Disclosures

- Presenter has no financial or non-financial interest to disclose.

- PESG staff, PVA staff, and planning/review committee members have no financial or non-financial interest to disclose.

- This continuing education activity is managed and accredited by Professional Education Services Group in cooperation with Paralyzed Veterans of America. PESG, PVA, and all accrediting organization do not support or endorse any product or service mentioned in this activity.
Learning Objectives

- Distinguish relapsing-remitting, secondary-progressive and primary-progressive MS subtypes
- Understand the new diagnostic criteria, 2017 McDonald criteria
- Be aware of the extensive differential diagnoses of MS
- Analyze and apply the results of various imaging and screening tools to monitor signs and manage symptoms associated with MS and disease progression.
What is Multiple Sclerosis?

- Inflammatory damage to myelin and axons in the central nervous system
- Multiple sclerosing lesions in the brain, optic nerves, spinal cord
- Symptoms are separated in space (DIS) and time (DIT)
What causes MS?

- Genetics
- Environment/Geographic location
- Vitamin D deficiency
- Diet
- Infectious etiology
Different subtypes of MS

CIS
Clinically Isolated Syndrome

SP
Secondary Progressive

PP
Primary Progressive

Relapses
Relapsing-Remitting

Handicap

Source: Servier
Diagnostic criteria over time

- 1916: Dawson criteria
- 1965: Schumacher criteria
- 1983: Poser criteria
- 2001 McDonald criteria
  - 2005 revision
  - 2010 revision
- 2016: MRI criteria: MAGNIMS
- 2017 revision McDonald criteria
Misdiagnosis of MS is Common

• Multicenter analysis of 110 misdiagnosed patients
  – Mayo (55%), UVM (25%), WUSL (11%), OHSU (9%)
  – 85% women, 15% men
  – Mean age 49 ± 11 years (range 21 – 77)

<table>
<thead>
<tr>
<th>Number of patients</th>
<th>Misdiagnosed by</th>
</tr>
</thead>
<tbody>
<tr>
<td>26 (24%)</td>
<td>Neurologist with MS fellowship training or practice focus</td>
</tr>
<tr>
<td>35 (32%)</td>
<td>Neurologist without MS fellowship training</td>
</tr>
<tr>
<td>3 (3%)</td>
<td>Non-neurologist</td>
</tr>
<tr>
<td>46 (42%)</td>
<td>Physician with unknown training</td>
</tr>
</tbody>
</table>

Conditions Mistaken for MS

- 70% of misdiagnosed patients received a DMT; 4% participated in an MS clinical trial
- 2/3 of all diagnoses:
  - 22% migraine in combination with other diagnoses
  - 15% fibromyalgia
  - 12% nonspecific symptoms with abnormal MRI
  - 11% conversion or psychogenic disorder
  - 6% NMOSD
<table>
<thead>
<tr>
<th>Infections of the CNS</th>
<th>Syphilis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Progressive multifocal leukoencephalopathy (PML)</td>
</tr>
<tr>
<td></td>
<td>Lyme disease</td>
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<tr>
<td></td>
<td>Human immunodeficiency virus (HIV)</td>
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<tr>
<td></td>
<td>Human T-cell lymphotrophic virus-1 (HTLV-1)</td>
</tr>
<tr>
<td>Inflammatory disorders of the CNS</td>
<td>Sjogren’s syndrome</td>
</tr>
<tr>
<td></td>
<td>Vasculitis</td>
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<tr>
<td></td>
<td>Systemic lupus erythematosus (SLE)</td>
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<tr>
<td></td>
<td>Neurosarcoïdosis</td>
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<tr>
<td></td>
<td>Behcet’s disease</td>
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<tr>
<td>Genetic disorders</td>
<td>Hereditary myelopathies</td>
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<tr>
<td></td>
<td>Cerebral Autosomal-Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy (CADASIL)</td>
</tr>
<tr>
<td></td>
<td>Leukodystrophies</td>
</tr>
<tr>
<td></td>
<td>Hereditary cerebellar degeneration</td>
</tr>
<tr>
<td></td>
<td>Mitochondrial disease</td>
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<tr>
<td>Brain tumors</td>
<td>Metastases</td>
</tr>
<tr>
<td></td>
<td>Lymphoma</td>
</tr>
<tr>
<td>Deficiencies</td>
<td>Copper deficiency</td>
</tr>
<tr>
<td></td>
<td>Vitamin B12 deficiency</td>
</tr>
<tr>
<td>Structural damage in brain or spinal cord</td>
<td>Cervical spondylosis</td>
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<tr>
<td></td>
<td>Hemiated disc</td>
</tr>
<tr>
<td></td>
<td>Chiari’s malformation</td>
</tr>
</tbody>
</table>

Lane et al, 2018
Why are patients misdiagnosed with MS?

- MS has heterogeneous clinical and imaging manifestation
- MRIs can show non-specific WM changes
- Pressure to diagnose to alleviate patient uncertainty and start DMT
- The authors felt that the MC cause for misdiagnosis was overcalling nonspecific symptoms, signs or MRIs that would not fit McDonald criteria
  - Use caution when accepting a historical event as a diagnosis in absence of current objective evidence
The International Panel on Diagnosis of MS convened for the International Advisory Committee on Clinical Trials in MS

To discuss “…issues related to misdiagnosis, differential diagnosis in diverse populations and in patients with atypical presentations.”
Role of MRI

- **Brain MRI:**
  - All patients

- **Spinal MRI**
  - Not mandatory
  - Advisable when history localizes to a spinal cord problem, primary progressive course, atypical population, or if you need more data
  - (Less helpful in children)
Role of CSF

- CSF recommended when:
  - Insufficient or atypical evidence
  - Presentation other than CIS (including progressive course at onset)
  - Populations in which MS is less common
  - CSF findings atypical for MS (elevated protein concentration of >100 mg/dL, pleocytosis with >50 cells per mm³, or the presence of neutrophils, eosinophils, or atypical cells)
  - 2 or more CSF OCBs more reliable than other measures (like IgG synthesis)
  - Proceed with caution with a panel with +IgG studies and -OCB; and with diagnosis of MS without OCBs (especially if the case is atypical)
### 2017 McDonald Criteria

<table>
<thead>
<tr>
<th>Number of lesions with objective clinical evidence</th>
<th>Additional data needed for a diagnosis of multiple sclerosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥2 clinical attacks</td>
<td>None*</td>
</tr>
<tr>
<td>≥2 clinical attacks (as well as clear-cut historical evidence of a previous attack involving a lesion in a distinct anatomical location)</td>
<td>None*</td>
</tr>
</tbody>
</table>
| ≥2 clinical attacks                               | Dissemination in space demonstrated by an additional clinical attack implicating a different CNS site or by MRI
| 1 clinical attack                                 | Dissemination in time demonstrated by an additional clinical attack or by MRI or demonstration of CSF-specific oligoclonal bands
| 1 clinical attack                                 | Dissemination in space demonstrated by an additional clinical attack implicating a different CNS site or by MRI

If the 2017 McDonald Criteria are fulfilled and there is no better explanation for the clinical presentation, the diagnosis is multiple sclerosis. If multiple sclerosis is suspected by virtue of a clinically isolated syndrome but the 2017 McDonald Criteria are not completely met, the diagnosis is possible multiple sclerosis. If another diagnosis arises during the evaluation that better explains the clinical presentation, the diagnosis is not multiple sclerosis. An attack is defined in panel 1. No additional tests are required to demonstrate dissemination in space and time. However, unless MRI is not possible, brain MRI should be obtained in all patients in whom the diagnosis of multiple sclerosis is being considered. In addition, spinal cord MRI or CSF examination should be considered in patients with insufficient clinical and MRI evidence supporting multiple sclerosis, with a presentation other than a typical clinically isolated syndrome, or with atypical features. If imaging or other tests (eg, CSF) are undertaken and are negative, caution needs to be taken before making a diagnosis of multiple sclerosis, and alternative diagnoses should be considered. A clinical diagnosis based on objective clinical findings for two attacks is most secure. Reasonable historical evidence for one past attack, in the absence of documented objective neurological findings, can include historical events with symptoms and evolution characteristic of a previous inflammatory demyelinating attack; at least one attack, however, must be supported by objective findings. In the absence of residual objective evidence, caution is needed. The MRI criteria for dissemination in space are described in panel 5. The MRI criteria for dissemination in time are described in panel 5. The presence of CSF-specific oligoclonal bands does not demonstrate dissemination in time per se but can substitute for the requirement for demonstration of this measure.

**Table:** The 2017 McDonald criteria for diagnosis of multiple sclerosis in patients with an attack at onset

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*Thompson et al, 2018 Lancet*
Panel 5: 2017 McDonald criteria for demonstration of dissemination in space and time by MRI in a patient with a clinically isolated syndrome

- Dissemination in space can be demonstrated by one or more T2-hyperintense lesions* that are characteristic of multiple sclerosis in two or more of four areas of the CNS: periventricular†, cortical or juxtacortical, and infratentorial brain regions, and the spinal cord
- Dissemination in time can be demonstrated by the simultaneous presence of gadolinium-enhancing and non-enhancing lesions* at any time or by a new T2-hyperintense or gadolinium-enhancing lesion on follow-up MRI, with reference to a baseline scan, irrespective of the timing of the baseline MRI

*Unlike the 2010 McDonald criteria, no distinction between symptomatic and asymptomatic MRI lesions is required. †For some patients—eg, individuals older than 50 years or those with vascular risk factors—it might be prudent for the clinician to seek a higher number of periventricular lesions
Panel 6: 2017 McDonald criteria for diagnosis of multiple sclerosis in patients with a disease course characterised by progression from onset (primary progressive multiple sclerosis)

Primary progressive multiple sclerosis can be diagnosed in patients with:
- 1 year of disability progression (retrospectively or prospectively determined) independent of clinical relapse

Plus two of the following criteria:
- One or more T2-hyperintense lesions* characteristic of multiple sclerosis in one or more of the following brain regions: periventricular, cortical or juxtacortical, or infratentorial
- Two or more T2-hyperintense lesions* in the spinal cord
- Presence of CSF-specific oligoclonal bands

*Unlike the 2010 McDonald criteria, no distinction between symptomatic and asymptomatic MRI lesions is required.
2017 Revisions compared to 2010 McDonald Criteria

- In a patient with CIS with DIS and no better explanation, CSF-specific OCBs allows an MS diagnosis without the previously required DIT
- Symptomatic and asymptomatic MRI lesions can be considered in determination of DIS or DIT
- Cortical and juxtacortical lesions can be used in fulfilling MRI criteria for DIS
- PPMS criteria the same, except removal of distinction between symptomatic and asymptomatic lesions and cortical lesions
Nonspecific symptoms
Exam findings not localizable to CNS

- Psychiatric disease
- Migraine
- Chronic pain disorders
- Ischemic microangiopathy
Hyperacute Presentation

- Ischemia
  - Ischemic optic neuropathies
- Cerebral or spinal cord stroke
- CADASIL
CADASIL

- External capsule involvement
- Cystic spaces in deep gray matter
- Anterior temporal lobe involvement

External capsule involvement

Cystic spaces in deep gray matter

Anterior temporal lobe involvement
1. Severe optic neuritis with poor recovery
2. Bilateral optic neuritis
3. Complete or LETM
   - A. Neuromyelitis Optica Spectrum Disorder

Other considerations
   - B. Systemic lupus erythematosus (SLE) and Sjogren’s
   - C. Idiopathic transverse myelitis
   - D. Leber’s hereditary optic neuropathy
A. Neuromyelitis Optica in Spine
A. NMO in Brain is different from MS: tumefactive brain lesions

Pittock et al. Arch Neurol. 2006;63(3)
A. NMO in Brain is different from MS: Diencephalic lesions

Pittock et al. Arch Neurol. 2006;63(3)
A. NMO in Brain is different from MS: Brainstem lesions

Pittock et al. Arch Neurol. 2006;63(3)
A. NMO Ancillary testing

- CSF - not specific
  - 20% have neutrophilic pleocytosis
  - <20% have oligoclonal bands or elevated IgG index/synth rate
- Anti-aquaporin 4 antibody - specific
  - Present in 70-80% of patients
  - ELISA ~5% false positive → cell based more accurate
  - Half of - AQP-4 will have + Anti-MOG
B. SLE and Sjogren’s

- Note: both may coexist with NMO
- Look for other neurologic sx
  - Encephalopathy
  - Headache
  - Seizures
  - Peripheral neuropathy (mononeuritis multiplex)
- Look for systemic manifestations
  - Typically precede neurologic sx
    - SLE: synovitis, fevers, photosensitive rashes
    - SS: sicca symptoms
C. Idiopathic transverse myelitis

- Complete transverse myelitis → <5-10% risk of conversion to MS
- Partial TM with characteristic MS brain lesions → >60-90% conversion risk to MS

D. Leber’s hereditary optic neuropathy

- Mitochondrial disorder (maternal transmission)
  - Degeneration of retinal ganglion cells and their axons
1. Multiple cranial neuropathies
2. Leptomeningeal disease/ MRI enhancement
3. Failure to remit
   - Lyme disease
     - ELISA $\rightarrow$ confirmatory western blot
     - Nerve-root or meningeal enhancement
   - Infiltrative processes
     - Neurosarcomaodis
     - Lymphomatosis
   - Other Carcinomatosis/Metastatic disease
     - Simultaneous development of carcinomatosis upon dissemination from a primary source
       - Often through seeding via CSF with involvement of leptomeninges
       - Adenocarcinoma most common
Neurosarcoidosis on Brain MRI
Neurosarcoidosis: Distinct MRI characteristics

Leptomeningeal enhancement
Basilar infiltration
Neurosarcoidosis in Spine

- Expansile
- Often peripheral cord location
- Extramedullary findings
  - Enhancing root nodules
  - Enhancement of cauda

STIR

T1 post-gad
Prominent cortical features and headache

- ADEM
- CNS angiitis (vasculitis)
  - Primary or secondary
- Infections
  - HSV, enterovirus, WNV
ADEM: A clinical diagnosis
CNS Vasculitis

- Cognitive decline, headache, seizures, and recurrent strokes
- MRI
  - Multiple infarcts
  - Multiple ages
  - Multiple territories
  - Multiple vessel calibers
- Consider Angiography
Susac’s Syndrome

- Small infarcts of cochlea, retina, and brain
- Triad
  - Encephalopathy
  - Sensorineural hearing loss
  - Branch retinal artery occlusions
  - Consider Fluoroscein angiogram
Progressive ataxia or Spastic Paraparesis

- Progressive MS
- Syphilis
- B12 and/or copper deficiency; NO toxicity
- HIV-associated vacuolar myelopathy
- Human T-cell lymphotropic virus type 1 (HTLV-1)
- Structural Lesion
- Dural AV fistula
- Hereditary spastic paraparesis (HSP)
- Primary lateral sclerosis
- Adult-onset sporadic isolated ataxias
Cognitive dysfunction

- Acquired and genetic leukodystrophies
- Consider neurodegenerative dementias in older patients with MS
Monitoring MS patients

- In past, trials were solely targeted at reducing number of relapses
- Relapses may not be a sufficient indicator of MS activity
- No evidence of disease activity (NEDA)
No Evidence of Disease Activity

- NEDA-3 defined as:
  1. No relapses
  2. No sustained disability progression
  3. No MRI activity
     - No New or enlarging T2 lesions
     - No Gd-enhancing lesions
- NEDA-4: Brain atrophy
- NEDA-NfL: Neurofilament light chain
Conclusions and Takeaways

- Multiple sclerosis is a chronic inflammatory disorder affecting the brain, optic nerve, and spinal cord.
- There are different types of MS with different presentations and natural histories.
- Although the 2017 McDonald criteria is very helpful in diagnosing MS, misdiagnosis of MS is common.
  - The differential diagnosis of MS is broad and there are many mimics.
- NEDA is an evolving concept that has implications in disease monitoring and DMT efficacy assessment.
References

Multiple Sclerosis
Treatment/Medication

AUGUST 2018
M.S.A. RICHARDSON MD FAC.P.
Learning Objectives

- To understand the factors affecting treatment decisions in MS
- To understand the available medications for MS treatment
- To discuss the treatment options available in 2018 for MS patients
- To learn the current recommendations for initiating and monitoring MS medications
Considerable changes in medication & Rx management
Now 15 medications with FDA approval
Goals of treatment have shifted
  - Decrease frequency & severity of relapses
  - Delay progression
Prevent new or enhancing lesions
  - NEDA (No evidence of disease activity)
Goals of Treatment

- Reduce incidence of relapses
- Reduce development of new or enhancing lesions on MRI
- Delay disease progression
- Enhance QoL

- NEDA = no relapses
  - No disability progression
  - No MRI activity
  - Brain volume loss <0.4%
Considerations in Treatment

- Lifestyle (compliance, self medication, routine)
- Work & Career (wellness)
- Travel (monitoring, access)
- Family
- Pregnancy
- Tolerance of Risk (side effects/new drug)
Current Treatment Algorithm

1st Line: reduce relapses
reduce MRI activity

2nd Line: 
relapse in 1st year
incomplete recovery
new/enhancing MRI activity
Escalation Approach to MS therapy

- **First-Line**
  - Interferon beta-1a, interferon beta-1b
  - Glatiramer acetate
  - Teriflunomide
  
- **Second-Line**
  - Fingolimod
  - Dimethyl fumarate

- **Third-Line**
  - Natalizumab
  - Alemtuzumab
  - Daclizumab
  - Ocrelizumab

- Avonex, Rebif, Plegridy, Betaseron,
- Copaxone
- Aubagio
- Gilenya
- Tecfidera
- Tysabri
- Lemtrada
- Zinbryta
- Ocrevus
Escalation Approach to MS therapy (2)

- Fourth-Line
  - Mitoxantrone
  - Cyclophosphamide

- Fifth-Line
  - Autologous stem cell transplant (experimental)

Ampyra (dalfampridine) has specific indication to improve walking speed

In VAMC the Pharmacy Benefits Management Service, Medical Advisory Panel has criteria for selection of therapy and preferred Agents when DMT switch is needed
Injectable Agents - First line DMT

- Subcutaneous, intramuscular
- Intermittent dosage, available with autoinjectors
- **Baseline monitoring** - CBC with diff, LFT, thyroid
- **On therapy monitoring** - q 3 monthly x 2 then yearly (betaseron may develop neutralizing antibodies)
- **Potentially serious AE** - anemia, leukopenia, depression, Sz, CHF, autoimmune disorders
- **Common AE** - injection site reaction, fatigue, myalgia, flu like sx

- Copaxone - has no monitoring but AE lipoatrophy and skin necrosis, and post injection flushing, SOB, hypersensitivity reaction
Injectable Agents (2)

- **Now pegylated interferon beta 1a**
  - Administered q O week
  - Prefilled syringe may be at room temp for one week
  - Monitoring etc is the same

- **Single monoclonal injectable daclizumab**
  - Administered monthly
  - Avoid in patients with Hx liver disease
  - Monitoring needed monthly and 6 months after d/c drug
  - AE - liver damage, anaphylaxis/angioedema, rash, eczema, URI
Oral Agents

**Fingolimod**
- 0.5 mg daily
- Baseline CBC, LFT, optical tomography
- Monitor CBC, LFT every 3-6 months
- First dose bradycardia, AV block
- PML, hepatitis, macular edema, worsening PFT

**Tecfidera**
- 120 mg bid and titrate to 240 mg
- Baseline CBC, LFT
- Monitor CBC with lymphocyte counts quarterly
- D/C if WBC <2000/m or lymph count <500/μL for > 4 weeks
- PML, decrease WBC, abd pain, flushing, diarrhea, nausea, pruritic
- High fat/high protein food/H2 blockers will help GI effects

**Teriflunomide**
- 14 mg once daily
- Avoid in pregnancy, abnormal LFTs, active infection
- Baseline CBC, LFT, PPD, Preg. Test
- Monitor monthly LFT x 6 months
- Hepatotoxicity, teratogenicity, ARF, neuropathy, SJ S
- Alopecia, nausea, diarrhea, headache, increase BP, parasthesia
## Infusible Agents

<table>
<thead>
<tr>
<th>Infusible Agent</th>
<th>Dosage and Administration</th>
<th>Precautions and Monitoring</th>
<th>Adverse Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Natalizumab</strong></td>
<td>300 mg IV monthly</td>
<td>Avoid if JC virus positive</td>
<td>Baseline CBC, LFT, JC virus</td>
</tr>
<tr>
<td><strong>Alemtuzumab</strong></td>
<td>12 mg IV daily x 5 days then 1 year later 12 mg daily x 3 days</td>
<td>Vaccination for varicella is negative</td>
<td>Baseline CBC, creatinine, TSH, varicella titer, skin exam</td>
</tr>
<tr>
<td><strong>Ocrelizumab</strong></td>
<td>300 mg infusion q 2 weeks x 2 then 600 mg infusion q 6 months</td>
<td>Avoid in HBV – need consultation</td>
<td>Baseline HBV, CBC</td>
</tr>
</tbody>
</table>
What are the considerations when choosing a treatment

<table>
<thead>
<tr>
<th>COST</th>
<th>LIFESTYLE</th>
<th>RISKS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lemtrada - $$$</td>
<td>Compliant/Adherence</td>
<td>Safety versus Efficacy</td>
</tr>
<tr>
<td>Tecfidera --$</td>
<td>Fear of injections/needles</td>
<td>Early adopter/late acceptor</td>
</tr>
<tr>
<td>Copaxone</td>
<td>Travel/Work</td>
<td>Tolerance for side effects</td>
</tr>
<tr>
<td>Avonex</td>
<td>Domestic responsibilities/Family</td>
<td>JCV</td>
</tr>
<tr>
<td>Pegasidy</td>
<td>Urban/Rural</td>
<td>Thyroid</td>
</tr>
<tr>
<td>Ocrelizumab</td>
<td>Access/Insurance/MS expertise</td>
<td>Pregnancy</td>
</tr>
<tr>
<td>Gilenya ---$</td>
<td></td>
<td>Liver Hepatitis</td>
</tr>
<tr>
<td>Rebif</td>
<td></td>
<td>Cardiac</td>
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<tr>
<td>Tysabri</td>
<td></td>
<td></td>
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<tr>
<td>Aubagio</td>
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</table>

Ocrelizumab - FDA approved for PPMS
How do you decide?

- Are there signs of highly active MS
  - Old, male, high dz burden, rapid progression
- Has there been a relapse while on one DMT
- Is there development of a contraindication
  - JCV, Liver Dz, Pregnancy, macular edema, hypersensitivity
- Is a side effect intolerable
- Is the signs/symptoms progressing
  - disability, cerebellar, memory,
## What’s Important – Pts differ from MDs

<table>
<thead>
<tr>
<th>Benefit</th>
<th>Patient</th>
<th>MD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reduction in MRI lesions</td>
<td>-</td>
<td>++</td>
</tr>
<tr>
<td>Long-term disability is reduced</td>
<td>-</td>
<td>++</td>
</tr>
<tr>
<td>Longer between/less freq. attacks</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>Decrease in severity of attacks</td>
<td>_</td>
<td>++</td>
</tr>
<tr>
<td>Reduction in disease progression</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>Maintain current status/condition</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Prevents symptoms getting worse</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Less reduction in total brain volume</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Improvement in quality of life</td>
<td>+</td>
<td>+</td>
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</tbody>
</table>

- = patient wanted more discussion
++ = MD thought discussion okay
Treatment Strategies

- No widely accepted algorithm for the treatment
- What is the patient’s prognosis
- Evidence based strategies should consider an early start to therapy
- Balance efficacy and safety to reduce relapses and MRI disease activity
- If DMTs are deemed ineffective or only partially effective, therapy is switched to second-line medications.
- RECOGNIZE A SUPOTIMAL RESPONSE AS SOON AS POSSIBLE

What about patients with active disease from the onset (incomplete recovery, freq relapses in past year, enhancing/increasing MRI lesions)?
Treatment Strategies

- Monitor for adverse effects
- Monitor for JCV virus
- MRI every 3-6 months
  - Seropositive JCV
  - Natalizumab >24 months
  - Immunosuppressed
- MRI every 6 – 12 months
  - DMT switch
- MRI every year
  - Stable symptoms
When to stop treatment??

- Treatment is failing
- Adverse events intolerable
- Patient noncompliant, unable to follow treatment plan
- Progressive EDSS > 7.5
- Aging stable patient (“burnt-out MS”)

Prognostic Considerations

- Male sex
- Older age onset
- Multifocal onset
- Motor cerebellar or bladder symptoms at onset
- Multiple contrast-enhancing and T2 lesions on MRI
- High score for evoked potential abnormalities
New Considerations.

- Should we consider initiating treatment with a highly efficacious therapy. Is the step approach detrimental to the patient response and prognosis?

- Are the monitors (clinical, routine MRI, labs) sufficient to determine which category of DMT is optimal? Is there a cost to the step approach?

- The risk-benefit profile is variable during the disease course e.g. age related comorbidities, MS lesion burden. How best to monitor and manage this risk-benefit profile. Is there a cost to exposure to several differing DMTs.

- With increasing knowledge of pathophysiology and availability of newer agents there is a greater hope for individualized therapy for MS patients.
Thanks