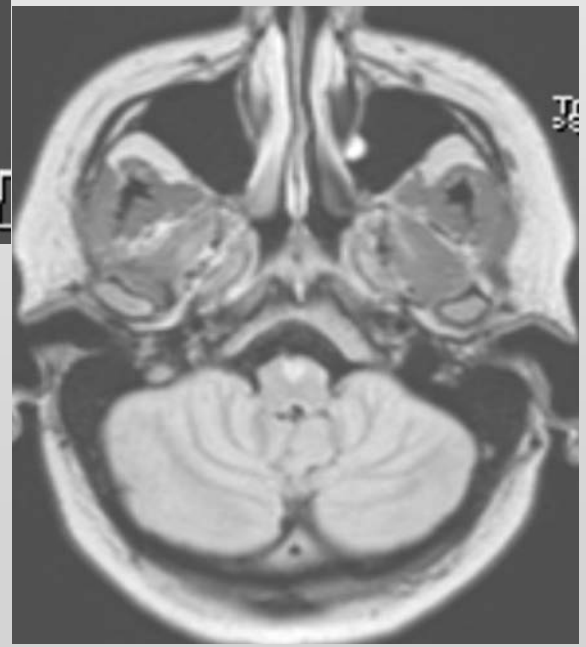
Swelling Left Optic Nerve





Ovoid Subcortial and Periventricular lesions

Periependymal Aqueduct Lesion



Images courtesy of LHSC Radiology Department.

Discussion Questions

- What other investigations would you consider for this patient?

Please provide responses in the chat feature

Additional Investigations

- Laboratory
  - Anti-AQP4 and anti-MOG serum negative
  - Anti-dsDNA, ANA, lupus anticoagulant negative
  - Angiotensin-converting enzyme serum negative
  - CSF
    - Protein 431 mg/L (200-400)
    - IgG 127 mg/L (10-30)
    - IgG/albumin 0.66 (0.00-0.23)
    - CSF index 2.95 (0.25-0.85)
    - Oligoclonal bands present (no bands in serum)

ANA = antinuclear antibody; CSF = cerebrospinal fluid; dsDNA = double-stranded DNA; Ig = immunoglobulin; MOG = myelin oligodendrocyte glycoprotein

Diagnostic Criteria

MS diagnosis is based on:

Patient susceptibility	Clinical history with symptoms consistent with inflammatory, demyelinating process	Objective neurological evidence on examination
Dissemination of CNS lesions in time and space	CSF specific for oligoclonal bands	Exclusion of other causes

Thompson AJ et al. *The Lancet Neurology.* 2018;17:162-173.

Confirmed Diagnosis

- Met 2017 McDonald diagnostic criteria for RRMS
  - Epidemiology risk factors: 28-years-old, female, White
    - Environmental: born in Canada, smoker
    - Genetics: aunt with MS
  - Dissemination in time: transverse myelitis and 3 months later an optic neuritis, multiple enhancing lesions on MRI
  - Dissemination in space: MRI findings, brain, optic nerve, and spinal cord
  - CSF: positive oligoclonal bands
  - Exclusion of other causes

RRMS = relapsing-remitting MS

Thompson AJ et al. *Lancet Neurol*. 2018;17(2):162-73.

Disease Phenotype

- Active MS
  - Relapsing-remitting disease
    - 2 clinical relapses in less than 6 months
    - MRI shows multiple enhancing lesions

Lublin F et al. *Neurology*. 2014;83(3):278-86.

MRI Predictors of Frequent Relapse

- High number of T2 white matter lesions
- Presence of gadolinium-enhancing lesions
- Presence of infratentorial or spinal cord lesions at first episode
- Presence of corpus callosum long-axis perpendicular lesions
- Increased ventricular volume loss

Bergamaschi R. *Int Rev Neurobiol*. 2007;79:423-427.

Factors Associated With Worse Prognosis at MS Diagnosis

Demographic	Radiological	Clinical
• Age >40 years • Male sex • Nonwhite ethnicity • Comorbidity	• New Gad-enhancing T1 or T2 weighted lesions • T2 lesion volume • Spinal cord lesion • Brain atrophy	• Relapse frequency • Relapse severity o >1 moderate to severe attack o Steroids/hospitalization o Impact on ADLs o >1 functional system o Severe motor/cerebellar/ brainstem involvement • Relapse recovery

Freedman MS et al. *Can J Neurol Sci*. 2020;474(4):437-55.

ADLs = activities of daily living

Treatment Initiation

When to Start an MS Therapy: Early vs Delayed

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Rationale to Treat Early

- Current DMTs target inflammatory demyelination
- Less effective in degenerative disease process
- Therapeutic window
  - Optimal treatment window closes early in disease course
    - Patient reaches EDSS 3.0
- Early treatment associated with better outcomes after 1st relapse
  - Reducing relapses and new MRI lesions
    - Delay or prevent disability accrual
- MSBase study found DMTs more effective in subgroups with shorter disease duration, lower EDSS, and lower relapse rate in relapsing MS phenotype

DMT = disease-modifying therapy

Freedman MS et al. *Mult Scler Relat Discord*. 2014;3(2):147-55. Kalincik T et al. *Neurology*. 2021;96(5):e783-97.

Rationale to Delay Treatment

- Confidence in MS diagnosis
- Patient readiness
- Psychological state: Emotional burden high at diagnosis
  - Risk for depression
    - Recently diagnosed patients have significantly poorer QoL
    - Younger patients and those with mild physical impairment have perceived lower QoL
  - Risk of poor treatment adherence or persistence
    - Mohr et al (1997): 41% with new or worsening depression discontinued treatment within 6 months

QoL = quality of life

Amati MP et al. *Mult Scler.* 2001;7(5):340-344. Janssens AC et al. *Acta Neurol Scand*. 2003;108(6):389-95. Mohr DC et al. *Arch Neurol*. 1997;54(3):531-3.

Treatment Strategies

Escalation Approach	Induction Approach
• Start with safest therapy • Possibly less efficacious • Minimize long-term safety risks • Escalate with breakthrough disease • Potential loss of therapeutic window benefit	• Start with highly efficacious therapy • Achieve disease stability early in disease course • Potential for future de-escalation • Risk of serious adverse events • Concern for therapeutic options for breakthrough disease

Smith AL et al. *Neurotherapeutics*. 2017;14(4):952-60.

Shared Decision Making

Ability to discuss treatments in the context of patient's values and preferences

Shared perspective between the patient and clinicians' healthcare goals

Improves treatment adherence

More likely to involve self-management practices

Heesen C et al. *J Neurol*. 2007;254(Suppl 2):11/116-11/121.

Treatment Initiation: Patient and Clinician Perspectives (Case)

- Patient Perspective
  - Concerned about her mood, poor sleep, work stress
  - Ongoing symptoms
    - Episodic leg pain, visual blurring, impaired cognition, and urinary frequency
  - Concerned for medication side effects and risks
  - Timing of 2nd pregnancy
- Clinician Perspective
  - Active disease: clinical and MRI
  - Lesion location: brainstem and extensive spinal cord
  - Incomplete relapse recovery
  - EDSS 2.0
  - Young and good health
  - Early treatment initiation promote better outcomes

Treatment Plan

- Decision made to initiate glatiramer acetate
- Refer to social worker for coping with diagnosis, anxiety and work stress
- Neurocognitive evaluation
- Offered symptomatic treatment

Treatment Plan Continued

- Follow-up
  - Hesitant to initiate DMT
  - Generalized symptom worsening, pain, memory, and wording difficulties
  - MRI: New and enhancing lesion
  - Neurocognitive testing: Normal in all domains, high anxiety, and reported significant increase in cannabis use since diagnosis
- Plan
  - Provide support and counseling
    - Participatory “guided treatment decision-making”
    - Support medical leave from work
    - Management of MS symptoms
    - Impact of cannabis (THC) and anxiety

Feinstein A et al. *Mult Scler*. 2021 Apr;27(4):636-639. Pavisian B et al. *Neurology*. 2014;82(21):1879-87.

Follow-up

- 4 months later
  - Mood and sleep improved
  - Delay 2nd pregnancy for at least 2 years
  - Decision to initiate ocrelizumab; started in April 2019
- 12 months later: Virtual visit
  - Reports possible relapse: disequilibrium, numbness, and thoracic hug lasting a few weeks
  - Notes worsening of mood x 4 weeks post-infusion
  - Describes worsening fatigue and symptoms 4 weeks prior to infusion “crap gap”
  - Concerns for COVID and ocrelizumab

Follow-up (cont)

- 1 relapse 12 months on treatment
- EDSS: unchanged
- MRI: 2 new lesions, enhancing pons, and thoracic cord 18 months on treatment
- Patient concerned about mood and “crap gap” side effects and wants to change therapy

Treatment Goals for MS

NEDA-3

- ❑No clinical relapses
- ❑No sustained disability
- ❑No Gad-enhancing or new or enlarging T2 lesions on head MR

NEDA-4

- ❑Brain volume atrophy <0.4%

AAN Guidelines

- ❑≤1 relapse 6-12 months
- ❑≤1 new MRI lesions (Gad or new T2) 6-12 months
- ❑No sustained disability over past 12 months

NEDA = no evidence of disease activity; Gad = gadolinium

Nixon R et al. *Adv Ther*. 2014;31(11):1134-54. Kappos L. *Mult Scler*. 2016;22(10):1297-1305. https://aan.com/Guidelines/home/GuidelineDetail/989. Accessed August 10, 2022.

Achieving Treatment Goals

- Is this patient meeting treatment goals?
  - 1 clinical relapse (minor)
  - No EDSS change
  - 2 new lesions on MRI (major)
    - 1 enhancing brainstem lesion
    - 1 spinal cord lesion
  - On therapy for >1 year
  - Patient not wanting to continue therapy

Summary Points

- Application of McDonald Diagnostic Criteria to support MS diagnosis
- Early treatment initiation to achieve better patient outcomes
- Participatory guidance and shared decision-making supports patient adherence and self-management skills
- Balance treating the disease versus treating the individual to achieve therapeutic goals
- Establish routine monitoring to achieve treat-to-target goals

Discussion Questions

- Do you agree with the treatment decisions made for this patient? Why or why not?
- What else would you do to help this patient?

- In general, how do you help ensure your patients achieve treat-to-target goals?

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Multiple Sclerosis Nurse Leadership Program

2022

TOPICS IN MS SYMPTOM MANAGEMENT

Constance B. Easterling, MSN, ARNP
Clinical and Research Consultant
MS Care Center of Neurological Services
Orlando, Florida

Provided by Academy for Continued Healthcare Learning and Annenberg Center for Health Sciences at Eisenhower

ACHL ACADEMY for CONTINUED HEALTHCARE LEARNING

ANNENBERG CENTER FOR HEALTH SCIENCES AT EISENHOWER

The program is supported through educational grants from Biogen, Bristol-Myers Squibb, Inc., and Novartis Pharmaceuticals Corporation.

Polling Question

Which of the following symptoms are the most concerning for your patients with multiple sclerosis (MS)?

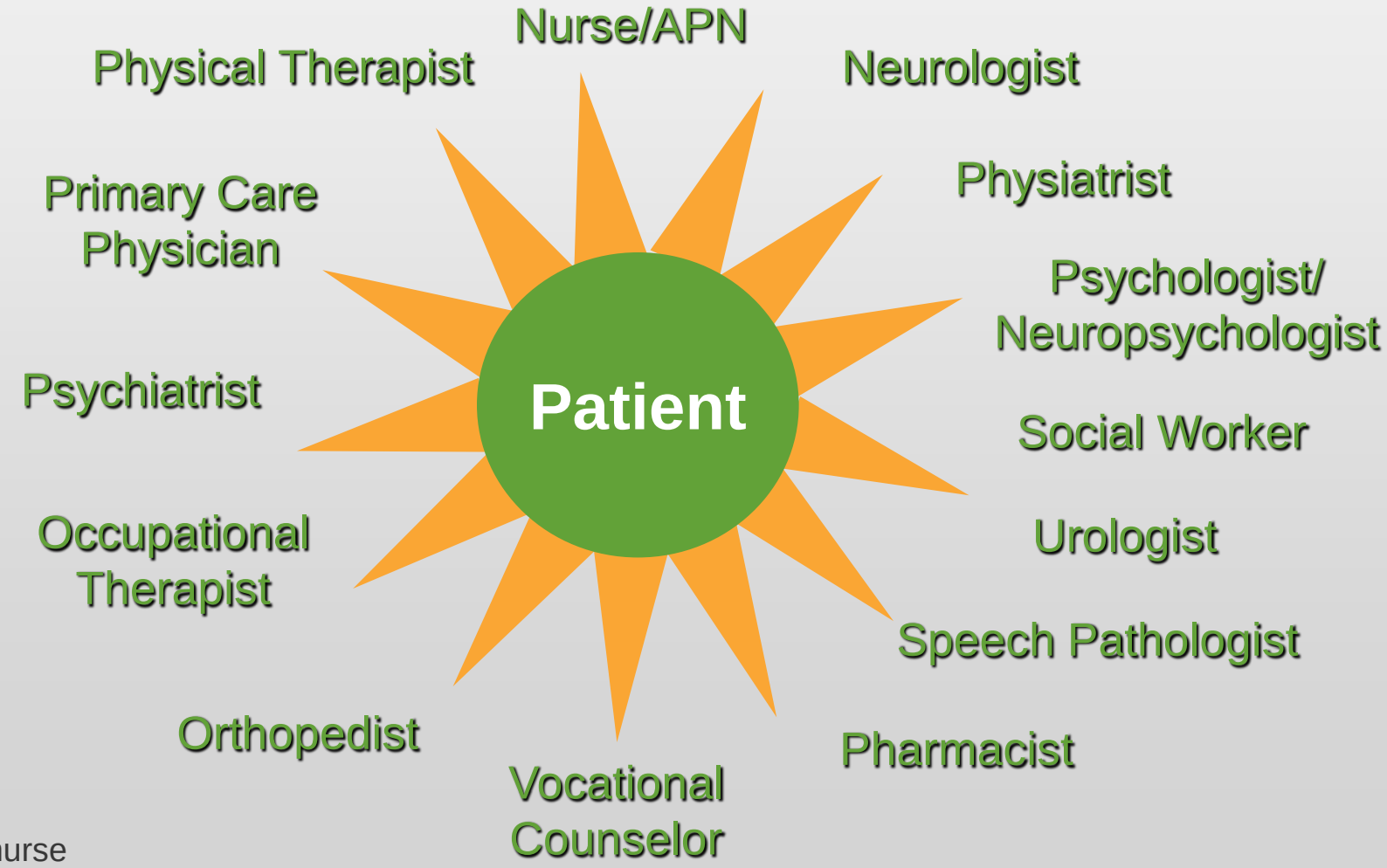
A. Fatigue
B. Pain
C. Sexual dysfunction
D. Cognitive difficulties
E. Spasticity
F. Bladder and bowel dysfunction

MS Symptom Overview

- Fatigue
- Loss of sensation
- Decreased visual acuity, diplopia
- Pain
- Sexual dysfunction
- Paresthesias
- Emotional disturbances
- Cognitive difficulties
- Heat sensitivity
- Spasticity
- Gait, balance, and coordination problems
- Speech/swallowing problems
- Tremor
- Weakness
- Bladder, bowel dysfunction

Halper J et al. *Nursing Practice in Multiple Sclerosis: A Core Curriculum*. 3rd ed. Springer Publishing Company; 2012.

Comprehensive Team Approach



APN = advanced practice nurse

https://www.nationalmssociety.org/Treating-MS/Comprehensive-Care/Developing-a-health-care-team. Accessed August 15, 2022.

WELLNESS

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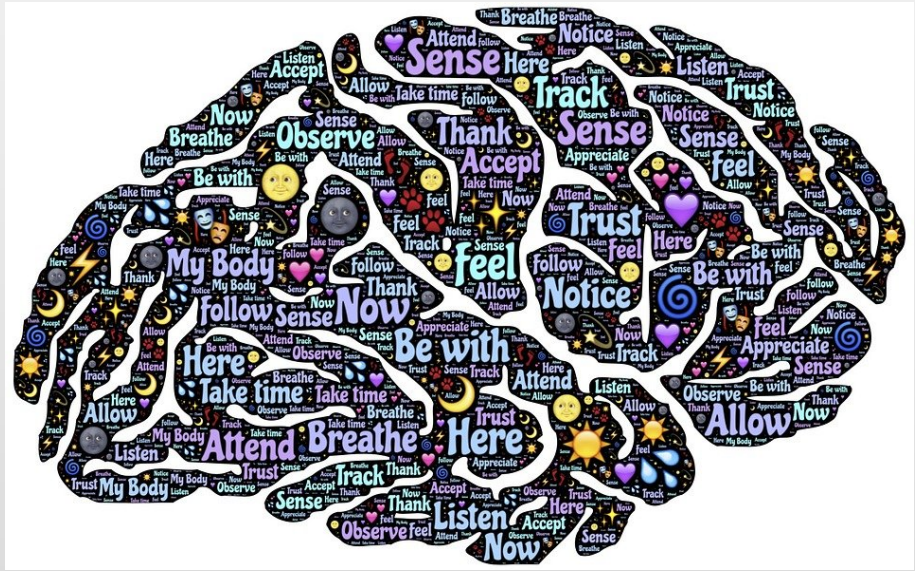
Wellness Promotion

- Maximize neurologic reserve
- Improve sleep quality
- Exercise
- Nutrition
- Vitamin D
- Manage chronic conditions or comorbidities
- Lifestyle changes
- Mindfulness
  - Maintaining a moment-to-moment awareness of our thoughts, feelings, bodily sensations, and surrounding environment, through a gentle nurturing lens
  - Mindfulness involves acceptance and paying attention to our thoughts and feelings without judgment



https://www.youtube.com/watch?v=puzAe4G6uDw. Accessed August 15, 2022. Zhang T et al. *Neurology*. 2016;86(14):1287-95.

FATIGUE

MS Fatigue

- “A subjective lack of physical and/or mental energy that is perceived by the individual or caregiver to interfere with usual and desired activities”
- Forms: lassitude, neuromuscular, cognitive
- Acute: new onset, related to a relapse
- Chronic: longer than 6 weeks; may last months

https://www.nationalmssociety.org/Symptoms-Diagnosis/MS-Symptoms/Fatigue. Accessed August 15, 2022.

MS Fatigue (cont)

- The most common and disabling symptom of MS
- Experienced by up to 95% of patients
- 50%-60% describe it as one of their most troubling symptoms
- Reported in all disease stages and phenotypes
- Some evidence that lesions in the basal ganglia and hypothalamus may play an important role

Schapiro RT. *Managing the Symptoms of Multiple Sclerosis*. 6th ed. Demos Medical Publishing, 2014. Amato P. *Exp Opin Pharmacother*. 2012;13(2):207-16. Halper J et al. *Nursing Practice in MS: A Core Curriculum*. 3rd ed. Springer Publishing; 2012.

Clinical Characteristics of Fatigue

- Overwhelming sense of sleepiness
- Constant sense of tiredness
- Lack of mental energy
- Feeling of exhaustion
- Not necessarily related to level of disability
- May affect motor function
- May affect cognitive function
- Not fully understood

Comi G et al. *Expert Rev Neurother*. 2002;2(6):867-76. Krupp LB. *CNS Drugs*. 2003;17(4):225-34.

Fatigue Management

- Exercise improves fatigue
- Address secondary causes
- Cooling techniques
- OT/PT: energy conservation techniques (eg, pacing)
- Stress management
- Pharmacotherapy

OT/PT = occupational and physical therapists

Amato P. *Expert Opin Pharmachother*. 2012;13(2):207-16. Bennett SE et al. *Int J MS Care*. 2014;16(suppl 1):S25-32.

Pharmacologic Management of MS Fatigue

Drug	Dose	Adverse Effect
Amantadine*	100 mg tid	Dry mouth, constipation, GI, poor appetite, agitation
Amantadine ER*	68-137 mg qd (titrate to 274 mg)	Depression, dizziness, confusion
Modafinil*	100-200 mg bid	Headache, nausea, anxiety
Armodafinil	150-250 mg qd	Headache, insomnia, CNS effects
Methylphenidate ER*	5-20 mg (titrate to 60 mg max qd)	Headache, insomnia, loss of appetite
Dextroamphetamines*	5-20 mg (titrate to 60 mg max qd)	Anorexia, insomnia, emotional lability
Fluoxetine*	10-60 mg qd	CNS stimulation, sexual dysfunction
Bupropion XL SR*	100-450 mg qd	Dry mouth, dizziness, agitation, tremor
Aspirin*	325 mg once qd	GI bleed. cardiovascular disease risk
Dalfampridine ER*	10 mg every 12 hours	Headache, dizziness, GI, insomnia, seizure

bid = twice daily; CNS = central nervous system; ER = extended-release; GI = gastrointestinal; qd = daily; SR = sustained release; tid = 3 times daily; XL = extended length

Amato P. *Expert Opin Pharmacother*. 2012;13(2):207-16.

*Off-label

COGNITION IN MS

Cognitive Dysfunction in MS

- May affect 45%-70% of people with MS
- Unrelated to physical disability
- Occurs in all phenotypes; early in disease
- Predicts limitations in the workplace and social settings
- Underrecognized, underdiagnosed, and more likely to be unemployed
- Confounded by mood disorders and/or fatigue, motor and visual impairment
- Does not affect intelligence, remote memory, reading comprehension

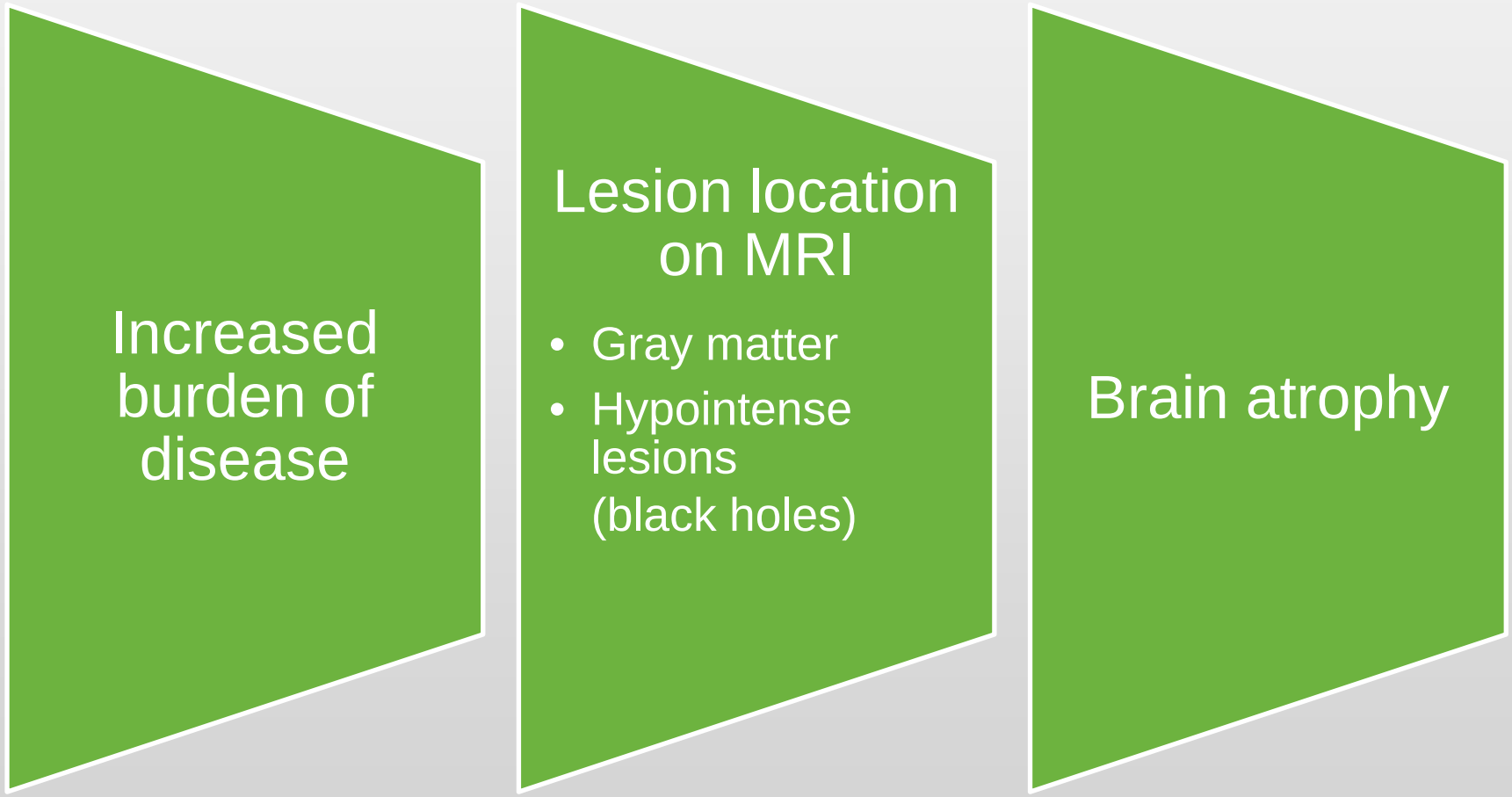
Kalb R et al. *Mult Scler*. 2018;24(13):1665-80.

Cognitive Domains

- Executive function
- Recent memory (short-term)
- Information processing speed
- Attention and concentration
- Visual-spatial organization
- Verbal fluency (word finding)
- Language

Kennedy P. *The Can Do Multiple Sclerosis Guide to Lifestyle Empowerment*. 1st ed. Demos Health; 2012.

Cognition and MRI Correlates



MRI = magnetic resonance imaging

https://uems-prm.eu/wp-content/uploads/2017/09/AIMS-cognitive-primer.pdf. Accessed August 15, 2022. Filippi M et al. *Neurology*. 2010;75(23):2121-8.

Signs of Cognitive Dysfunction

- Poor performance reviews at work
- Taking longer to accomplish a familiar task
- Difficulty starting and finishing a project
- Problems balancing a checkbook
- Problems following a recipe
- Automobile accidents
- Emotional changes
- Poor initiation of self-care activities
- Trouble remembering
- Difficulty following directions
- Inability to make decisions
- Inability to solve problems
- Difficulty finding the right words
- Losing a thought midsentence
- Difficulty in following a conversation
- Slowness in understanding what is heard or written

Kalb R et al. *Mult Scler*. 2018;24(13):1665-80. Kennedy P. *The Can Do Multiple Sclerosis Guide to Lifestyle Empowerment*. 1st ed. Demos Health; 2012. Benedict R. *Int J MS Care*. 2012;14(2):55-7.

Nursing Interventions

- Observe for signs during office visits
  - Part of the neurologic evaluation
- Question patient and family members
- Consider effects of medications
  - Anticholinergics, topiramate, clonazepam, tizanidine, tricyclic antidepressants
- Perform cognitive screening; screen for depression (annually)
- Refer for formal testing and cognitive rehabilitation (compensatory strategies)
  - Occupational therapist
  - Speech and language pathologist
  - Neuropsychologist

Benedict R. *Int J MS Care*. 2012;14(2):55-7.

Nursing Interventions (cont)

- Encourage disease-modifying therapy early
- Manage fatigue
- Treat depression and mood disorders
- Medications
  - Minimal benefit: amantadine, amphetamines,
  - Research indicates benefit: donepezil, rivastigmine
    - Reversible acetylcholine (ACh) inhibitors (neurotransmitter that facilitates learning and memory processes)

Drug	Dose	Adverse Effect
Donepezil	5-10 mg qd	Nausea, insomnia, fatigue, muscle cramps
Rivastigmine	1.5-6 mg bid	Nausea, anorexia, asthenia, GI, dizziness

He D et al. *Cochrane Database Syst Rev*. 2011;(10):CD008876. Krupp LR et al. *Neurology.* 2004;63(9):1579-85.

Cognitive Screening

- Annual reassessment with same instruments
- Montreal Cognitive Assessment (MOCA; 5-6 minutes)
  - Open domain
- Symbol Digit Modalities Test (SDMT; 5 minutes)
- MS Neuropsychological Screening Questionnaire (MSNSQ; 5 minutes)
- Paced Auditory Serial Additions Test (10-15 min)
  - Part of the MS Functional Composite (MS Society website)
- Supplemental screening: Fatigue Impact Scale, Beck Depression Index

Morrow SA et al. *Mult Scler*. 2010;16(11):1385-92. Kalb R et al. *Mult Scler*. 2018;24(13):1665-80.

MS AND DEPRESSION

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Clinical Characteristics

- Feeling sad or empty
- Irritable or crying most of the day
- Poor concentration
- Loss of energy/fatigue
- Loss of interest or pleasure in most activities
- Significant change in appetite and weight
- Unusual sleep behavior
- Decreased sex drive
- Suicidal thoughts

Siegert RJ et al. *J Neurol Neurosurg Psychiatry*. 2005;76(4):469-75.
http://www.nationalmssociety.org/Symptoms-Diagnosis/MS-Symptoms/Depression. Accessed August 15, 2022.

Screening for Depression

- Beck Depression Inventory
- Beck Depression Inventory: Fast Screen
- Beck Depression Inventory-II
- Depression Scale (CES-D)
- Chicago Multi-Scale Depression Inventory

Goldman Consensus Group. *Mult Scler*. 2005;11(3):328-37. Crawford P et al. *Int J MS Care*. 2009;11(4):167-73.

Comprehensive Management

- Provide a supportive therapeutic environment
- Identify risk factors (screening, self report, environmental factors, family history)
- Combination of psychotherapy and antidepressants works best
- Wellness focus (exercise, mindfulness)
- Be alert for suicidal ideation/plan
- Assess and reassess continually
- Adjust medications appropriately
- Refer to psychiatry

Bashir K et al. *Handbook of Multiple Sclerosis*. Lippincott, Williams & Wilkins; 2002. Patten SB. *Int J MS Care*. 2009;11(4):174-9.

Pharmacologic Treatment

SSRI	Dose	Adverse Effect
Fluoxetine	20-80 mg/d	Nausea, insomnia, diminished libido
Sertraline	25-200 mg/d	Nausea, fatigue, diminished libido
Paroxetine	20-50 mg/d	Nausea, insomnia, diminished libido
Citalopram	20-40 mg/d	Nausea, somnolence, diminished libido
Escitalopram	10-20 mg/d	Nausea, insomnia, diminished libido
SNRI	**Dose**	**Adverse Effect**
Venlafaxine	75-225 mg/d	Nausea, dizziness
Duloxetine	40-60 mg/d	Nausea, insomnia

Aminoketone	Dose	Adverse Effect
Bupropion XL/SR	100-300 mg/d	Dry mouth. Insomnia, nausea, dizziness

SNRI = serotonin/norepinephrine reuptake inhibitor; SSRI = selective serotonin reuptake inhibitor

Schapiro RT. *Neurorehabil Neural Repair*. 2002;16(3):223-31. http://www.nlm.nih.gov/medlineplus/druginformation.html. Accessed August 15, 2022.

Esketamine

- FDA approved March 2019 in 28-mg-per-spray formula (2 sprays per device)
- N-methyl-D-aspartate (NMDA) receptor agonist
- Blocks receptors for glutamate, a neuroexcitatory transmitter in the brain, and prevents reuptake of dopamine
- Form: nasal spray *only used under strict medical supervision* in a clinic
- Dosed twice per week for 4 weeks, then once per week for 4 weeks, then monthly
- 2-hour postdosing observation
- Highly habit forming (black box)
- Adverse effects: increased blood pressure, anxiety, dizziness, sedation, poor attention, dissociation, suicidal behaviors
- Indicated for individuals who failed at least 2 antidepressants

https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/211243lbl.pdf. Accessed August 15, 2022.

MS AND PAIN

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Pain and MS

- Pain prevalence reports vary from 29%-86% of patients with MS
- More than 50% of patients with MS find pain to be a problem; for 10%-20%, it is a significant problem
- Pain is estimated to comprise nearly 30% of all symptomatic treatment
- Underrecognized and often inadequately managed
  - Manageable in most patients

http://www.nationalmssociety.org/NationalMSSociety/media/MSNationalFiles/Brochures/Clinical-Bulletin-Maloni-Pain.pdf. Accessed August 15, 2022. Solaro C et al. *Neurology*. 2004;63(5):919-21. Beiske AG et al. *Eur J Neurol*. 2004;11(7):479-82. Schapiro RT. *Managing the Symptoms of MS*. 6th ed. Demos Medical Publishing; 2014. Solaro C et al. *Nat Rev*. 2011;7(9):519-27. Hoffman KJ. *Way Ahead*. 2005;9(1):8-9.

Pain Risk Factors

- Older age
- Comorbidities
- Longer disease duration
- Greater disease severity
- Men and women are equally likely to experience pain, but women tend to have greater severity of pain
- Progressive forms of MS

O'Connor AB et al. *Pain*. 2008;137(1):96-111.
http://www.nationalmssociety.org/NationalMSSociety/media/MSNationalFiles/Brochures/Clinical-Bulletin-Maloni-Pain.pdf. Accessed August 15, 2022.

Pain Subtypes Common in MS

Continuous central neuropathic	• Burning, tingling, aching, throbbing, band-like • Dysesthetic extremity pain, extremity cramps, impaired balance
Intermittent central neuropathic	• Spontaneous, paroxysmal, shooting, stabbing, shock-like • Trigeminal neuralgia, Lhermitte's sign, migraine headaches
Mixed neuropathic	• Tonic spasms, spasticity
Nonneuropathic	• Musculoskeletal pain, low back pain

O'Connor AB et al. *Pain*. 2008;137(1):96-111
http://www.nationalmssociety.org/NationalMSSociety/media/MSNationalFiles/Brochures/Clinical-Bulletin-Maloni-Pain.pdf. Accessed August 15, 2022. Solaro C et al. *Nat Rev Neurol*. 2011;7(9):519-27.

Common Causes of MS Pain

- Mechanism based
- Ongoing extremity pain
- Lhermitte’s sign
- Tonic spasms
- Spasticity
- Trigeminal neuralgia
- Optic neuritis
- Headache/migraine/ tension
- Musculoskeletal pain

Solaro C et al. *Nat Rev Neurol*. 2011;7(9):519-27.
http://www.nationalmssociety.org/NationalMSSociety/media/MSNationalFiles/Brochures/Clinical-Bulletin-Maloni-Pain.pdf. Accessed August 15, 2022.

Pain Management

- Biopsychosocial model
  - Integrates health practices into conventional medicine
  - Recognizes a mind-body relationship and uses a holistic approach to pain management
  - Pain self-management is the goal
  - Self-taught techniques of mindfulness, meditation, and behavior change empower pain coping
  - Behavior self-management: relaxation training, cognitive-talk therapy, adaptive coping, pacing activities, and behavior activation
    - Best learned through an integrated team approach
    - Social and physical activities decrease intensity of pain
    - Hypnosis can modulate pain experience
    - Guided imagery, breathing, and progressive muscle relaxation techniques

Solaro C et al. *Nat Rev Neurol*. 2011;7(9):519-27. http://www.nationalmssociety.org/NationalMSSociety/media/MSNationalFiles/Brochures/Clinical-Bulletin-Maloni-Pain.pdf. Accessed August 15, 2022.

Complementary and Integrative Health (Wellness)

- Acupuncture
- Acupressure
- Yoga
- Relaxation practices
- Meditation
- Massage therapy
- Chiropractic
- Tai chi, qigong, Reiki
- Stretching for spasticity
- Distraction
- Cooling
- Guided imagery
- Distraction techniques
- Rehabilitation: OT/PT
- Hypnosis

OT = occupational therapy; PT = physical therapy

http://www.nationalmssociety.org/NationalMSSociety/media/MSNationalFiles/Brochures/Clinical-Bulletin-Maloni-Pain.pdf. Accessed August 15, 2022.
https://www.nccih.nih.gov/. Accessed August 15, 2022.

Pharmacologic Management of Neuropathic Pain: Antidepressants

- Antidepressants as 1st-line therapies
  - Serotonin and norepinephrine reuptake inhibitors for continuous central neuropathic pain
    - Duloxetine 60-120 mg qd treats pain of allodynia
      - Adverse effects: nausea, somnolence, dry mouth, sweating, dizziness, decreased appetite, diarrhea
    - Venlafaxine 150-225 mg most effective in neuropathic pain
      - Adverse effects include hypertension at high doses, nausea, headache, insomnia, palpitations, hyperhidrosis
  - Tricyclics for burning, aching, central neuropathic pain; headaches (used at lower doses)
    - Nortriptyline and imipramine are better tolerated
    - Effective doses range from 25-150 mg; starting dose 10 mg
    - Adverse effects: somnolence, weight gain, anticholinergic effects

Solaro C et al. *Nat Rev Neurol*. 2011;7(9):519-27. http://www.nationalmssociety.org/NationalMSSociety/media/MSNationalFiles/Brochures/Clinical-Bulletin-Maloni-Pain.pdf. Accessed August 15, 2022.

Pharmacologic Management of Neuropathic Pain: Antiepileptics

Drug	Dose	Adverse Effect
Gabapentin (100-800 mg)	Titrate to 1200 mg tid; higher doses are well tolerated	Dizziness, peripheral edema, weight gain, headache, asthenia, somnolence, fatigue
Pregabalin (25-300 mg)	Titrate to 150-600 mg qd	Dizziness, peripheral edema, weight gain, headache, dry mouth, constipation
Enacarbil (300 mg, 600 mg) (gabapentinoid)	1200-3600 mg in 2 divided doses qd	Dizziness, peripheral edema, weight gain, headache, fatigue
Carbamazepine	200-1600 mg qd	Dizziness, drowsiness, nausea, unsteady gait

Bates D et al. *Pain Med*. 2019;20(suppl 1):S2-12.

Pharmacologics: 2nd- and 3rd-Line

Drug	Dosage	Adverse Effect
Capsaicin 8% patches (high-quality evidence); safety concerns for long-term use	1-4 patches to painful areas for 30-60 minutes	Site irritation, burning
Lidocaine patches 4%-6% (weak quality of evidence)	1-3 patches to region of pain qd for 12 hours	Excellent safety profile
Tramadol (25 mg, 50 mg, 100 mg) CIV; extended dose available; weak opioid; mu receptor agonist	200-400 mg in 2 or 3 divided doses (ER formula)	Habit-forming; drowsiness, headache, dizziness, nausea, constipation, dry mouth
Botulinum toxin A OnabotulinumtoxinA DaxibotulinumtoxinA (long acting)	50-200 U to painful area every 3 months Lasts up to 6 months	Pain, swelling, bruising, headaches, muscle weakness
Opioids	Individual titration	Risk for abuse with high doses; overdose mortality; misuse and morbidity

Bates D et al. *Pain Med*. 2019;20(suppl 1):S2-12.

Migraine

- Migraines are supported by MS lesions in the midbrain, C2 dorsal horn, and periaqueductal grey matter; most common headache in MS, higher than general population; CNS disruption may predispose migraines in MS
  - May be associated with exacerbation of MS symptoms
  - Prevalence >50%
  - Increased depression and additional sensory-related pain syndromes
  - Treatment: follow existing clinical guidelines for headache type from American Headache Society
    - Episodic vs prevention management: medications
    - Mindfulness and stress management

https://americanheadachesociety.org/resources/guidelines/guidelines-position-statements-evidence-assessments-and-consensus-opinions/. Accessed August 15, 2022.

Migraine Management

Multiple medications are available for treatment and prevention

- NSAIDs
- Analgesics with and without narcotics
- Triptans
- Ergot alkaloids
- Antiepileptic drugs
- Beta blockers
- CGRP activity blockers

CGRP = calcitonin gene-related peptide; NSAID = nonsteroidal anti-inflammatory drug

Yang CP et al. *JAMA Netw Open*. 2021;4(10):e2128544.

MS AND MOVEMENT DISORDERS

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Altered Mobility in MS

Occurs in up to 87% of persons with MS

Possible Causes

- Spasticity, spasms
- Weakness
- Imbalance
- Sensory loss
- Vision changes
- Restless leg syndrome
- Tremors

Risks

- Decreased safety: falls
- Impaired biomechanics
- Pain
- Immobility
- Social isolation
- Reduced quality of life

Bennett SE et al. *Int J MS Care*. 2014;16(suppl 1):S1-11. Halper J et al. *Int J MS Care*. 2010;12(1):13-6. Rae-Grant AD et al. *Multiple Sclerosis and Related Disorders: Clinical Guide to Diagnosis, Medical Management, and Rehabilitation*. Demos Medical Publishing; 2013:226-34.

Management of Altered Mobility

- Rehabilitation therapy (PT and OT)
- Assistive devices, orthotics, and adaptive equipment
- Cooling measures for heat sensitivity
- Exercise and stretching daily
- Medications: “The Walking Pill”
- Surgery (orthopedic surgery or neurosurgical interventions)
- Translingual neurostimulation for chronic balance deficit

Rae-Grant AD et al. *Multiple Sclerosis and Related Disorders: Clinical Guide to Diagnosis, Medical Management, and Rehabilitation*. Demos Medical Publishing; 2013:226-34. Bennett SE et al. *Int J MS Care*. 2014; 16(suppl 1):S1-11.

The Walking Pill

- Dalfampridine 10 mg PO bid (4-aminopyridine)
  - Potassium channel blocker (blocks loss of potassium on naked axons)
  - Improves walking speed
  - Contraindicated in patients with seizure history, severe renal impairment, or concomitant use with 4-aminopyridine
  - Adverse effects: anaphylaxis, urticaria, angioedema of throat or tongue, UTIs, insomnia, dizziness, nausea, paresthesia, constipation

PO = by mouth; UTI = urinary tract infection

https://www.accessdata.fda.gov/drugsatfda_docs/label/2013/022250s006lbl.pdf. Accessed August 15, 2022.

Spasticity in MS

- Hypertonicity of muscles; “tightness, pulling, tugging, aching”
- Results from demyelination in descending CNS pathways
- Different muscle groups involved depending on lesion location
- Spasticity may increase over time without new CNS lesions
- Results in:
  - Increased resistance to stretch
  - Accentuation of deep tendon reflexes and clonus
  - Uncontrolled flexor responses and extensor spasms
  - Limited mobility
  - Excessive energy expenditure
  - Pain and discomfort

Bennett S et al. *Int J MS Care*. 2014;16(suppl 1):S12-8. Crayton H et al. *Neurology*. 2004; 63(11 suppl 5):S12-8. Halper J. *Advanced Concepts in Multiple Sclerosis Nursing Care*. 2nd ed. Springer Publishing Company; 2007.

Factors That May Increase Spasticity

- UTIs
- Menses
- Bowel impaction/flatus
- Deep vein thrombosis
- Infection
- Disease progression
- Stress/anxiety
- Depression
- Restrictive clothing
- Fatigue
- Heat exposure

Bennett S et al. *Int J MS Care*. 2014;16(suppl 1):S12-8.;Crayton H et al. *Neurology*. 2004;63(11 suppl 5):S12-8.; Halper J. *Advanced Concepts in Multiple Sclerosis Nursing Care*. 2nd ed. Springer Publishing Company; 2007.

Spasticity Management

- Goals
  - Improve functional ability and independence
  - Decrease pain
  - Improve ambulation
- Multidisciplinary
  - Stepladder approach
    - Intrathecal baclofen
    - Oral medications
    - Orthopedic treatments
    - Rehabilitation therapy
    - Remove noxious stimuli

Bennett S et al. *Int J MS Care*. 2014;16(suppl 1):S12-8. Crayton H et al. *Neurology*. 2004;63(11 suppl 5):S12-8. Halper J. *Advanced Concepts in Multiple Sclerosis Nursing Care*. 2nd ed. Springer Publishing Company; 2007.

Rehabilitation Therapy

Stretching	Weight bearing	Positioning	Range of motion
Seating	Orthotics	Serial casting	Aquatics

Bennett S et al. *Int J MS Care*. 2014;16(suppl 1):S12-8.

Pharmacologics for Spasticity

Medication	Dose	Adverse Effect
Baclofen (titrate dose to effect)	5-60 mg qd	Dizziness, weakness, confusion, headache
Tizanidine	2-4 mg (tablets) 6 mg qd	Dizziness, weakness, depression, GI
Diazepam	2-10 mg (max 40 mg)	Drowsiness, muscle weakness, CNS
Clonazepam	0.5-2 mg (max 4 mg)	Somnolence, depression, confusion
OnabotulinumtoxinA	100 U-200 U (max 400 U per 3 months)	Infection, weakness; for bladder: UTIs, dysuria, retention
Intrathecal baclofen	Depends on response to trial	Lower-extremity weakness
Cannabinoids dronabinol, nabiximols	No FDA guidelines	

http://www.nationalmssociety.org/NationalMSSociety/media/MSNationalFiles/Brochures/Clinical-Bulletin-Maloni-Pain.pdf. Accessed August 15, 2022. https://www.youtube.com/watch?v=Vbt0wdlPkmU. Accessed August 15, 2022.

Pharmacokinetics of Baclofen

Oral baclofen

- 60 mg (60,000 mcg) dose: 0.024 mcg/mL IT lumbar concentration
- Half-life 3-4 hours

Intrathecal baclofen

- 600 mcg/d dose: 1.24 mcg/mL IT lumbar concentration
- Lumbar to cervical concentration is 4:1
- Half-life 4-5 hours
- Benefits
  - Reversible
  - Fewer systemic side effects
  - Programmable for optimal benefit
  - Effective in upper and lower extremities

IT - intrathecal

https://www.youtube.com/watch?v=Vbt0wdlPkmU. Accessed August 15, 2022.

Intrathecal Baclofen Therapy (ITB™)

- Catheter delivers drug to intrathecal (subarachnoid) space in the spinal cord
- Pump infuses baclofen at programmed rate
- Programmer allows for precise easily adjustable dosing
- Thought to act at gamma-aminobutyric acid (GABA) receptor sites
- Lower doses are effective than are required orally
- Potential for fewer systemic side effects

Crayton H et al. *Neurology*. 2004;63(11 suppl 5):S12-8. https://www.youtube.com/watch?v=Vbt0wdlPkmU. Accessed August 15, 2022.

Nabiximols

- Derived from the *Cannabis sativa* plant
- In phase 3 development for MS spasticity
  - Currently approved for use in over 25 ex-US countries (UK 2010)
- Efficacy has been shown in multiple clinical trials
  - In 1 recent study:
    - After 4 weeks of treatment, responders to nabiximols had a mean 44% decrease on spasticity numeric rating scale vs 3% for nonresponders
    - Those treated with nabiximols also had a 44% mean decrease in muscle spasm frequency compared with 24% on placebo (*P*=0.006)

Aust Prescr. 2018;41(6):203-4. https://practicalneurology.com/news/cannabis-derived-nabiximols-well-tolerated-and-effective-for-spasticity-in-multiple-sclerosis. Accessed August 15, 2022.

TREMORS

Cerebellar Dysfunction

- Cerebellum coordinates movements
- Dysfunction caused by MS lesions in cerebellar pathways

Dysmetria	Tremor	Nystagmus
Ataxic gait	Tremorous speech	Titubation

Wilkins A. *Front Neurol*. 2017;8:312.

Treatment of Cerebellar Dysfunction

- Rehabilitation PT/OT
  - Proximal stability
  - Self-care strategies
  - Weight-bearing activities
  - Weighting (utensils, assistive devices)
  - Coordination exercises
  - Assistive devices
- Deep brain stimulation (DBS)
- Surgically implanted magnetic resonance (MR)−guided focused ultrasound treatment
  - Does not treat underlying diagnosis or prevent progression of symptoms
  - Indicated for essential tremors
  - Adverse effects: imbalance, headache, numbness/tingling

Wilkins A. *Front Neurol*. 2017;8:312.

Treatment of Cerebellar Dysfunction Medications

Drug	Dose	Adverse Effect
Primidone*	100-250 mg tid	Drowsiness, dizziness, nausea, emotional disorders, impotence
Clonazepam*	0.25-1 mg tid (2-mg tablets available)	Somnolence, nausea, dry mouth, headache, decreased libido, erectile dysfunction, constipation
Topiramate*	25-200 mg	Paresthesia, weight loss, dizziness, cognitive decline, somnolence, fatigue
Propranolol*	40-120 mg bid	Hypotension, bronchospasm, bradycardia, fatigue, dizziness, GI
Gabapentin*	100-1200 mg bid	Dizziness, peripheral edema, weight gain, headache, asthenia, somnolence, fatigue
Amantadine ER* (dyskinesia in Parkinson's disease)	137-274 mg hs	Drowsiness, depression, dry mouth, constipation, edema, hallucinations, orthostatic hypotension, unusual behaviors
Acetyl-DL-leucine* (France)	5 g qd orally	None reported

HS = at bedtime

https://www.youtube.com/watch?v=Vbt0wdlPkmU. Accessed August 16, 2022.

*Off label

ELIMINATION AND SEXUAL DYSFUNCTION

Assessment for Bladder/Bowel Incontinence

- Mental/cognitive status
- Functional status
  - Walking ability, spasticity, hand coordination, ADLs, ability to self-catheterize
- Access to bathroom
- Fluid and fiber intake
- Diet (bladder irritants)
- Frequency of urination and bowel movements
- Concurrent illnesses: UTIs

ADLs = activities of daily living

https://www.ics.org/Publications/ICI_4/files-book/comite-5A-B.pdf. Accessed August 16, 2022.

Types of Bladder Dysfunction in MS

Inability to Store	Inability to Empty	Combination/DSD
Symptoms	Symptoms	Symptoms
Urgency/frequency	Urgency, hesitancy	Urgency, hesitancy
Incontinence	Double voiding	Double voiding
PVR <100 cc	Frequency	Incomplete emptying
	Incomplete emptying	Dribbling incontinence
	Nocturia	
	UTIs	Diagnosed by urodynamic studies
	PVR >100 cc	

DSD = detrusor sphincter dyssynergia; PVR = postvoid residual

DasGupta R et al. *Drugs.* 2003;63(2):153-66. Fowler CJ et al. *Postgrad Med J.* 2009;85(1008):552-9. Schapiro RT. *Int J MS Care*. 2011;13 (suppl 4):S12-9. O'Leary ML et al. *J Neurosci Nurs*. 2010;42(2):E8-23. Betts CD et al. *J Neurol Neurosurg Psychiatry*. 1993;56(3):245-50. Bennett SE et al. *Int J MS Care*. 2014;16(suppl 1):S19-24.

Assessment of Bladder Function

Thorough history: patient's main concern

- Voiding patterns (voiding diary)
- Fluid intake

Measurement of PVR

- Determines amount retained in the bladder after voluntary emptying
- Evaluated by catheterization OR bladder ultrasound

Other causes of bladder dysfunction

- UTIs
- Pelvic-floor relaxation in women and men
- Benign prostatic hyperplasia (BPH) in men

Consortium of Multiple Sclerosis Centers. *Int J MS Care*. 2012;14(suppl 1):8-14.

Treatments: Inability to Store

- Limit fluid intake
- Timed voids (every 2-3 hours)
- Access to bathroom
- Pads or protective undergarments
- Decrease use of bladder irritants (caffeine, aspartame, alcohol)
- Botulinum toxin injections
- Pelvic-floor exercises per PT
- Anticholinergic: oxybutynin oral, oxybutynin transdermal, imipramine
- Antimuscarinic: tolterodine, solifenacin succinate, trospium chloride, darifenacin, fesoterodine fumarate
- Beta-3 adrenergic agonist: mirabegron, vibegron
- Intermittent self-catheterization (INS)
- Percutaneous tibial nerve stimulation (PTNS)
- Sacral neuromodulation system

Consortium of Multiple Sclerosis Centers. *Int J MS Care*. 2012;14(suppl 1):S8-14.

Treatments: Inability to Empty

- Adequate fluid intake
- Structured, timed voidings
- Intermittent catheterization or indwelling catheter
- Botulinum toxin A
- Antispasticity agents/nerve blocks
- Alpha blocking agents to promote the flow of urine
  - Tamsulosin
  - Doxazosin
  - Alfuzosin
  - Silodosin
- Sacral neuromodulation system

Consortium of Multiple Sclerosis Centers. *Int J MS Care*. 2012;14(suppl 1):S8-14.

What Patients Need to Know

- Adequate fluid intake is one and a half to 2 quarts/d (48-64 oz); water is best, decaf ok, juices
- Urge to void occurs about one and a half to 2 hours after drinking something
- Caffeine, aspartame, and alcohol are bladder irritants
- Smoking is a bladder irritant
- Drink fluids all at once. If you “sip, sip, sip,” you will feel the urge to go often
- Try to void about one and a half to 2 hours after you drink
- Stop drinking fluids about 2 hours before bedtime
- Void right before bedtime
- It is not normal to leak urine, wake up more than once at night to void, or have frequent UTIs
- Symptoms of UTIs and their effect on MS

Consortium of Multiple Sclerosis Centers. *Int J MS Care*. 2012;14(suppl 1):S8-14.

Bowel Dysfunction in MS

- 60% of persons with MS may experience problems with bowel function
- Common symptoms include constipation, chronic diarrhea, incontinence
- Symptoms may be intermittent or constant
- Symptoms can occur at any time in the disease process

DasGupta R et al. *Drugs*. 2003;63(2):153-66. Bennett SE et al. *Int J MS Care*. 2014;16(suppl 1):S19-24.

Bowel Dysfunction (cont)

Constipation

- Slow bowel
- Medication side effects
- Impaired motility
- Dietary/water restrictions

Bowel Incontinence

- Diminished sphincter control
- Hyperreflexic bowel

Consortium of Multiple Sclerosis Centers. *Int J MS Care*. 2012;14(suppl 1):S15-20.

Bowel Management in MS

Constipation

- Fluids: one and a half quarts/d
- Daily fiber: 20-30 g/d
- Bulk-forming agents
- Stool softeners/stimulants
- Laxatives
- Suppositories/mini-enemas

Diarrhea

- Monitor electrolytes, weight, diet
- Monitor skin and skin care
  - •Bulk-forming agents/fiber
  - •Anticholinergics and/or opiates

Bowel Incontinence

- Diet
- Bowel training
- Medications/ suppositories
- Sacral neuromodulation system

CONSULT GASTROENTEROLOGY

Namey M. *Comprehensive Nursing Care in Multiple Sclerosis*. 2nd ed. Demos Medical Publishing; 2002.

Sexual Dysfunction in MS

- Approximately 80% of women with MS
- Approximately 75% of men with MS
- A significant impact on quality of life
- Can occur at any phase of the sexual response cycle
- 4 categories:

Desire disorders	Arousal disorders	Orgasmic disorders	Pain disorders

Demirkiran M et al. *Mult Scler*. 2006;12(2):209-14. Crayton H et al. *Neurology*. 2004;63(11 suppl 5):S12-8.

Primary Sexual Dysfunction in MS

Men and women can experience difficulties

- ↓ Libido
- ↓ Altered genital sensation
- ↓ Frequency/intensity of orgasms
- ↓ Vaginal lubrication/clitoral engorgement
- ↑ Erectile dysfunction/ejaculation
- ↑ Bladder spasticity
- ↑ Depression/anxiety/fear

Halper J et al. *Nursing Practice in Multiple Sclerosis: A Core Curriculum*. 3rd ed. Springer Publishing Company; 2012. Crayton H et al. *Neurology*. 2004;63(11 suppl 5):S12-8.

Sexual Dysfunction Management

- Exclude metabolic causes (eg, diabetes, heart, and vascular)
- Management strategies include:
  - Pharmacologic management
  - Treat underlying symptoms/secondary dysfunction
    - Spasticity, fatigue, paresthesias, bladder/bowel
  - Positioning
  - Lifestyle changes
  - Mechanical aids: vacuum or inflatable devices, penile implants
- Key to successful management is open communication
- Psychotherapy and culturally sensitive support

Halper J et al. *Nursing Practice in Multiple Sclerosis: A Core Curriculum*. 3rd ed. Springer Publishing Company; 2012. Crayton H et al. *Neurology*. 2004;63(11 suppl 5):S12-8. National MS Society. *Patient Education, Sex Life and MS*.

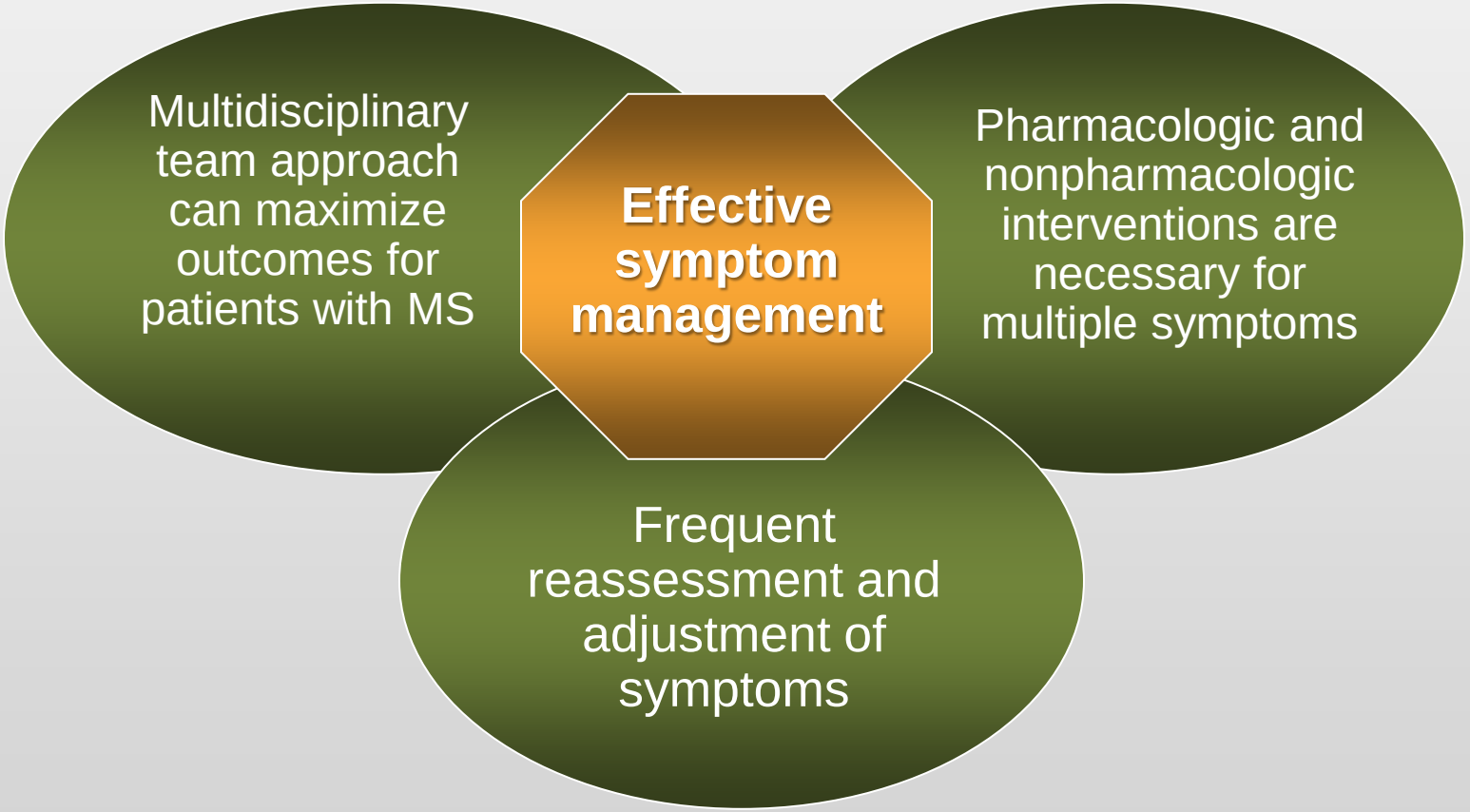
Pharmacologic Management of Sexual Dysfunction

Drug	Dose	Indication
Bupropion	150-300 mg/d	Decreased libido Decreased orgasm
Sildenafil	50-100 mg/d	Erectile dysfunction
Vardenafil	5-20 mg/d	Erectile dysfunction
Tadalafil	5-20 mg/72 hours	Erectile dysfunction
Avanafil	100 mg qd	Erectile dysfunction
Estrogens	Vaginal preparations Topical creams	Vaginal dryness Clitoral sensitivity
Ospemifene	Daily tablet	Painful intercourse/dryness
Flibanserin	Daily pill	Decreased libido
Bremelanotide	Injection before sex activity	Decreased libido

Note:
Flibanserin and bremelanotide are only used in *premenopausal* women

https://www.nationalmssociety.org/NationalMSSociety/media/MSNationalFiles/Brochures/Clinical_Bulletin_Sexual-Dysfunction-in-MS.pdf. Accessed August 16, 2022.

Conclusions



Careful management can improve quality of life, promote *EMPOWERMENT,* and inspire HOPE

THE 13TH ANNUAL LINDA MORGANTE

Multiple Sclerosis Nurse Leadership Program

2022

MS SYMPTOM MANAGEMENT: A CASE STUDY

Beverly Layton, RN, BSN, CCRC, MSCN

Michelle Keating, RN, MSCN

Provided by Academy for Continued Healthcare Learning and Annenberg Center for Health Sciences at Eisenhower

ACHL ACADEMY for CONTINUED HEALTHCARE LEARNING

ANNENBERG CENTER FOR HEALTH SCIENCES AT EISENHOWER

The program is supported through educational grants from Biogen, Bristol-Myers Squibb, Inc., and Novartis Pharmaceuticals Corporation.

Patient Case: Michelle

- Relapsing-remitting multiple sclerosis (RRMS) diagnosed in 1981

Symptoms Along the Journey	Current Symptoms
• Numbness and tingling • Fatigue • Mobility • Hand and arm weakness • Depression • Scotoma	• Bladder and bowel dysfunction • Mobility dysfunction • Spasticity

DMT History

1993-1999	• Interferon β-1b
1999-2002	• Interferon β-1a x 2x week, 3x week
2000-2004	• Mitoxantrone
2002-2013	• Interferon β-1a
2013	• Natalizumab consideration
May 2013-Sept 2018	• Dimethyl fumarate
Since 2018	• Disease-modifying therapy (DMT) discussions

https://www.nationalmssociety.org/Treating-MS/Medications. Accessed August 11, 2022.

Current Treatments

Oral Medications

- Levothyroxine
- Dalfampridine
- Levetiracetam
- Metoprolol succinate
- Baclofen
- Polyethylene glycol

Bladder Injection

- Botulinum toxin 300 IU q5mo (bladder injection)

Orthoses

- Forearm crutches, plastic-hinged left ankle-foot orthosis (AFO)
- Carbon-fiber right AFO

Exercise Regimen

- Walking
- Cycling
- Stretching
- Strength training

IU = international units; q5mo = every 5 months

The Office Visit

- What brings you to the office today?
- Assessment begins as she comes into the exam room
- “Top 3” discussion
- Review includes social/family/work updates
- COVID-19: Review of exposures, infections, and vaccines

Symptom Management

- Most common provider intervention
- Chronic vs new
- Review of current/past symptom treatments
- Quality of life (QoL) impact

Functional Review

- Mobility
- Activities of daily living
- Speech
- Swallowing
- Vision
- Fatigue
- Cognition
- Mood
- Bladder
- Bowel
- Sexual function

Gait Deviations in MS

- MS is highly heterogeneous
- No “typical” MS gait
- Performance is likely to fluctuate from day to day or even within a day
  - Your exam is just a snapshot of 1 point in time

Factors Contributing to Walking Dysfunction

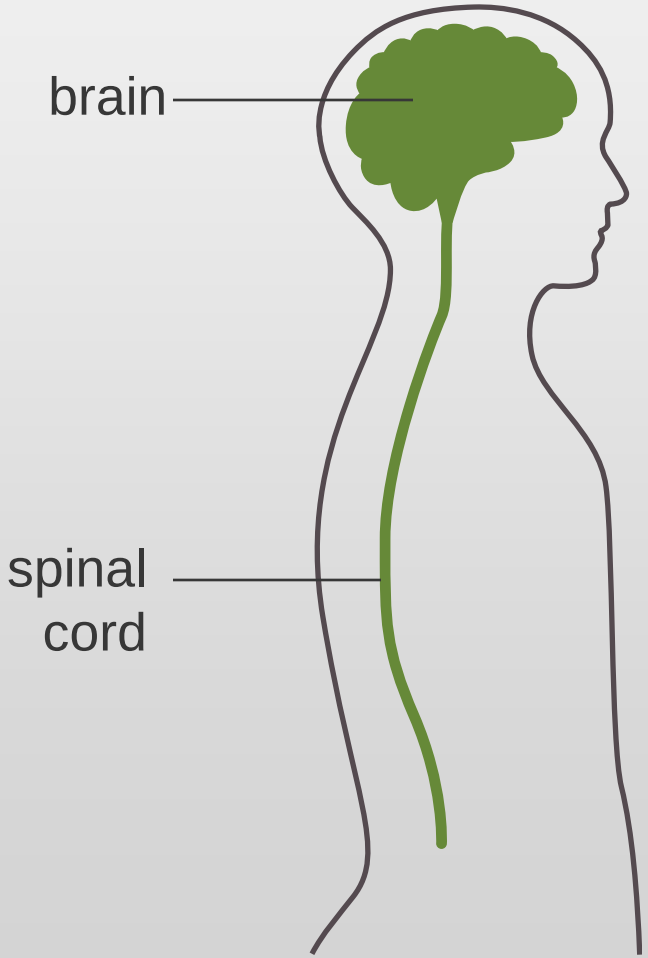
- Weakness
- Fatigue
- Altered balance
- Sensory dysfunction
- Spasticity
- Fear of falling
- Pain
- Vestibular dysfunction
- Limited range of motion
- Heat sensitivity
- Vision impairment
- Ataxia/impaired coordination
- Upper-extremity and trunk impairments
- Cognitive dysfunction
- Environmental barriers
- Comorbidities

MS and Bladder Function

- Bladder problems are common, sometimes sporadic, and interfere with lifestyle
  - Many describe as one of the most distressing symptoms
- Bladder issues can usually be managed
- Bladder symptoms, while aggravating, limiting, and isolating, can lead to more serious urinary tract problems if left unmanaged

https://www.nationalmssociety.org/Symptoms-Diagnosis/MS-Symptoms/Bladder-Dysfunction. Accessed August 11, 2021.

What Creates Bladder Problems?



- Lesions in brain and spinal cord
- Cord lesions cause most problems
- Brain lesions cause difficulty with voluntary control
- There is a correlation between disability level and bladder problems

https://www.nationalmssociety.org/Symptoms-Diagnosis/MS-Symptoms/Bladder-Dysfunction. Accessed August 11, 2021.

Botulinum Toxin (Type A): What Does It Do?

- Injections into bladder muscle will cause small areas to be inactive, which will decrease significant overactivity
- Injections will need to be repeated after several months
- Many patients will need to do intermittent catheterization to empty the bladder, but find great relief from the treatment

https://www.drugs.com/pro/botox.html. Accessed August 11, 2022.

Bowel Dysfunction

- Constipation: hard stool that is difficult to pass
  - Stool frequency: daily to every 3 days best
  - Causes
    - Medications, impaired motility, inactivity, poor diet, and inattention to signals
- Diarrhea
  - Infection, fecal impaction, medications, food intolerance, and malabsorption
- Involuntary bowel
  - Diminished sphincter control and overactive bowel (another patient-reported distressing symptom)

Improving Bowel Function

Move your body more

Eat regularly and include more high-fiber foods

Increase fluids

Establish a bowel program

Bowel Program

- Establish a schedule
  - Daily? Every 2 days? Every 3 days?
- Choose a time of day that works for you
  - Morning is best for most people
- Sit on the toilet on schedule, even without a sense of needing to
- Do not sit on toilet longer than 15 minutes
- Squatty Potty is an option for some

Tips to Improve Bowel Program

- If stool is hard, add a bulk agent and increase water and fiber
  - OTC products: Metamucil/Benefiber, other psyllium products
- To get stool moving, add stimulation to the rectum
  - Digital stimulation with a gloved finger, glycerin suppositories
- Utilize foods
  - Prunes, oatmeal, fruit, and whole grains
- Allow a few weeks for the program to work well
- If not successful, discuss with your provider

OTC = over-the-counter

Conclusion

- MS symptoms can affect QoL
- Symptoms may stabilize, fluctuate, or progress
- How do you recognize and discuss symptoms with your patients and their care team?
- Management should be individualized with ongoing assessments of interventions
- Careful management can improve QoL and promote realistic HOPE!

Discussion

- What are the primary symptom concerns with your patients with MS?
- Are there any other strategies that you employ for MS symptom management that were not mentioned in this talk?
- Do you discuss COVID-19/vaccines with your patients?

Discussion (cont)

- How do you hope to change the care of your patients with MS after attending this curriculum?

- What is one key takeaway that you learned from this curriculum?

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Multiple Sclerosis Nurse Leadership Program

2022

THE EVOLVING ROLE OF THE MS NURSE: MULTIPLE SCLEROSIS IN THE 21ST CENTURY

June Halper, MSN, APN-C, MSCN, FAAN

Provided by Academy for Continued Healthcare Learning and Annenberg Center for Health Sciences at Eisenhower

ACHL ACADEMY for CONTINUED HEALTHCARE LEARNING

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Florence Nightingale as Our Example

- “Lady of the Lamp”
- Best known for:
  - Work during the Crimean War
  - Passion for patient rights
  - Research in hospitals
  - Philosophy of nursing

Florence Nightingale's Contributions to Nursing

- Provided direct care to patients and families
- Advocated on behalf of her patients
  - Improved sanitation
- Improved the nursing profession
  - Introduced nurses into military hospitals
  - Established the Nightingale School for Nurses in London
- Conducted extensive research and developed statistical reporting methods
- Published over 200 books including, "Notes on Hospitals" and "Notes on Nursing"

https://www.history.com/topics/womens-history/florence-nightingale-1. Accessed August 8, 2022.

2020 INTERNATIONAL YEAR OF THE NURSE AND THE MIDWIFE

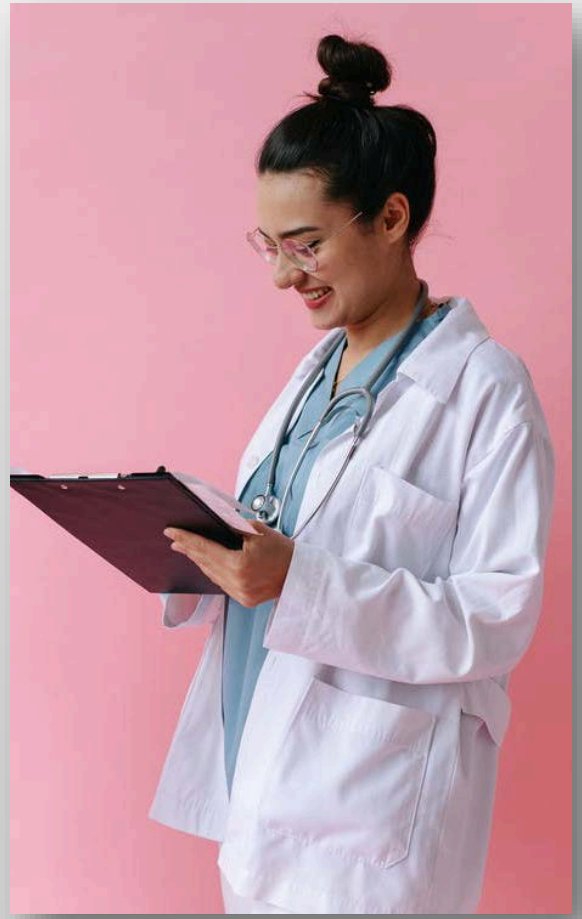
2020 was the 1st time in history the nations of the world united in celebration of the **benefits that nurses and midwifery bring** to the health of the global populations.

- Coincided with the **200th anniversary** of the birth of **Florence Nightingale**, one of the founders of modern nursing
- Nurses and midwives make **up more than half of the healthcare workforce** worldwide
- During this global pandemic, **celebrating and honoring** our nurses is even more important
- Time to focus on nursing in the modern context of healthcare
- **2022 and onward: the importance of nursing remains!**

THE 13TH ANNUAL LINDA MORGANTE MS Nurse Leadership Program

https://www.who.int/campaigns/annual-theme/year-of-the-nurse-and-the-midwife-2020. Accessed August 8, 2022.

The Evolving Role of the MS Nursing Professional



MS = multiple sclerosis

What Is an MS Nurse?

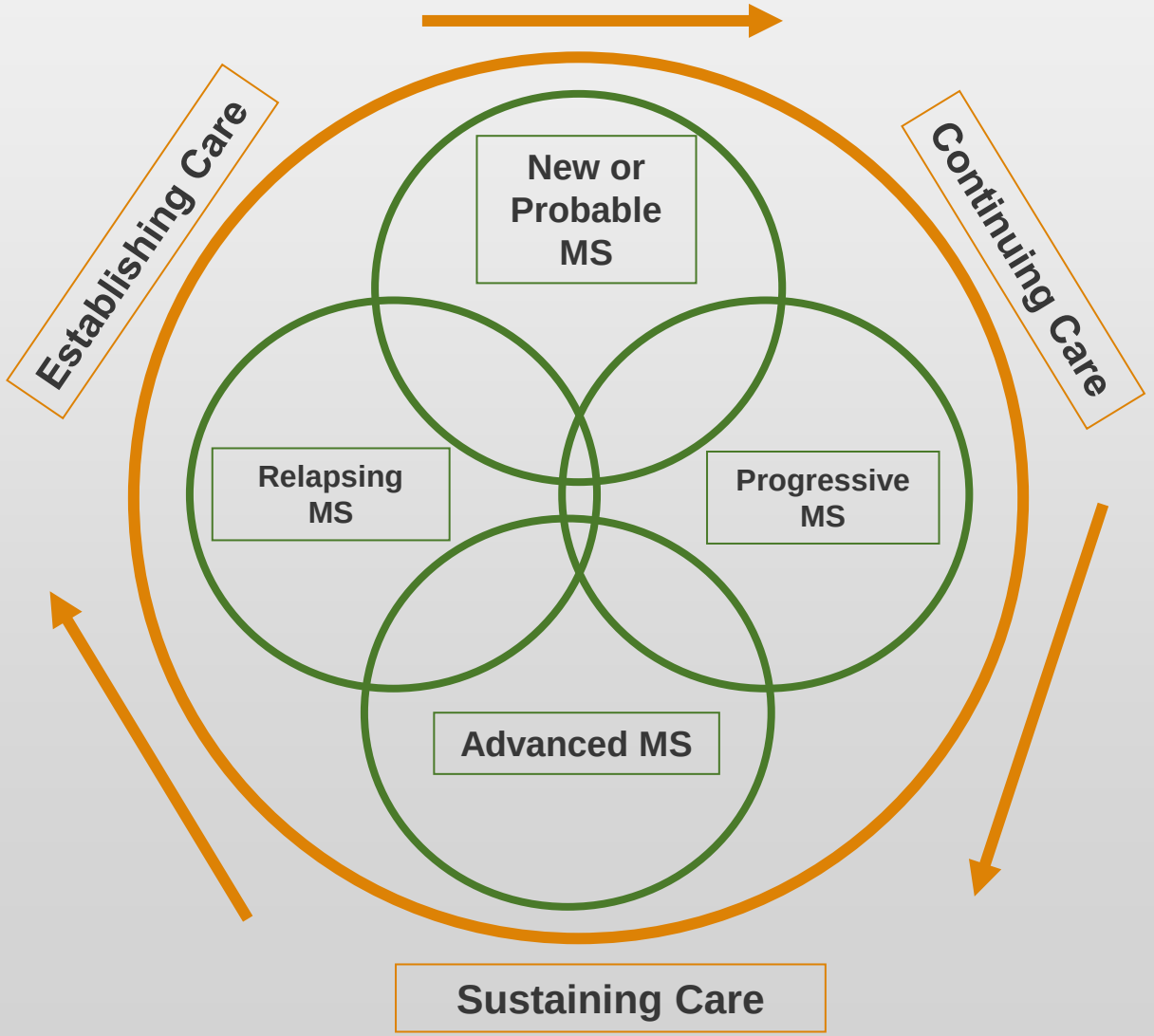
- An MS nurse is a competent expert who collaborates with those affected by MS and shares knowledge, strength, and hope
- MS nurses can enhance adaptive and coping skills, facilitate empowerment and a sense of control, and thereby engender hope and positive attitudes among those affected by MS

Philosophy of MS Nursing

- The philosophy of MS nursing is for the MS nurse is to:
  - Shape the course of the disease by facilitating treatment that interrupts acute episodes
  - Delay progression of pathology
  - Facilitate the management of MS symptoms

MS nurses enhance and promote safe, maximal, and (where possible) independent function.

Model of Nursing Care in MS



Establishing Care

- Relationship building
- Open communication
- Building trust
- Sharing information
- Assessment

Continuing Care

- Encouraging self-care strategies
- Assisting with vocational issues
- Preserving independence/interdependence
- Educating patients/families/community-at-large
  - Shared decision-making
  - Symptomatic care
  - Side-effect management

Sustaining Care

- Maintaining patient well-being
- Coordinating referrals
- Identifying community resources
- Ensuring comprehensive MS care
- Sustaining ongoing trusting relationships
- Inspiring HOPE

Key MS Nursing Domains

- The nurse-patient partnership
- Comprehensive care throughout the health-illness continuum
- Professional persona
- Scholarly inquiry

Key MS Nursing Activities

- **Identifying** patient care needs along a continuum of health as part of holistic care
- **Recognizing** (not necessarily treating) the patient's symptoms and non-MS–related conditions
- **Referring** to appropriate providers
- **Assessing** outcomes during subsequent visits
- **Educating** patients and healthcare providers about health and wellness within the context of MS

The Nurse as an Advocate

- To advocate is to speak or act on behalf of another
- Education is an important part of advocacy
- It is important to inform patients and families
- Patients need to know why they are taking special medications or undertaking special treatments, as well as how to take medication
  - They need to know who to call when they need help

Creating an Expert Patient With MS

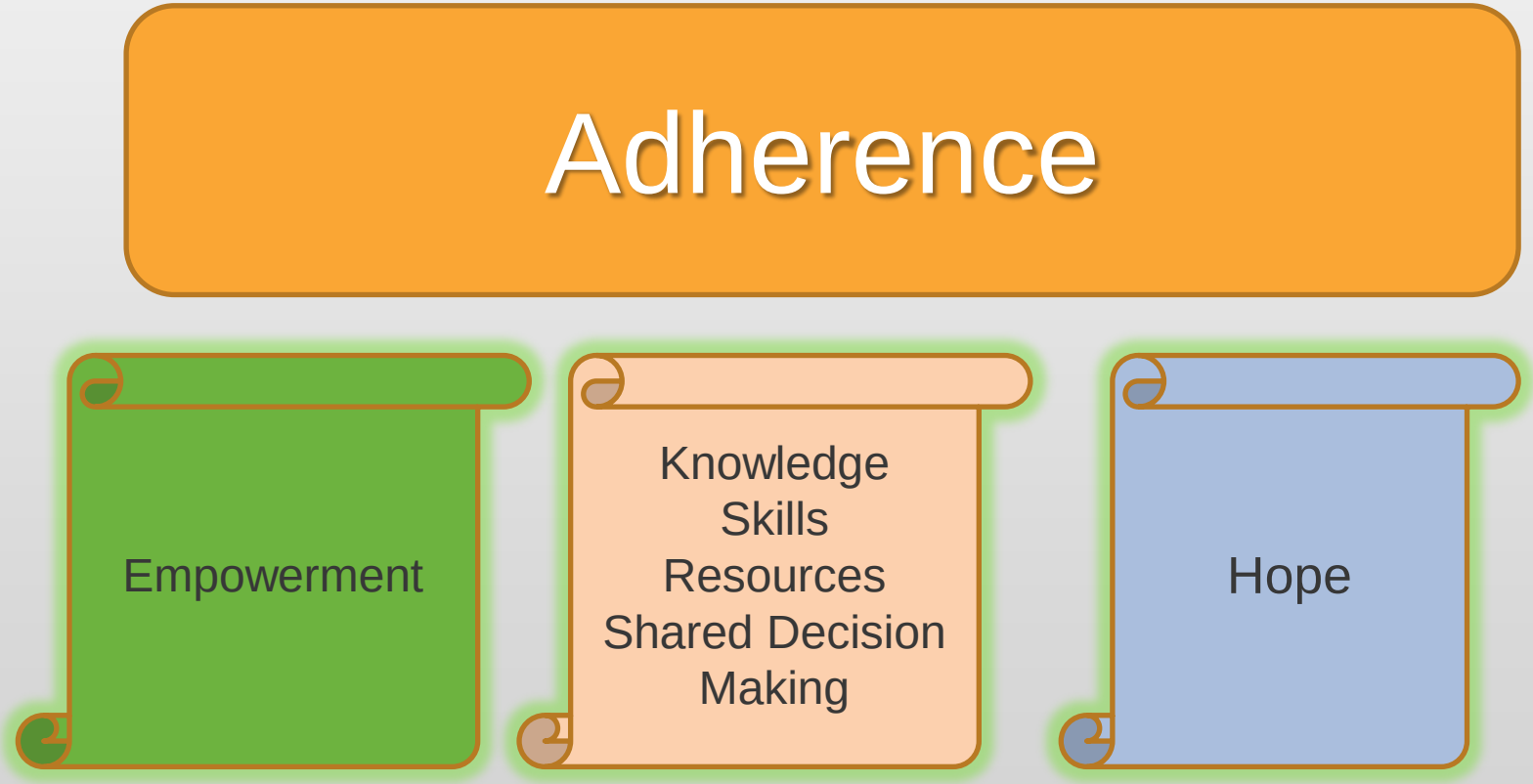
ADHERENCE

Adherence Defined

- An active, voluntary, and collaborative participation of the patient in a mutually agreeable course of behavior or treatment that results in a desired preventative or therapeutic outcome
- Adherence means staying on treatment (eg, medications, rehabilitation, symptomatic care, or wellness)

Harris C, et al. *Moving Forward: Adherence to Therapy and the Role of Nursing in Multiple Sclerosis*. Hackensack, NJ: International Organization of Multiple Sclerosis Nurses; 2013.

Pillars of Adherence



Hope

- Hope is a significant factor in coping, especially spiritual hope
- Allport (1951) theorized that a person needs unifying religious belief or a philosophy to effectively cope
- Those with spiritual hope have been found to be better able to set goals and have stronger relationships and supports
- Linda Morgante, one of the IOMSN founders, used the mantra of HOPE with her patients and families

IOMSN = International Organization of Multiple Sclerosis Nurses

Image courtesy of June Halper, MSN, APN-C, MSCN, FAAN. https://www.simplypsychology.org/contact-hypothesis.html. Accessed August 8, 2022.

Hope + Empowerment = Adherence

- Empowerment and hope are related concepts that can lead to adherence to therapy
- Empowerment gives people the recognition of strengths and resources
- Empowerment involves knowledge, skills development, coping, mastery over the environment, and flexibility
- These are the tools we give to our patients and families

What Is our Professional Role in MS Care?

- Become an expert in understanding and treating MS
- Educate patients, families, and the community
- Understand which services and programs are available to patients
- Network with MS nurses and other professionals
- Take care of yourself, learn, listen, grow personally, and professionally
- Seek MSCN certification

MSCN = MS-certified nurse

The Evolving Role of the MS Nurse

- Our knowledge of the disease has expanded to include:
  - Basic immunopathology, MRI techniques, diagnostic criteria
  - Mechanism of action of DMTs, as well as symptomatic treatments and rehabilitation strategies
- We must attend to our own education about MS, as we are constantly called upon to provide education and counseling

DMT = disease-modifying therapies; MRI = magnetic resonance imaging

The Evolving Role of the MS Nurse (cont)

- As new treatments emerge, the role of the nurse as a clinician, educator, advocate, and counselor will continue to grow more complex
- The risks of treatments are likely to be higher, as will the expectations of greater efficacy
- Through these changes, we will sustain our goal of improving the lives of those affected by MS
- MS NURSES CAN DO IT!

International Organization of Multiple Sclerosis Nurses (IOMSN)

www.IOMSN.org

Only **nursing organization representing MS nursing** professionals who practice in North America and globally, with **over 1500 members worldwide** across 19 countries

IOMSN addresses the following domains of MS nursing:

IOMSN
International Organization of Multiple Sclerosis Nurses

Clinical Care

- Mentorship opportunities
- Case-based learning and annual congress
- Publications: www.iomsn.org

Education

- Regional programs
- Annual programs
- DVDs
- Webinars

Research for nurses and clinical practice

- Outcomes research
- Protocol development
- Benefits of certification
- Formal and informal nursing surveys

Advocacy

- Networking
- Advocating for new and emerging therapies
- Collaboration with MS Coalition
- Establishing and validating the role of nurses

IOMSN Nightingale Initiatives

- 2020: 10 US nurses received grants to fund unique programs for nurses, patients, or the community
- 2020: 10 nurses who practiced globally also received funding for similar activities
- 2021: IOMSN presented an 8-week program titled the *MS Nurse Immersion Institute*
- 2022: 10 US nurses received Nightingale Awards to support special projects
- 2022: 10 international nurses will be awarded funding

In Summary…

- MS nurses incorporate the qualities of:
  - Teacher
  - Leader
  - Advocate
  - Caregiver
  - Social worker
  - Cheerleader

THE 13TH ANNUAL LINDA MORGANTE

Multiple Sclerosis Nurse Leadership Program

2022

THE LIVED EXPERIENCE OF MULTIPLE SCLEROSIS

Michelle Keating, RN, MSCN
Multiple Sclerosis Nurse Consultant

Provided by Academy for Continued Healthcare Learning and Annenberg Center for Health Sciences at Eisenhower

ACHL ACADEMY for CONTINUED HEALTHCARE LEARNING

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Beginning With the Diagnosis

- What do you think is wrong?
- Feelings of fear
  - What will happen to me?
- Grief
  - Who am I now?
- Anxiety
  - Can I have children?
- Support from family and friends

MS Is…

- Unpredictable
- Part of life, though not all of it
- Manageable

Images courtesy of Michelle Keating, RN, MSCN

The Early Years

1981-1986	• “5-year prognosis”
1986-1989	• Only complete remission
1986-1993	• 1 to 2 relapses per year

Disease-Modifying Treatment as the Years Continue

- Living through relapses and steroid treatments
- 1993: I am a “pioneer” in treatment with interferon β-1b as a patient and nurse educator
- 1st hospitalization in 1999 for injection-site cellulitis/panniculitis
- The “difficult” years: hospitalization 1999, 2000, 2003, 2005, 2007, 2009, and treatment changes
- With treatment experience of interferon β-1b and 1a, mitoxantrone, dalfampridine, and dimethyl fumarate

“Whether you think you can or think you can’t, you’re right."
–Henry Ford

Images courtesy of Michelle Keating, RN, MSCN

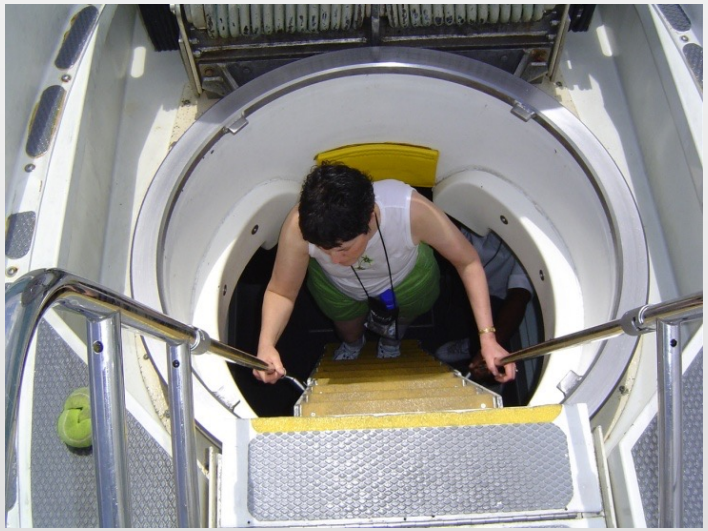
Vacationing on the Beach With MS

2000

2013

Images courtesy of Michelle Keating, RN, MSCN

Experiencing the Caribbean “Out of” and “In” the Water



Images courtesy of Michelle Keating, RN, MSCN

What has kept me going on my journey with MS?

- Being positive
- Exercise!
- Accepting change and readjusting life schedule
- Having faith and humor
- Asking for and accepting help

Image courtesy of Michelle Keating, RN, MSCN

Managing My Symptoms

- Dealing with the silent symptoms: “You look so good”
- Difficulty walking (spasticity, weakness, balance)
- Bowel and bladder
- Fatigue
- Heat

Images courtesy of Michelle Keating, RN, MSCN

Hope With MS: Comes From My Career as a Nurse

- Oncology nurse navigator for 29 years at Mercy and 13 years at another hospital
- Educating as an MSCN
- Pharmaceutical support nurse

Images courtesy of Michelle Keating, RN, MSCN

Hope: Comes From My Family

Images courtesy of Michelle Keating, RN, MSCN

Hope: Comes From Accepting and Giving Support

- Friends
- Coworkers
- MS community
- Faith community

Images courtesy of Michelle Keating, RN, MSCN

Hope: Comes From Health Professionals

- Mercy coworkers
  - Mary, Carol, Elissa
- My “MS team”
- CanDoMS

Images courtesy of Michelle Keating, RN, MSCN

Later Years Living With MS

- No relapses
- Focus on wellness
- Better walking

Images courtesy of Michelle Keating, RN, MSCN

Supporting the MS Community

- National MS Society volunteer roles as patient and nurse
- Relentless MS fundraising “Star” with MS Walk and MS bracelets and my 50th birthday bash with Teri Garr
- Quilt projects

Images courtesy of Michelle Keating, RN, MSCN

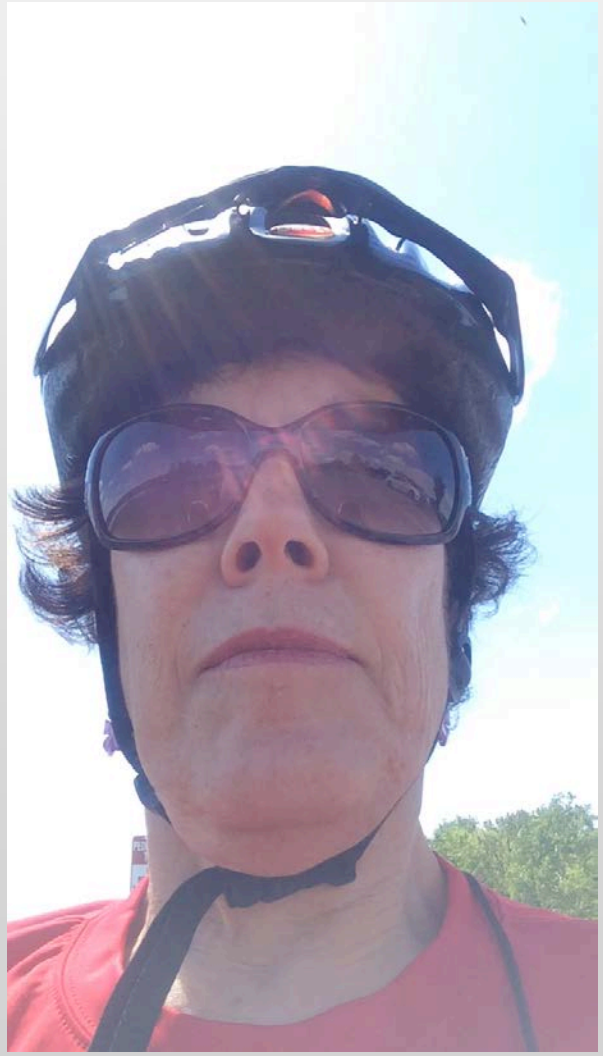
Hope in My Life

- Imagine the best
- Is the cup half full or half empty?
- A happy and healthy life is possible

Images courtesy of Michelle Keating, RN, MSCN

Hope: It Continues for the Future!
Recent Years

- PDSS ↓↓↓
  - Significantly improved mobility, upper body function, bowel and bladder control



PDSS = Patient-Derived Multiple Sclerosis Severity Score

Images courtesy of Michelle Keating, RN, MSCN

MS Bright Spots of Hope: Created May 2016

- Mission: educate, empower, spark creativity, and enhance wellness for the MS community
- Programs: MS Evening of Hope, Many Steps Towards Hope, MS Creative Arts with MS Cruisers, Many Steps Fitness Fun, Dance Movement, and more

Images courtesy of Michelle Keating, RN, MSCN

MS Bright Spots of Hope

- https://www.youtube.com/channel/UCCm2bmIacARjkU_Zom2fsZg
- And then there was 2020…

Images courtesy of Michelle Keating, RN, MSCN

New Programs in 2021

- https://www.youtube.com/watch?v=oogUMcFOYHY&t=24s
- https://www.youtube.com/watch?v=c7NLljGaQIw&t=2s

Image courtesy of Michelle Keating, RN, MSCN

THE 13TH ANNUAL LINDA MORGANTE

Multiple Sclerosis Nurse Leadership Program

2022

EXPERT DISCUSSION #2

Provided by Academy for Continued Healthcare Learning and Annenberg Center for Health Sciences at Eisenhower

ACHL ACADEMY for CONTINUED HEALTHCARE LEARNING

ANNENBERG CENTER FOR HEALTH SCIENCES AT EISENHOWER

The program is supported through educational grants from Biogen, Bristol-Myers Squibb, Inc., and Novartis Pharmaceuticals Corporation.

Expert Discussion Questions

- How do you define the role of the nurse in MS care?
- How have you seen the role of the MS nurse evolve in recent years?
- What insights did you learn listening to Michelle’s personal journey?
- Are there additional ways you get involved in MS patient advocacy?

MS = multiple sclerosis