# Updating MS Diagnosis: The 2024 McDonald Criteria Explained

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Ochsner Neuroscience Symposium

# Disclosures

- TG Therapeutics: Speaker, Consultant
- Sanofi: Speaker, Consultant
- EMD Serono: Speaker, Consultant
- Genentech: Consultant

Position Paper

# Diagnosis of multiple sclerosis: 2024 revisions of the McDonald criteria

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This online publication has been corrected. The first corrected version appeared at thelancet.com/neurology on September 23, 2025, the second corrected version appeared at thelancet.com/neurology on XXX, 2026

See Comment pages 807 and 808

See Personal View pages 866 and 880

Multiple Sclerosis Centre of Catalonia and Department of Neurology (Prof X Montalban MD, G Arrambide MD,

**Advances in the understanding of multiple sclerosis and the development of biomarkers of pathophysiology prompted a substantial revision of the 2017 McDonald diagnostic criteria. The new 2024 McDonald criteria provide a unified approach for diagnosing multiple sclerosis in individuals with relapsing or progressive courses throughout the lifespan (ie, from paediatric to late-life presentations). The optic nerve can now serve as a fifth anatomical location within the CNS for diagnosis. The central vein sign, paramagnetic rim lesions, and kappa free-light chain concentrations in CSF can be used, when available, to provide supportive evidence and confer specificity for a diagnosis of multiple sclerosis in specific situations. In certain cases, radiologically isolated syndrome or neurological symptoms that do not constitute a clear attack or progression of disability can fulfil the criteria for a multiple sclerosis diagnosis. We also provide guidance for the diagnosis of multiple sclerosis in older individuals (≥50 years) and those with comorbidities. The 2024 revised criteria should expedite the diagnosis of multiple sclerosis, while maintaining specificity.**

## Introduction

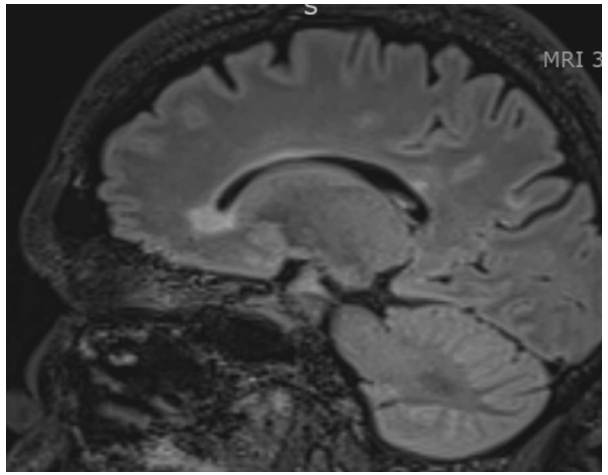
Diagnosing multiple sclerosis requires a balance between facilitating early recognition of disease and avoiding

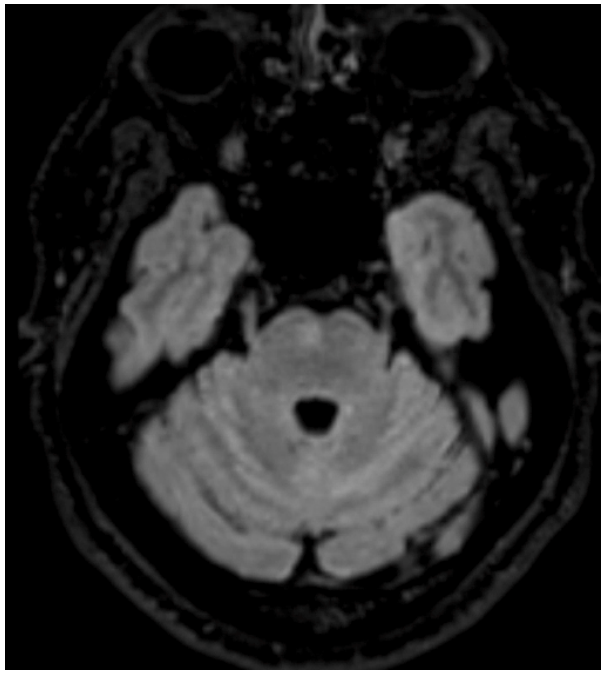
CSF-oligoclonal bands as a substitute for dissemination in time (DIT) in patients fulfilling only criteria for dissemination in space (DIS). Cortical lesions and both

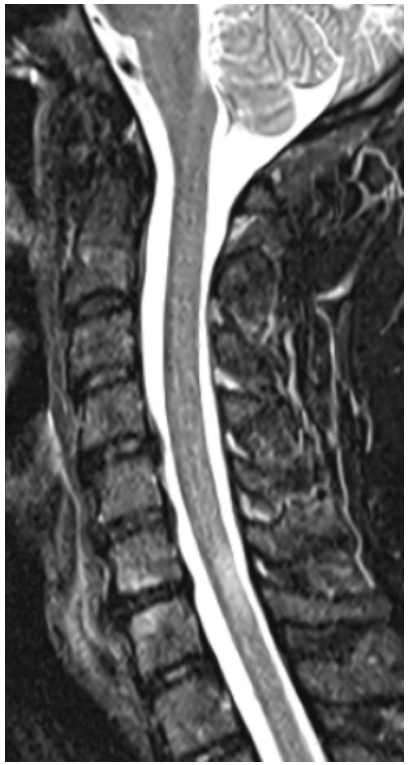
# Case 1

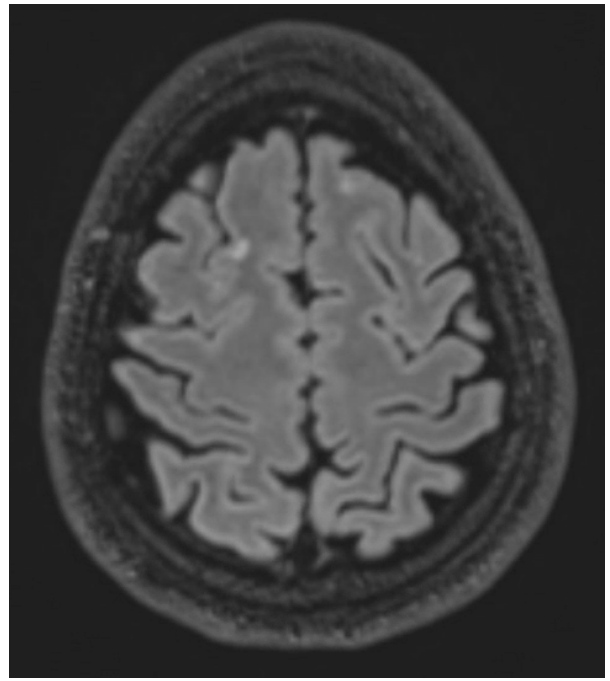
- 43 y/o woman developed diffuse numbness of upper arm lasting 1 week in 2020
- MRIs showed lesions of the brain and spine, non-enhancing. LP recommended, but she deferred and was lost to follow up.
- Back to MS clinic in 2026 to follow up on possible MS diagnosis. No clinical events since 2020. No sense of neurologic impairment.
- Normal neurologic exam
- MRI lesions: juxtacortical, periventricular, spinal cord and brainstem, all gad negative

# Case 1







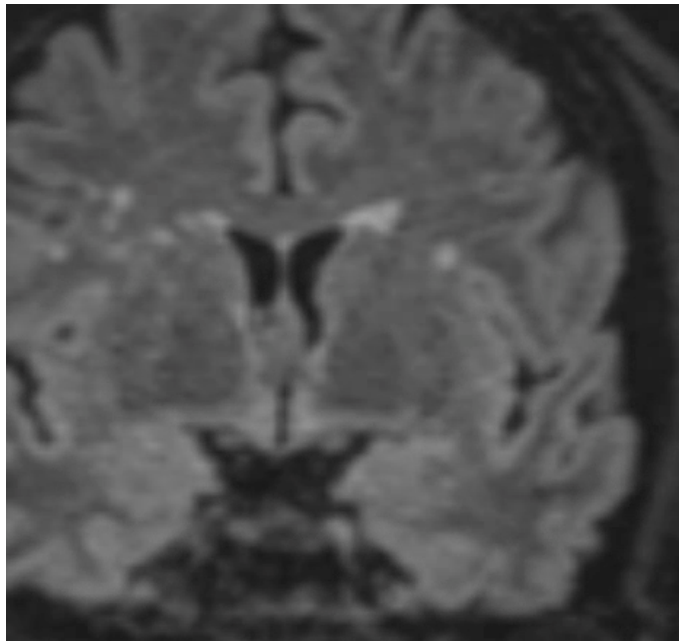


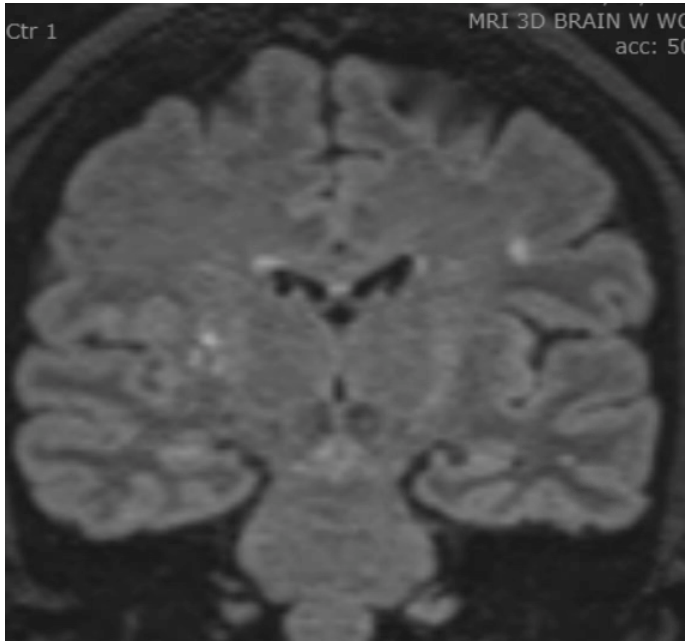
# Case 1

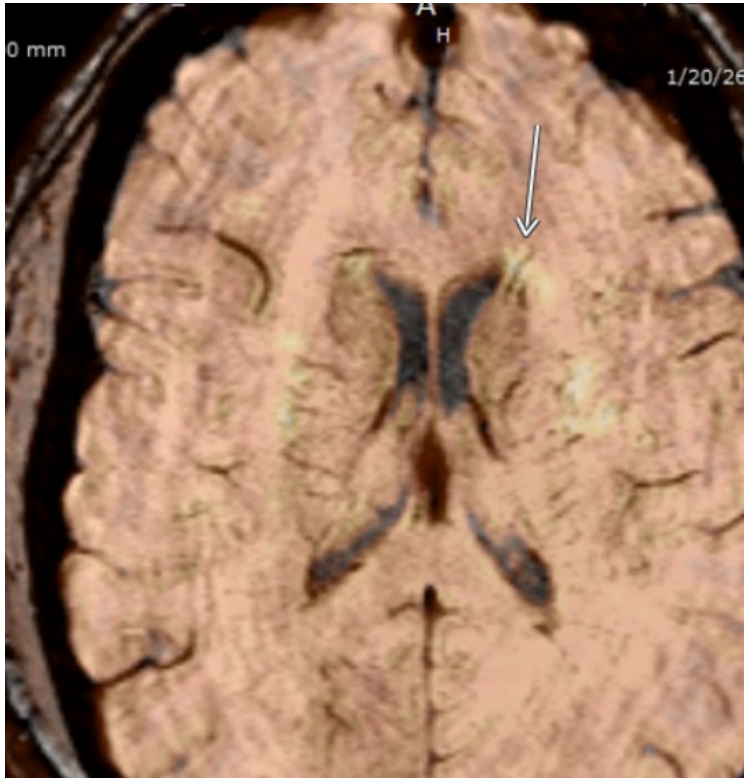
- Does patient have MS by:
  - 2017 McDonald criteria?
  - 2024 McDonald criteria?

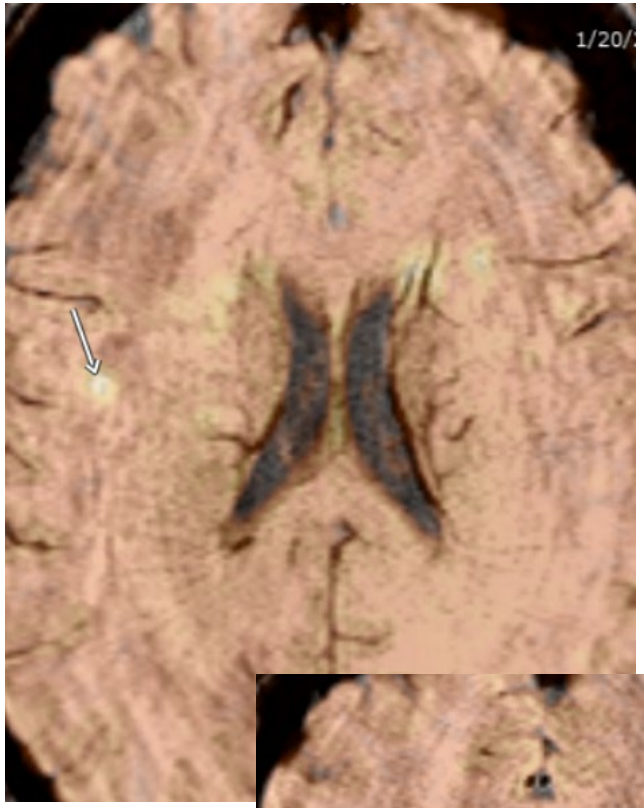
# Case 2

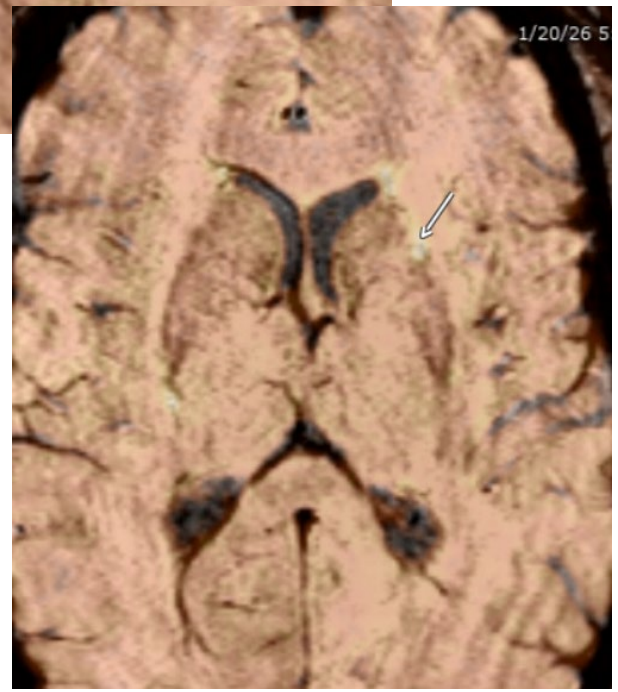
- 45 y/o woman referred with symptoms of intermittent lightheadedness, vertigo, brain fog, headaches and fatigue.
- VNG suggested a CNS etiology to vertigo
- EXAM: positive Romberg
- MRI: white matter lesions:
  - periventricular,
  - Juxtacortical
  - + CVS






# Case 2

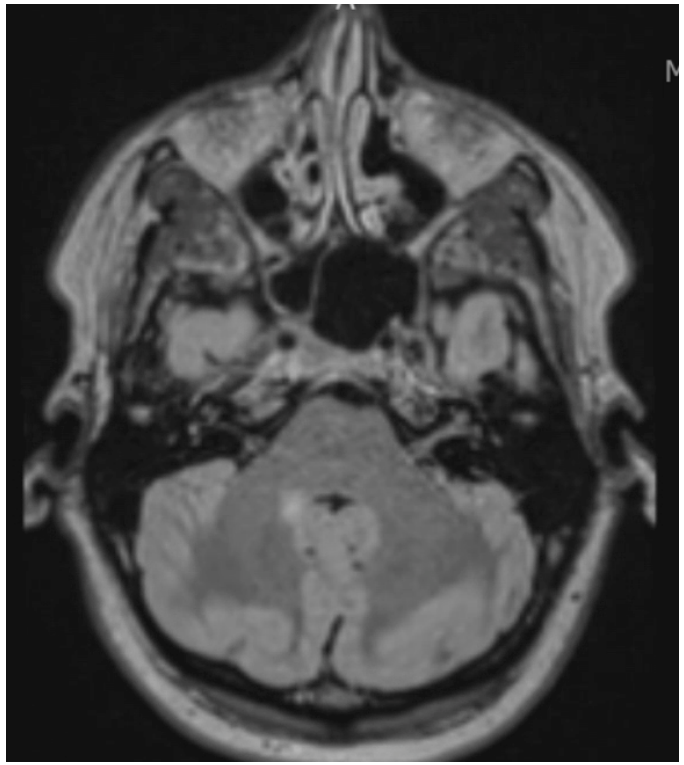
# Case 2

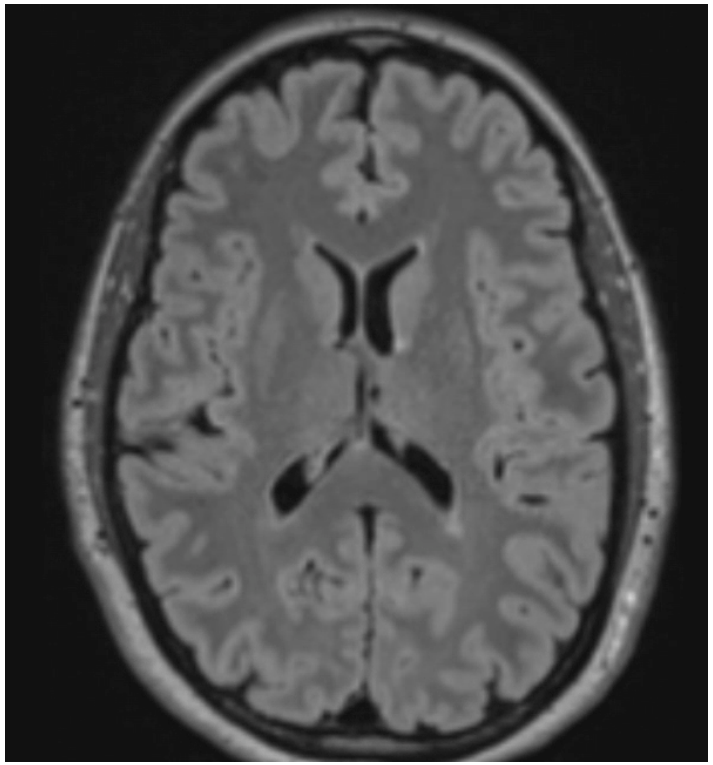
- Does patient have MS by:
  - 2017 McDonald criteria?
  - 2024 McDonald criteria?

# Case 3

- 48 y/o woman developed double vision, nausea, vertigo, and gait disturbance.
- Admitted – MRI brain with demyelinating lesion in the right MCP, lesion in left PV region
- LP - + OCB
- Mimics negative

# Case 3





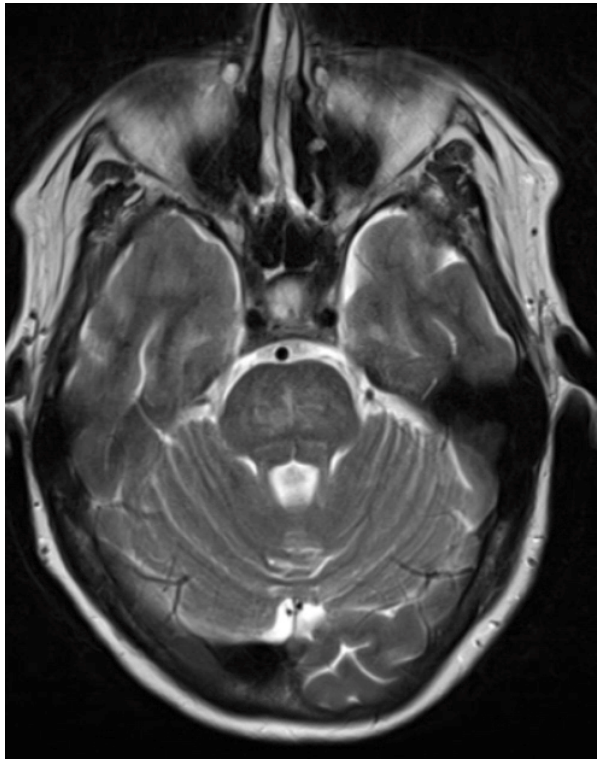
# Case 3

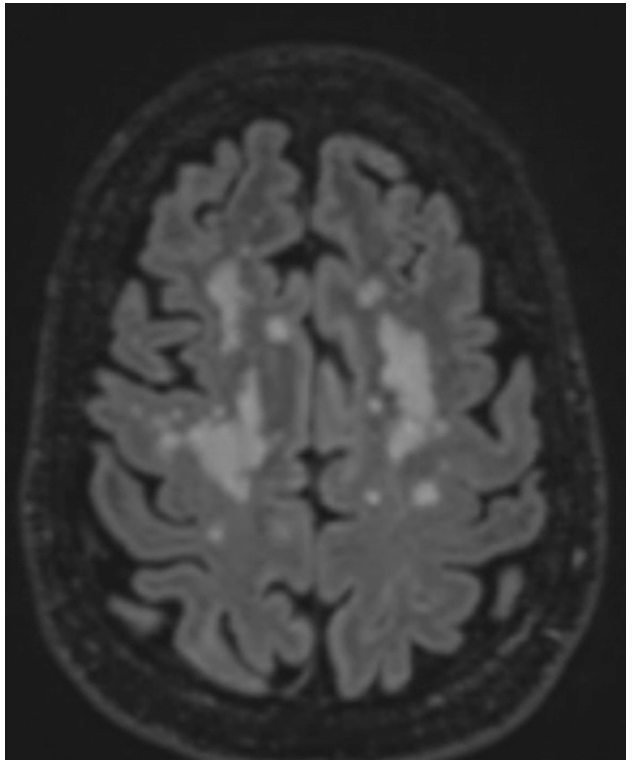
- Does patient have MS by:
  - 2017 McDonald criteria?
  - 2024 McDonald criteria?

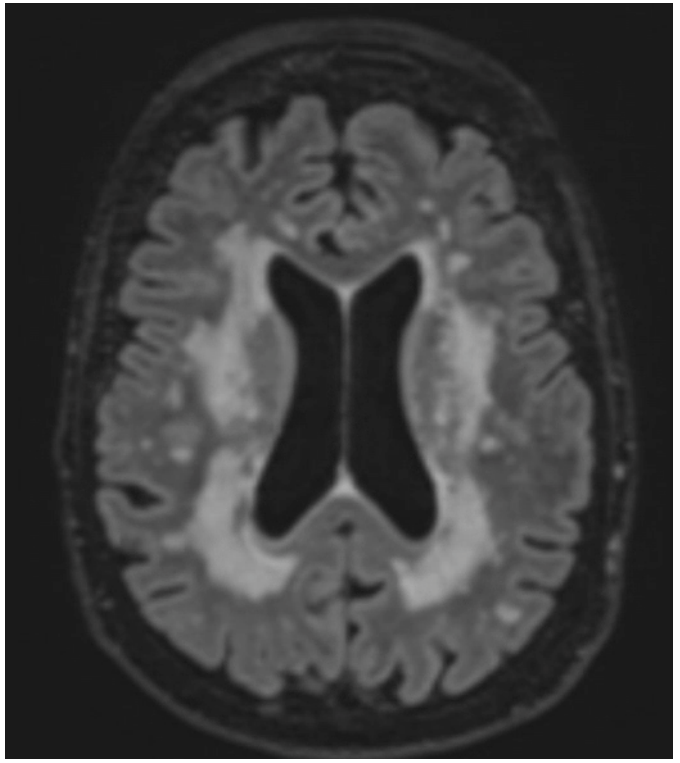
# Case 4

- 76 y/o woman with symptoms of tremor and abnormal MRI brain.
- Had five minute episode of double vision in 2017, and a prolonged episode of vertigo lasting weeks 30 years ago.
- Reports symptoms of progressive gait disturbance
- Admits to deconditioning and orthopedic issues
- PMH: HTN, Hyperlipidemia, CKD, CAD
- EXAM: absent AJ bilaterally, esotropia, decrease vibration in feet bil, slow walk
- B12 – 144 in 2025, other labs/mimics negative
- MRI- patchy and confluent WM abnormalities

# Case 4







# Case 4

- Does patient have MS by:
  - 2017 McDonald criteria?
  - 2024 McDonald criteria?

# Evolution of the McDonald Criteria for MS

- 2001 – Original McDonald Criteria
  - MRI formally incorporated into MS diagnosis
  - Introduced MRI concepts of:
    - DIS = Dissemination in Space
    - DIT = Dissemination in Time

- 2005 – Revised McDonald Criteria
  - Simplified MRI requirements
  - Greater emphasis on the Barkhof/Tintoré MRI criteria for DIS

Trend over time: increasing sensitivity, earlier diagnosis, and greater integration of imaging + biomarkers.

# Evolution of the McDonald Criteria for MS

- 2010 – Major MRI Simplification
  - A single MRI could fulfill both DIS and DIT
  - Symptomatic lesions counted
- 2017 – Increased Diagnostic Sensitivity
  - Cortical lesions added to DIS criteria
  - CSF oligoclonal bands (OCBs) allowed to substitute for DIT

Trend over time: increasing sensitivity, earlier diagnosis, and greater integration of imaging + biomarkers.

# Evolution of the McDonald Criteria for MS

- 2024 – Updated Revisions
  - Continued movement toward earlier biologically based diagnosis
  - Greater recognition of:
    - optic nerve involvement
    - central vein sign
    - paramagnetic rim lesions
    - kappa free light chains

Trend over time: increasing sensitivity, earlier diagnosis, and greater integration of imaging + biomarkers.

# Goals of the 2024 McDonald Workgroup

- Increase sensitivity so that MS can be diagnosed even earlier than it could be with 2017 criteria
- Maintain specificity so that MS can be ruled out with the same accuracy as with the 2017 criteria
- Big Shift – MS diagnosis to be based more on a biological framework and less on clinical framework

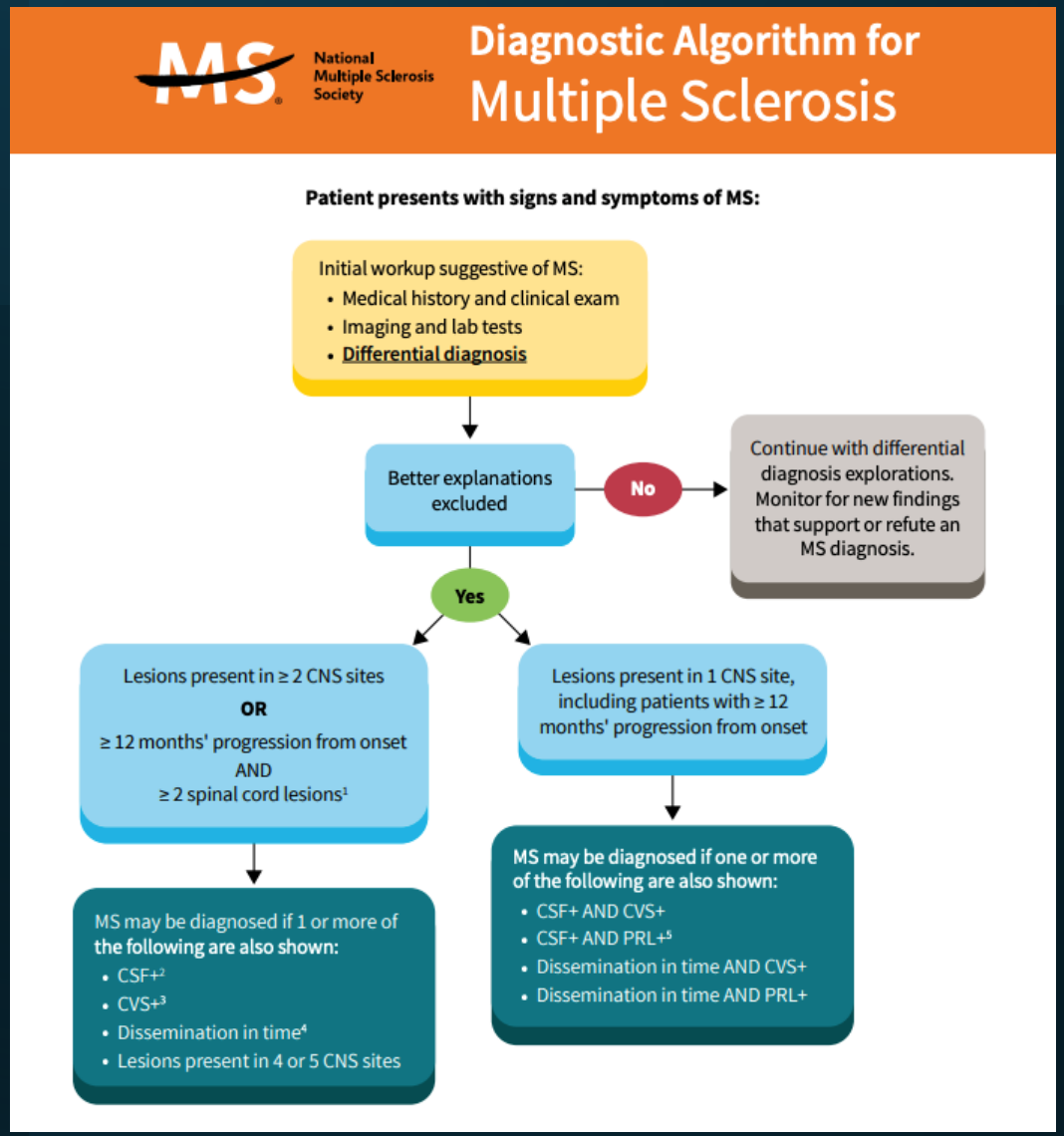
# Summary of Major Changes – 2024 McDonald Criteria

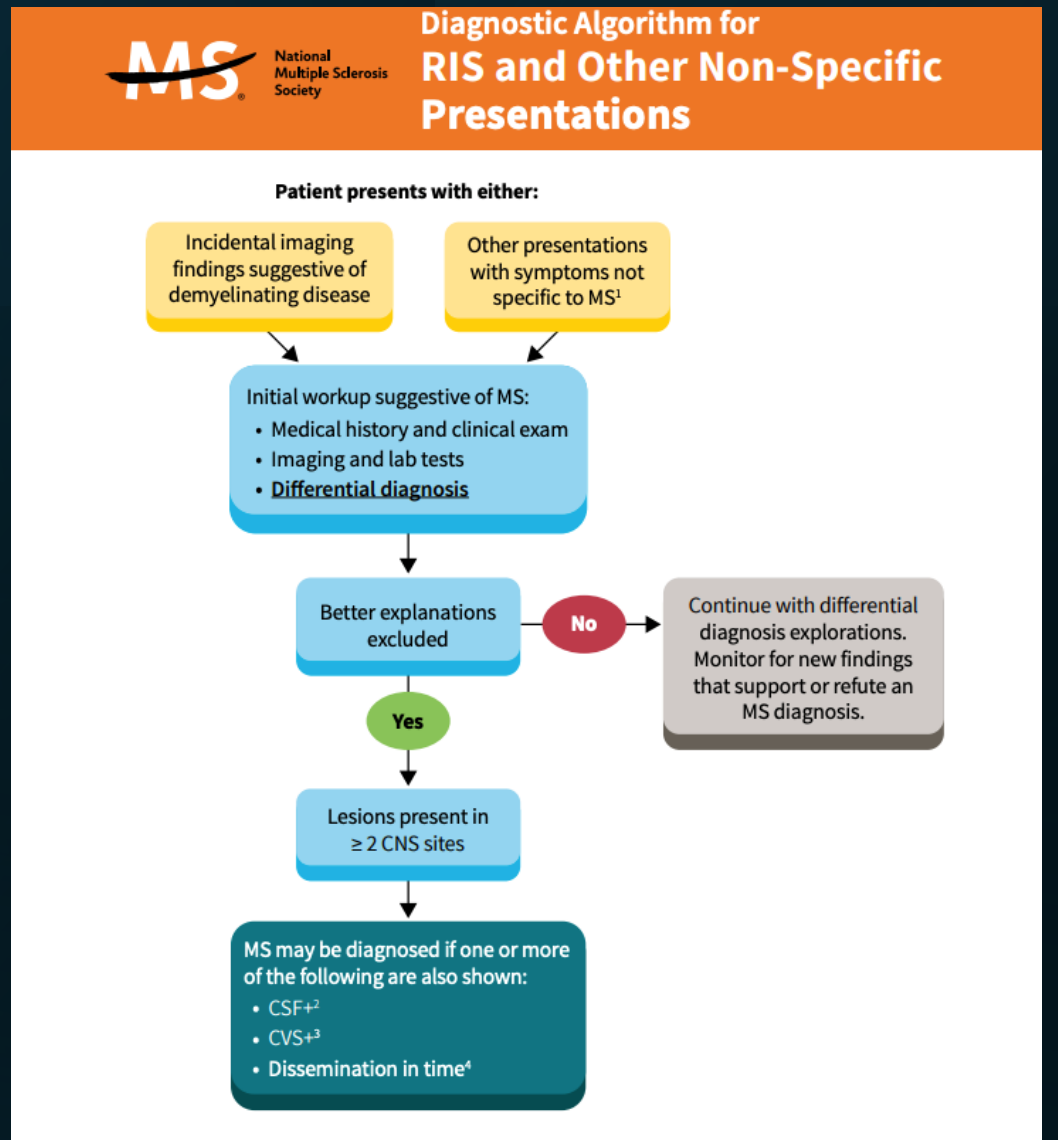
- The optic nerve may serve a fifth anatomical location
- DIS is fulfilled when two of five anatomical locations show typical lesions
- DIT is no longer mandatory for a diagnosis of MS
- The Central vein sign (CVS) on MRI can be used
- Paramagnetic rim lesions (PRLs) on MRI can be used
- The Kappa free-light chair index is interchangeable with OCB in CSF, and can replace it to diagnose MS
- Radiologically isolated syndrome and other non-specific clinical presentations can be MS when specific criteria are met
- Pediatric onset MS and adult onset have same diagnostic framework
- Progressive and relapsing MS represent a unified diagnosis and require unified diagnostic criteria
- Additional criteria are recommended when diagnosing MS in people over 50 years or with vascular comorbidities

# 2024 McDonald Criteria

- 2017 McDonald criteria are still valid, the 2024 criteria simply adds sensitivity and maintains specificity
- Paraclinical testing is now required for the diagnosis, MRI being the most useful
- The greatest value in the revised criteria applies to individuals with only one attack (CIS), no attacks (RIS), or non-specific clinical presentations

# Two main diagnostic algorithms based on clinical presentation
1. Typical signs/symptoms of MS
2. RIS or non-specific symptoms of MS



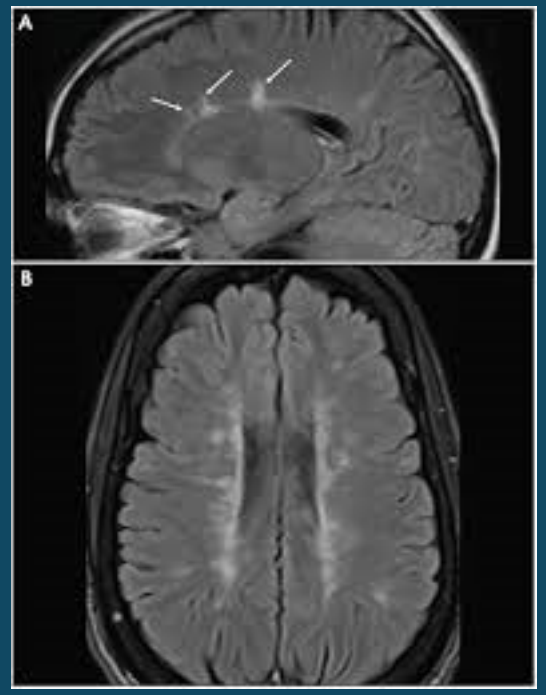
# Typical vs Atypical Presentation

| Typical | Atypical or Nonspecific |
| --- | --- |
| Unilateral optic neuritis<br>Focal brainstem syndrome<br>Partial myelopathy<br>Focal supratentorial syndrome<br><br>Persists continuously for at least 24 hours | Bilateral ON<br>Headache<br>Fatigue<br>Isolated vertigo<br>Complete transverse myelopathy<br>Ophthalmoplegia<br>Encephalopathy |

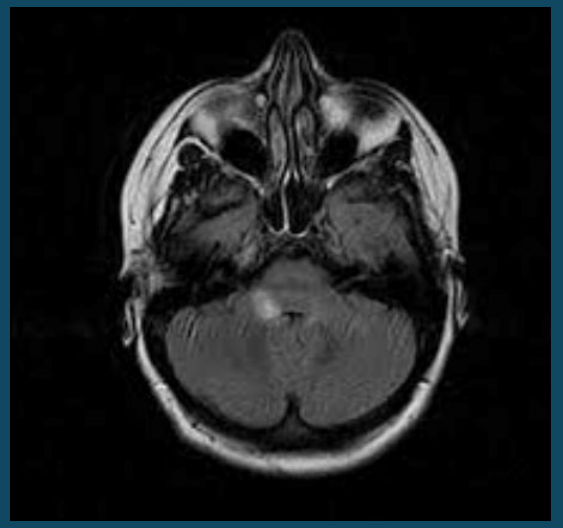
# Anatomic Location – Five MS Specific Regions

1. Periventricular
   - Lesions touch lateral ventricles
   - Includes classic Dawson's fingers
2. Juxtacortical / Cortical
   - Lesions touch the cortex
3. Infratentorial
   - Brainstem or cerebellar lesions
4. Spinal Cord
   - Typically, short-segment
5. Optic Nerve (new 2024 revisions)
   - Can use MRI, OCT or VEP to satisfy criteria

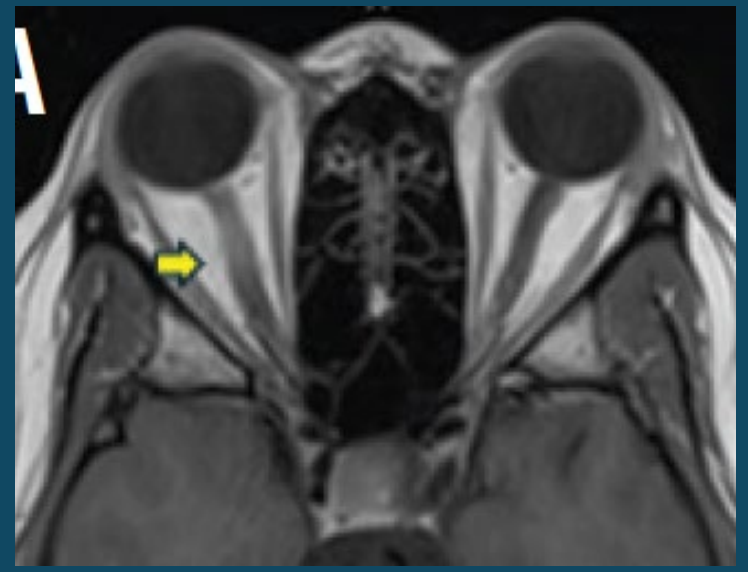
- Subcortical lesions are NOT counted because they are not specific to MS



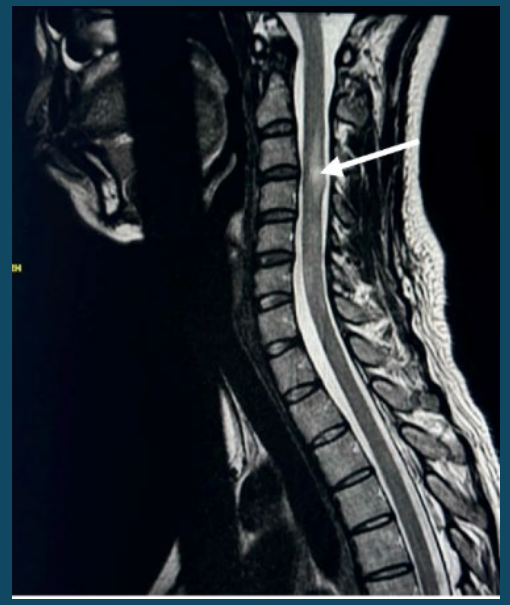

Periventricular



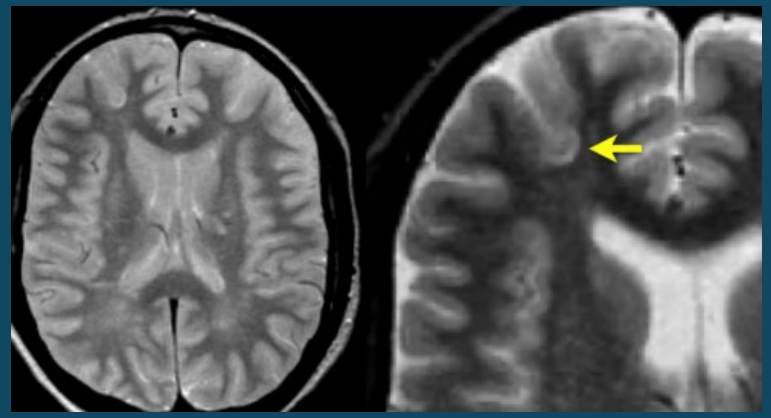
Infratentorial



Optic Nerve



Spinal Cord

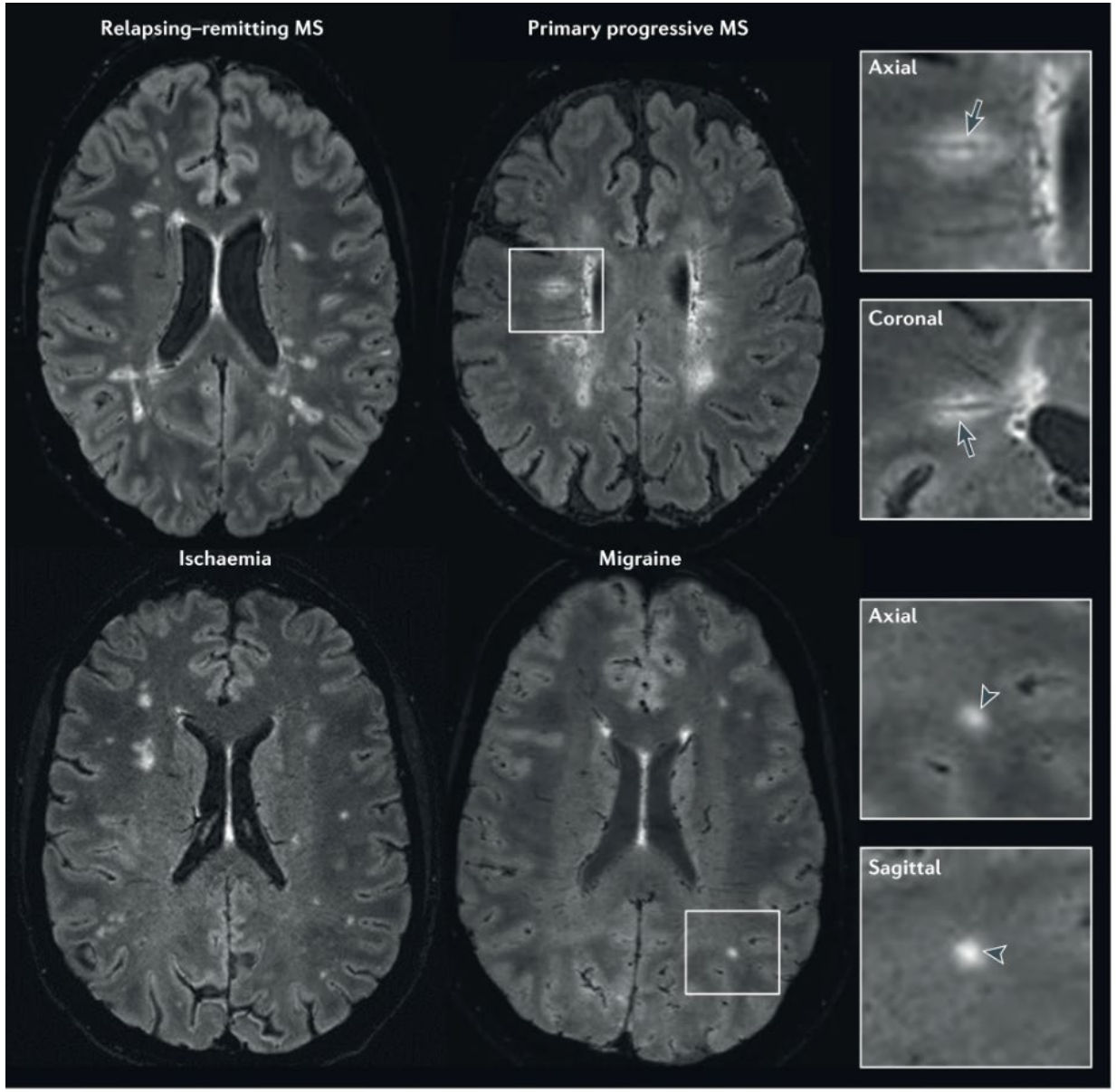


Juxtacortical / Cortical

# Central Vein Sign (CVS)

- CVS is present in in 70-80% of MS lesions
- Uncommon in conditions that mimic MS = highly specific for MS
- Best seen on axial T2 weighted or SWI (susceptibility-based) images
  - Small hypointense vein within lesion
  - Vein traverses lesion centrally
  - Best appreciated on axial images
  - Often confirmed on ≥2 contiguous slices
- Anatomic correlate of perivenular inflammation which is pathologic hallmark of MS
- Lesions in conditions that mimics MS (small vessel ischemic disease, migraine-related white matter lesions, NMOSD, Vasculitis, ADEM) do NOT have central vein on MRI
- Can be used in diagnosis, but NOT REQUIRED

# Central Vein Sign




Sati, P. et al. Nat Rev Neurol 12, 714–722 (2016)

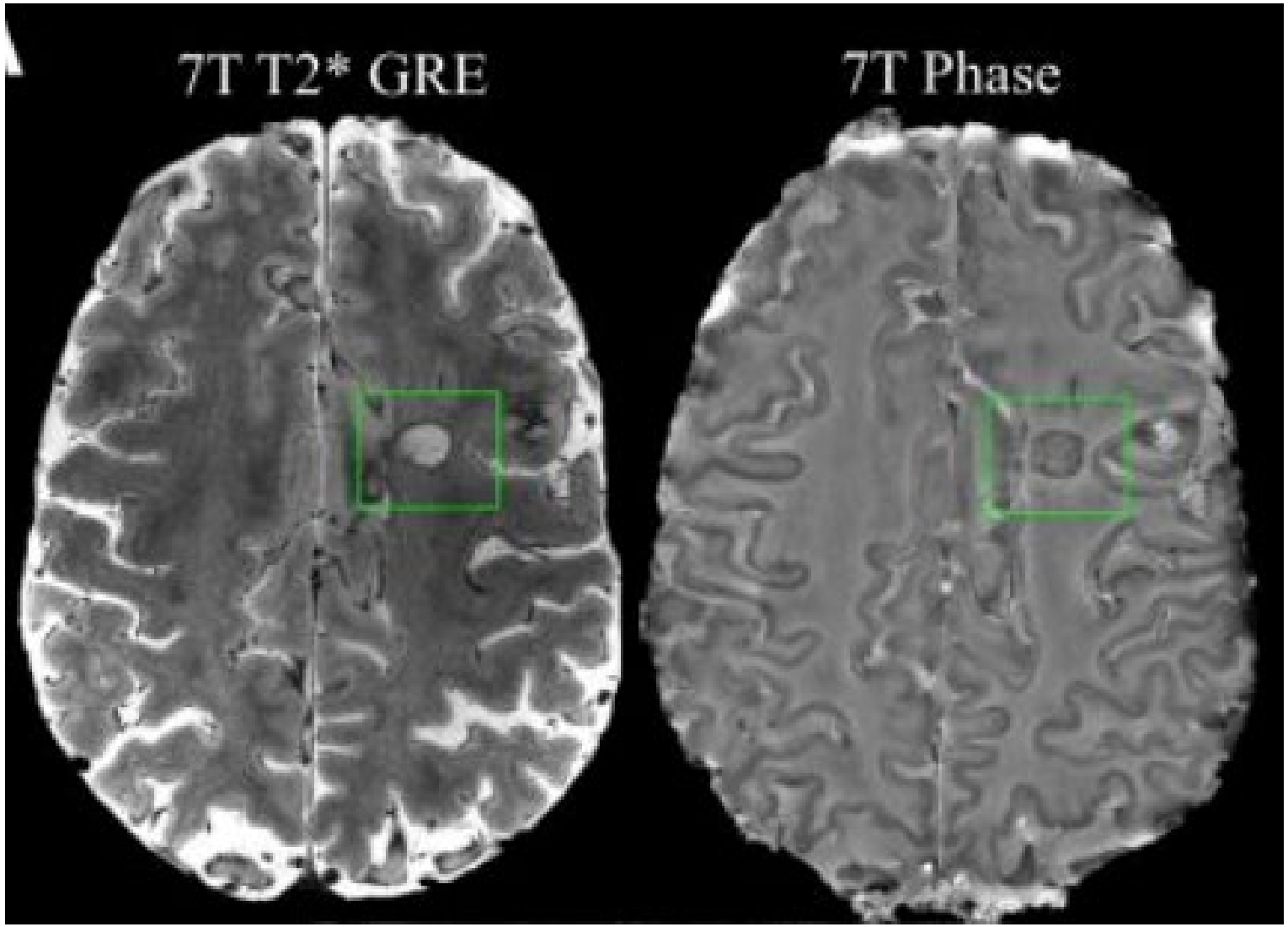
# CVS – Select 6 Rule

- If ≥6 white matter lesions contain a central vein, MRI is considered supportive of MS
- If the patient has <6 total lesions, then the majority of lesions should demonstrate a central vein for the MRI to be considered supportive of MS

# Paramagnetic Rim Lesion - PRL

- MS lesions with a hypointense paramagnetic rim on susceptibility-weighted imaging (SWI)
- Reflect iron-laden activated microglia/macrophages at the lesion edge
- Considered markers of chronic active (“smoldering”) inflammation
- Clinically, associated with greater disability and progressive MS biology
- PRLs on SWI
  - Dark rim surrounding a white matter lesion
  - Persistent over time
  - Often slowly expanding
- Can be used in diagnosis, but NOT REQUIRED

# Paramagnetic Rim Lesion




Bagnato et al. BRAIN 2024: 147; 2913-2933

# Special Populations

- Late onset MS -over age 50
  - Strongly recommended to look for additional features: CSF, spinal cord lesions, CVS
- Patients with headaches or vascular comorbidities

  Strongly recommended to look for additional features: CSF, spinal cord lesions, CVS
- Pediatric populations
  - Check MOG IgG using a cell-based assay in children < 12 years
  - Check MOG IgG in children > or = 12 years if atypical presentation for MS
  - If ADEM presentation, a second clinical attack or new T2 lesion >90 days post-onset is required before MS can be diagnosed
  - CVS – >50% of lesions have CVS in children / adolescents <18 years strongly supports a diagnosis of MS

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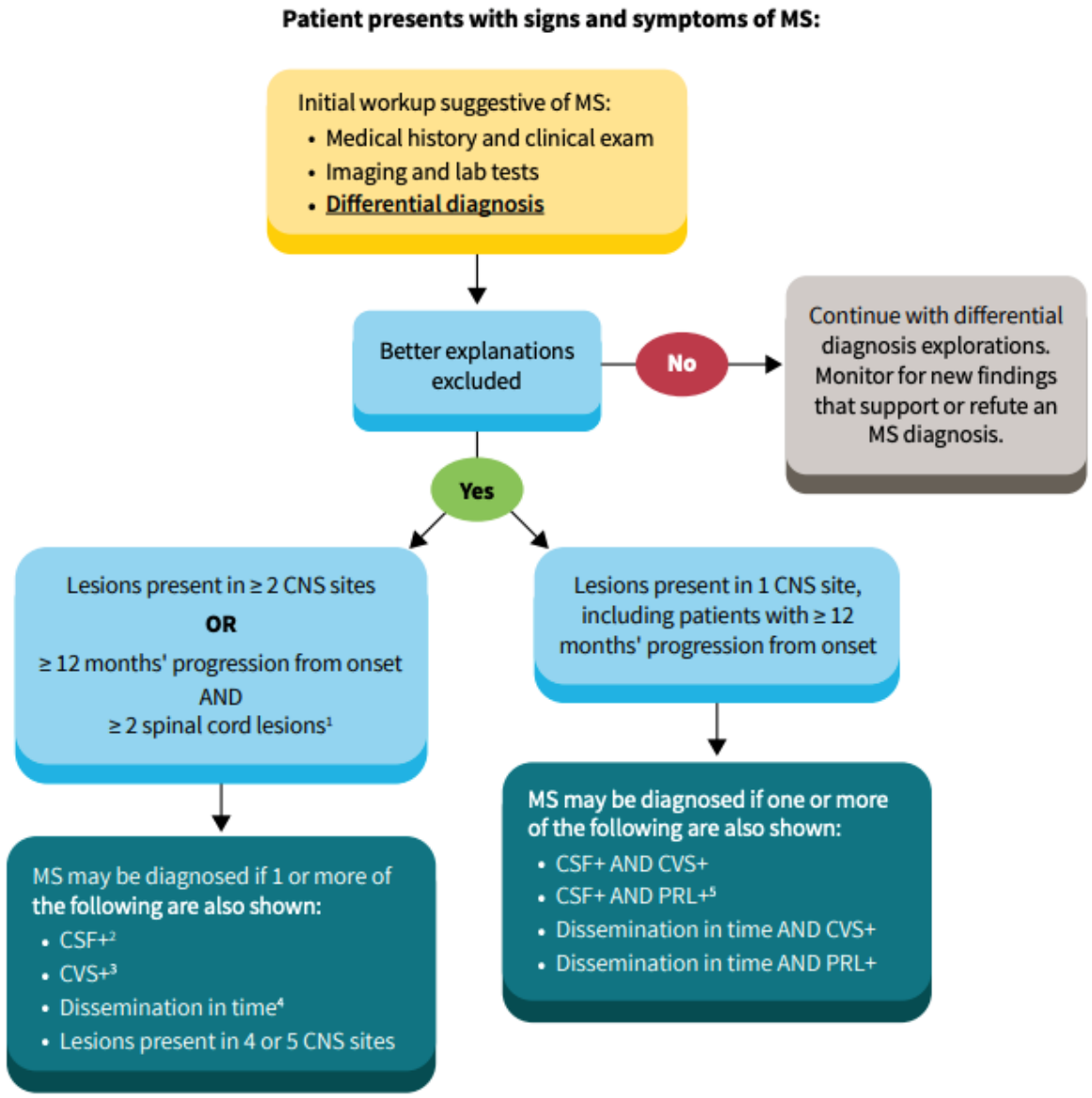
# Diagnostic Algorithm for Multiple Sclerosis



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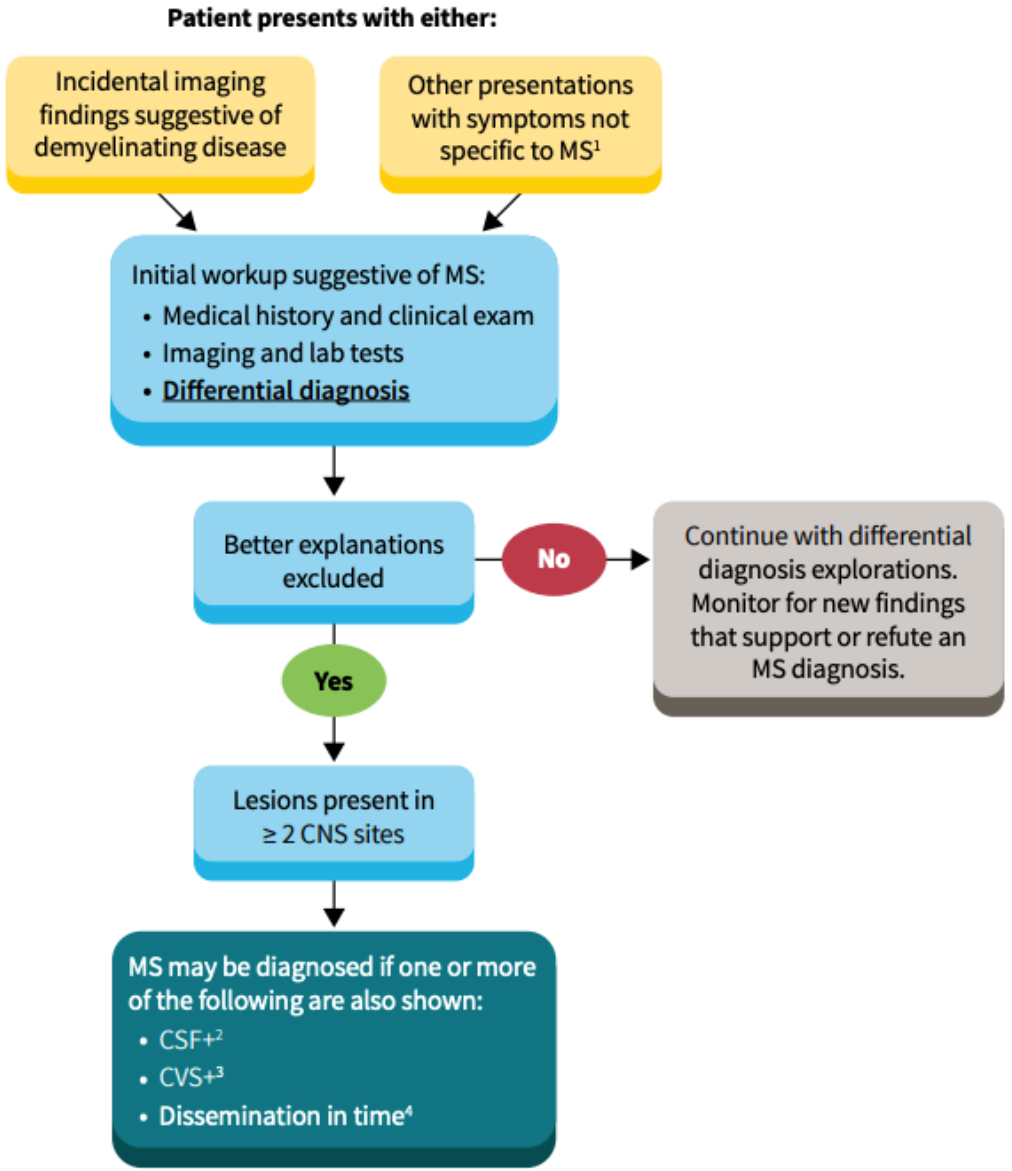
# Diagnostic Algorithm for RIS and Other Non-Specific Presentations



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# Requirements for Diagnosing MS

## Requirements for Diagnosing MS Based on the Number of DIS Anatomical Locations

| DIS Topographies | Attack or Progressive Onset | RIS and Other Non-Specific Presentations |
|---|---|---|
| **4–5** | No further criteria needed | Any 1 of the following:<br>• DIT<br>• CSF<br>• CVS |
| **2–3** | Any 1 of the following:<br>• DIT<br>• CSF<br>• CVS | Any 1 of the following:<br>• DIT<br>• CSF<br>• CVS |
| **1** | Combination of the following:<br>• DIT or CSF, and<br>• CVS or PRL<br><br>In patients with progression from onset (≥ 12 months), the following also applies:<br>• ≥ 2 spinal cord lesions and any 1 of the following:<br>  • DIT<br>  • CSF<br>  • CVS | Not able to make diagnosis |
| **0** | Not able to make diagnosis | Not able to make diagnosis |

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- Normal neurologic exam
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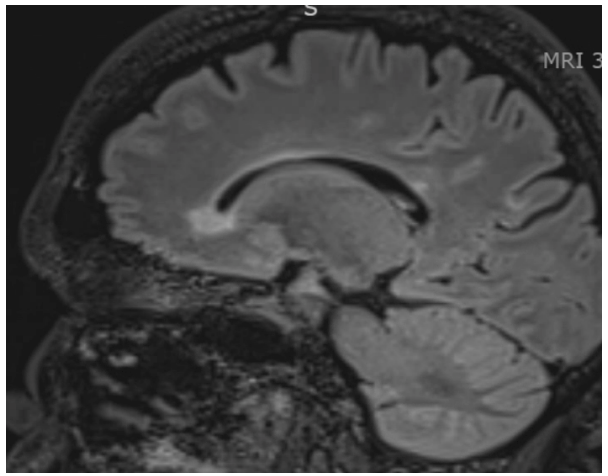


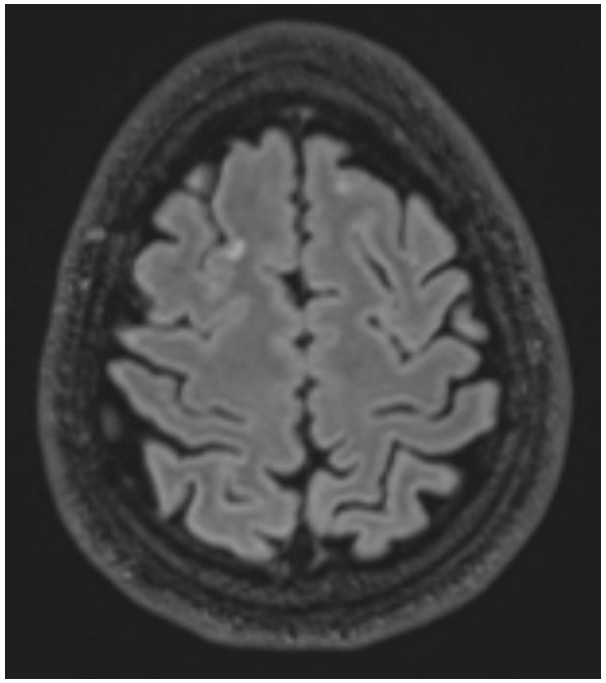

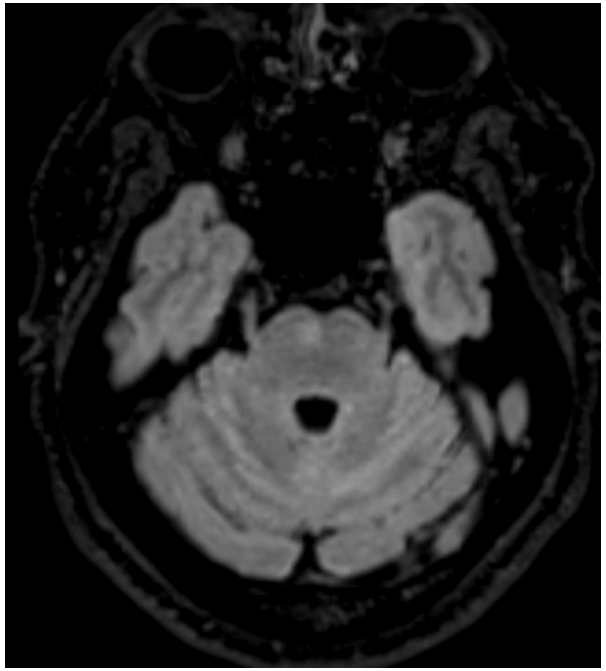

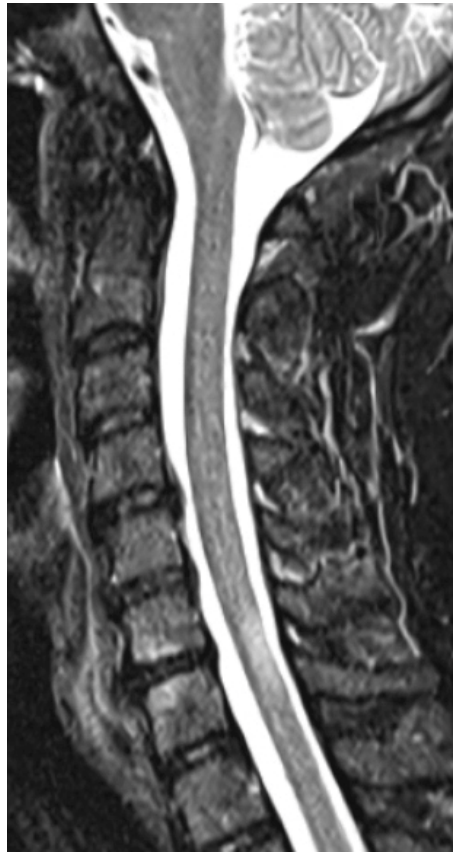

# Case 1

# Case 1

- Does patient have MS by:
  - 2017 McDonald criteria? No
    - DIT not met
  - 2024 McDonald criteria? Yes
    - Lesions in 4 MS typical regions
    - Typical clinical presentation
    - DIT no longer necessary

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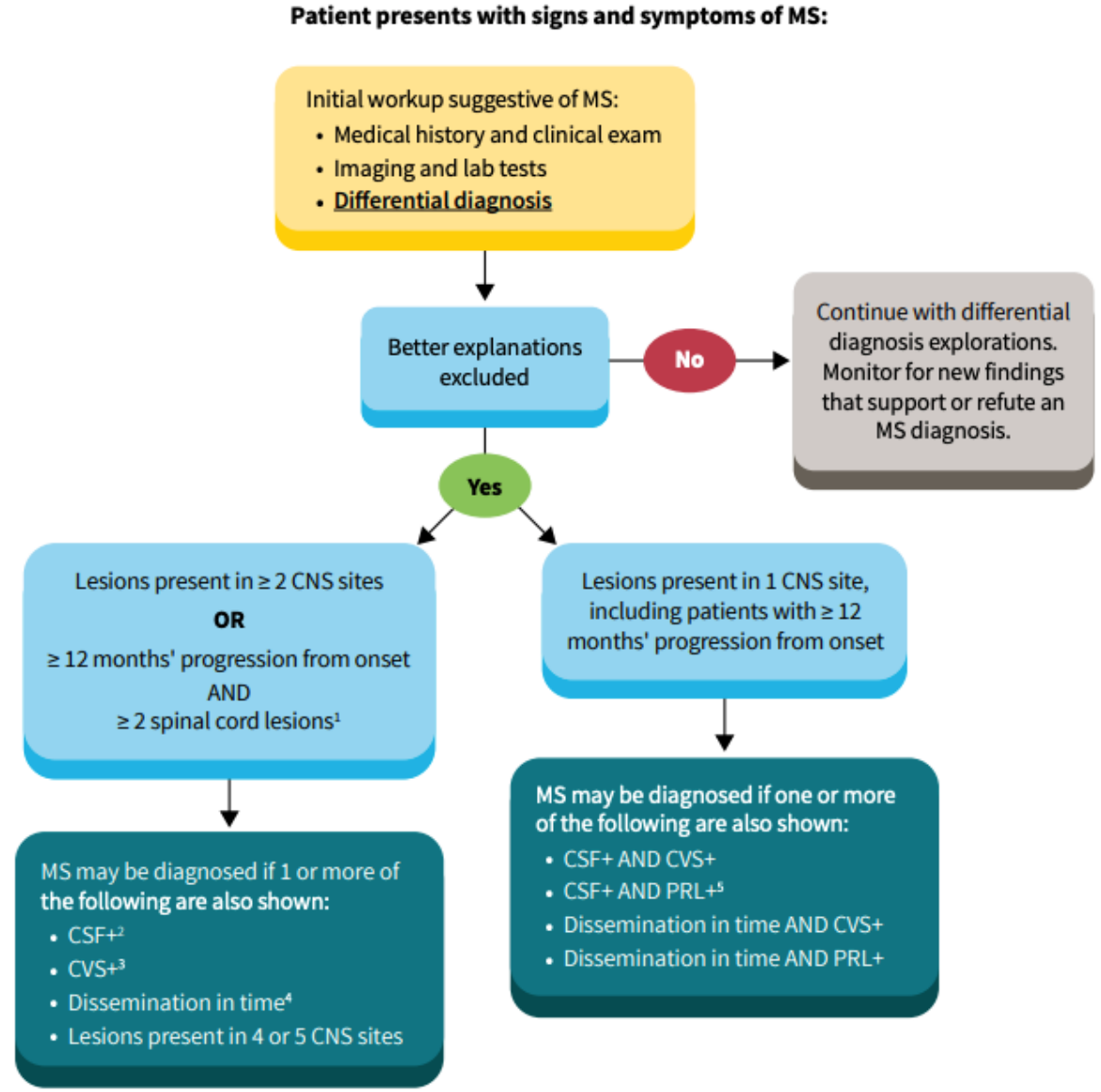
# Diagnostic Algorithm for Multiple Sclerosis



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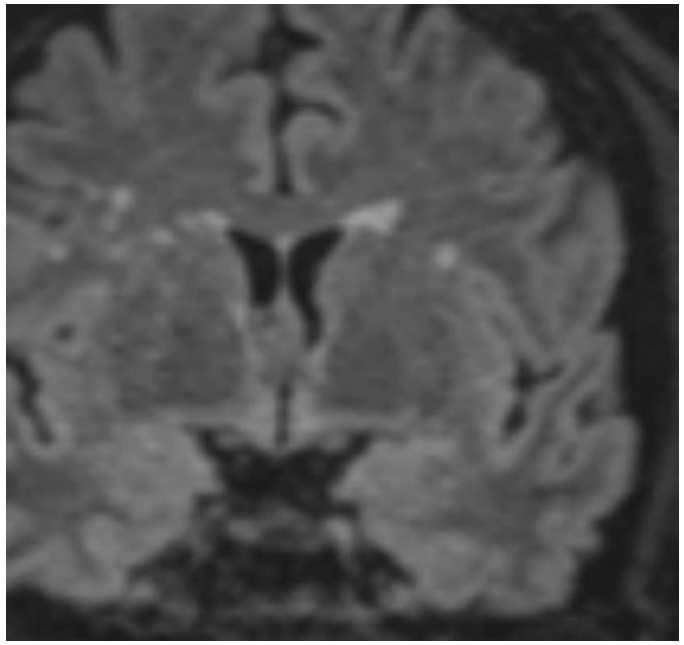
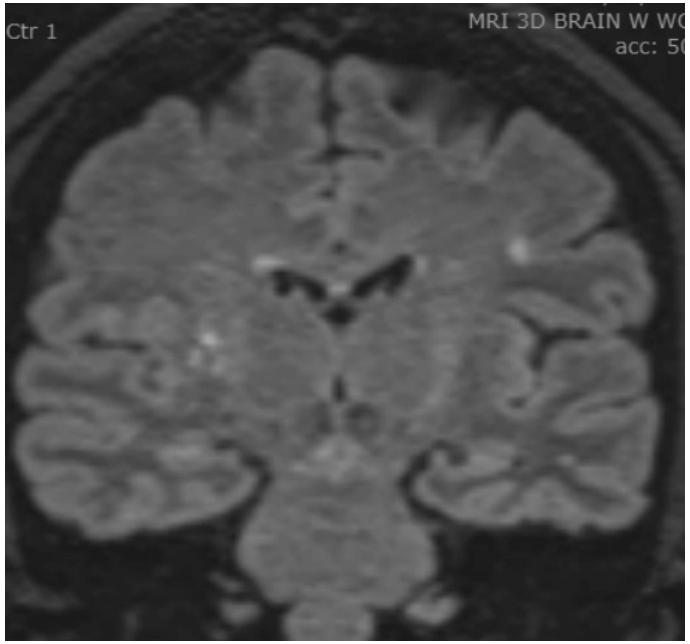
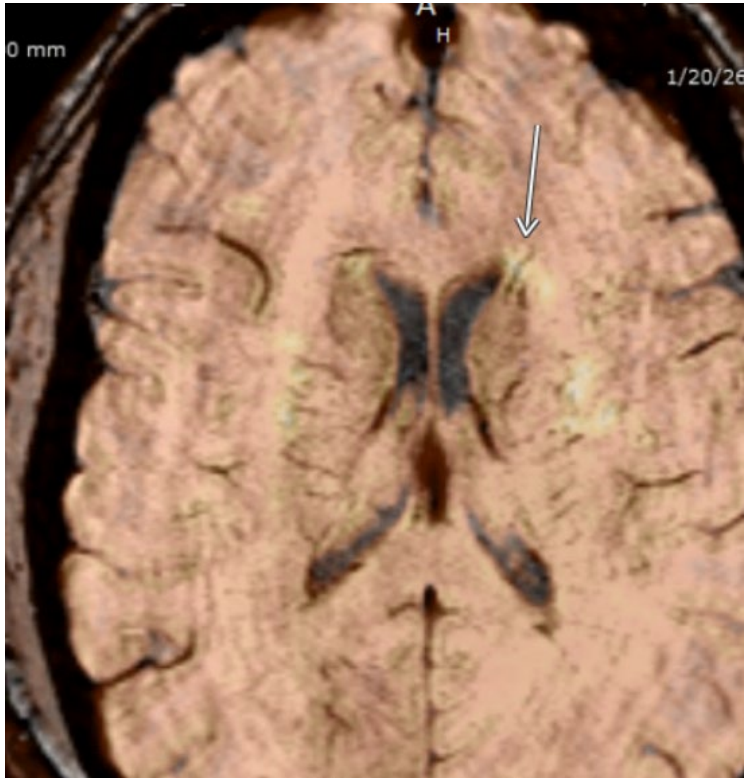
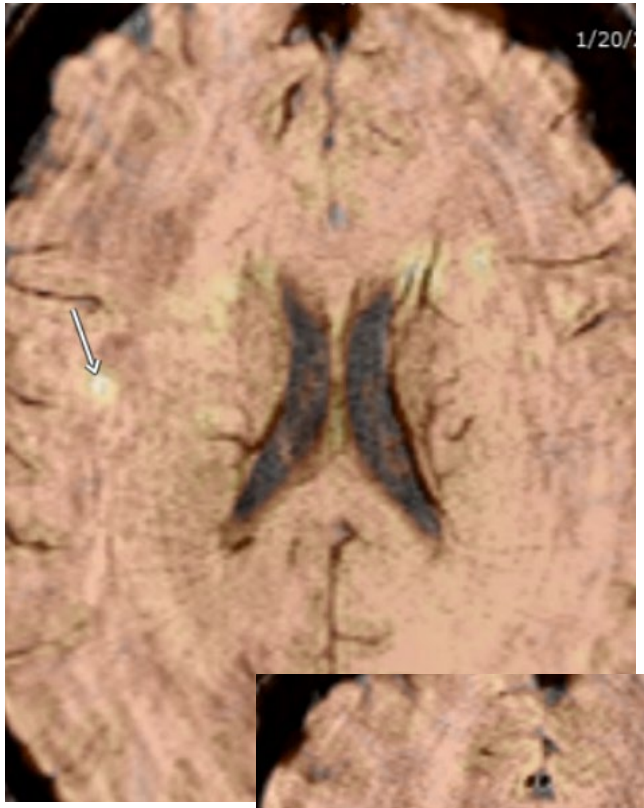
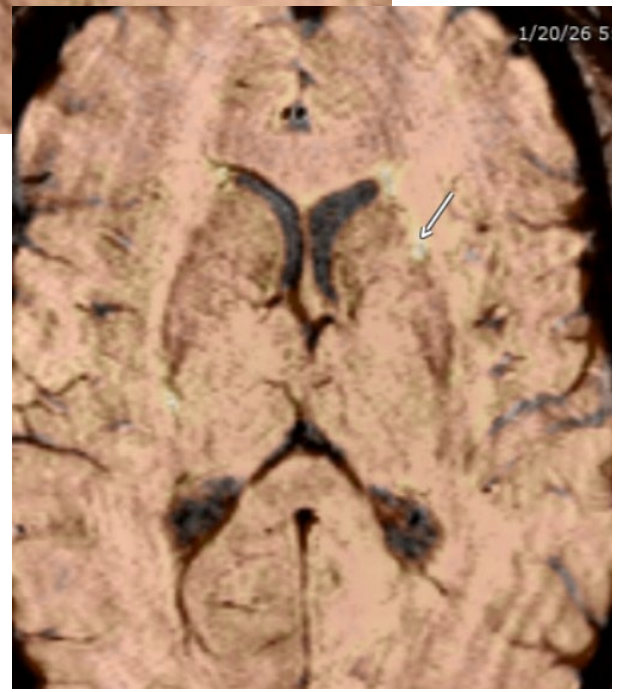




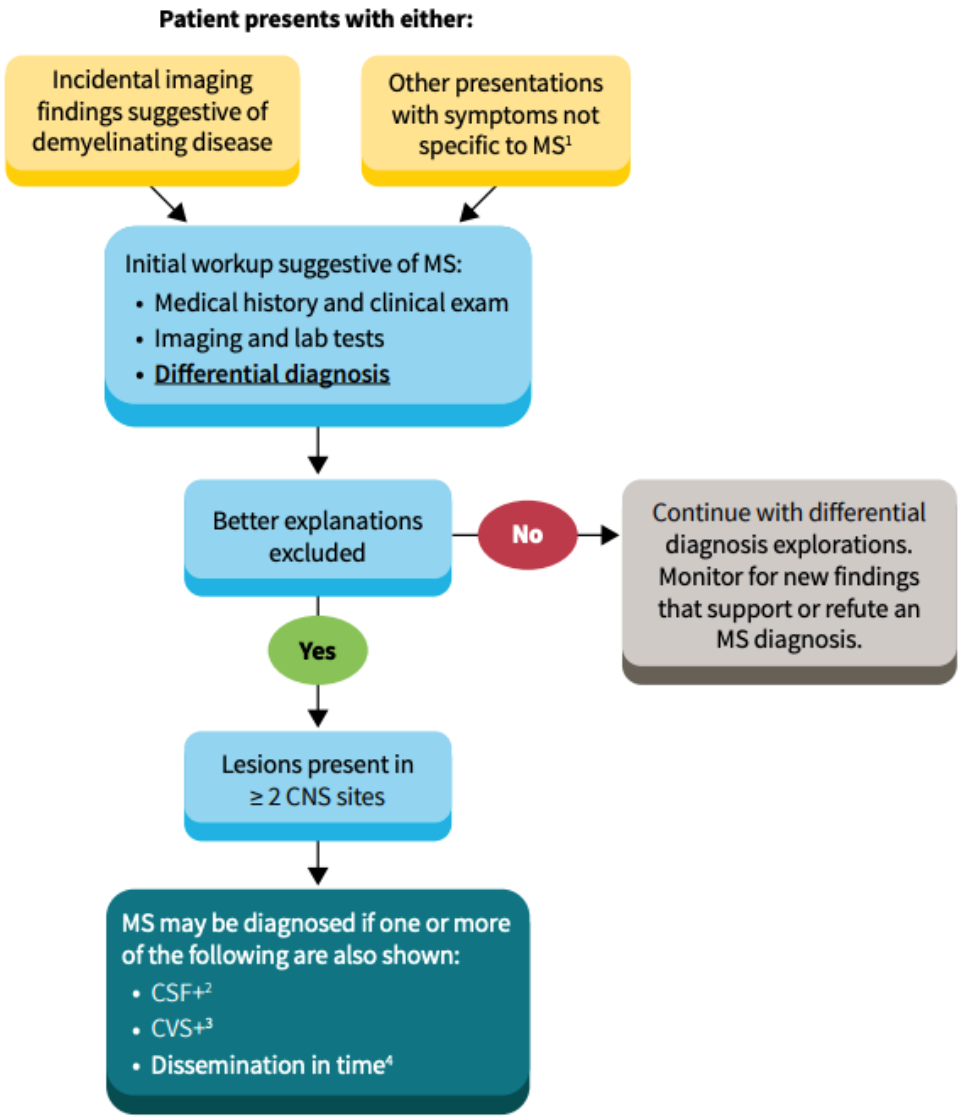

# Case 2

# Case 2

- Does patient have MS by:
  - 2017 McDonald criteria?
    - No, no typical clinical event
    - No DIT
  - 2024 McDonald criteria?
    - Yes, lesions in 2 MS typical regions and CVS+

National Multiple Sclerosis Society

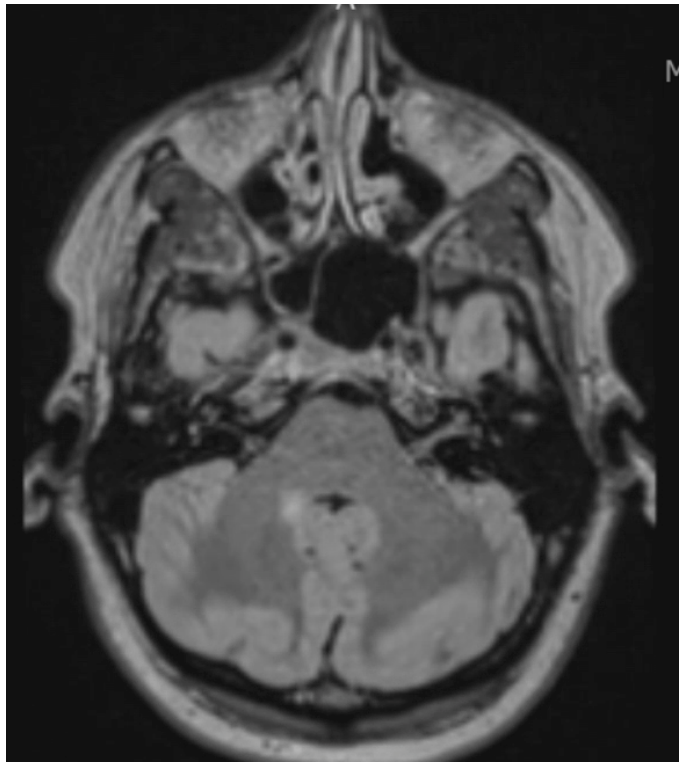
# Diagnostic Algorithm for RIS and Other Non-Specific Presentations

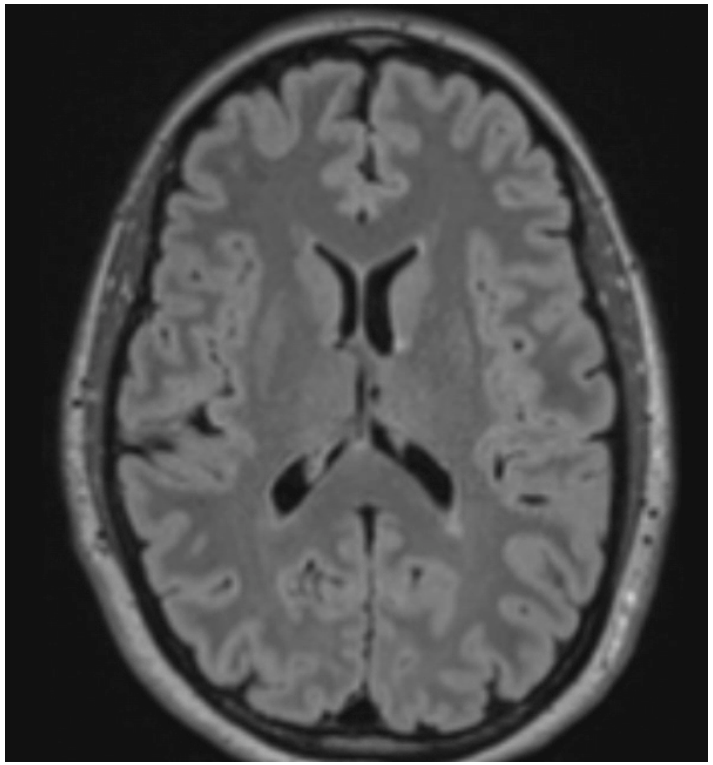


# Case 3

- 48 y/o woman developed double vision, nausea, vertigo, and gait disturbance.
- Admitted – MRI brain with demyelinating lesion in the right MCP, lesion in left PV region
- LP - + OCB
- Mimics negative

# Case 3



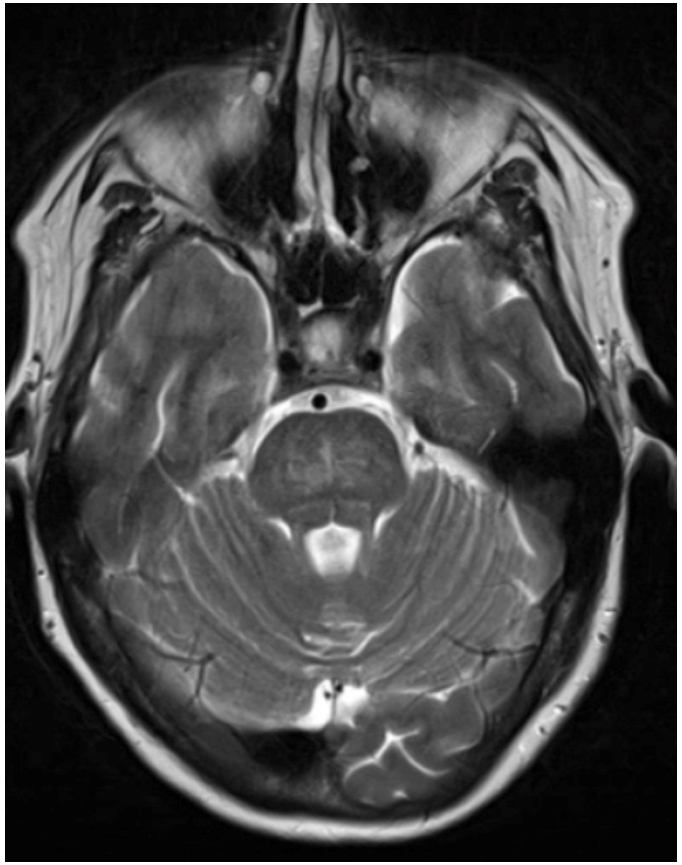
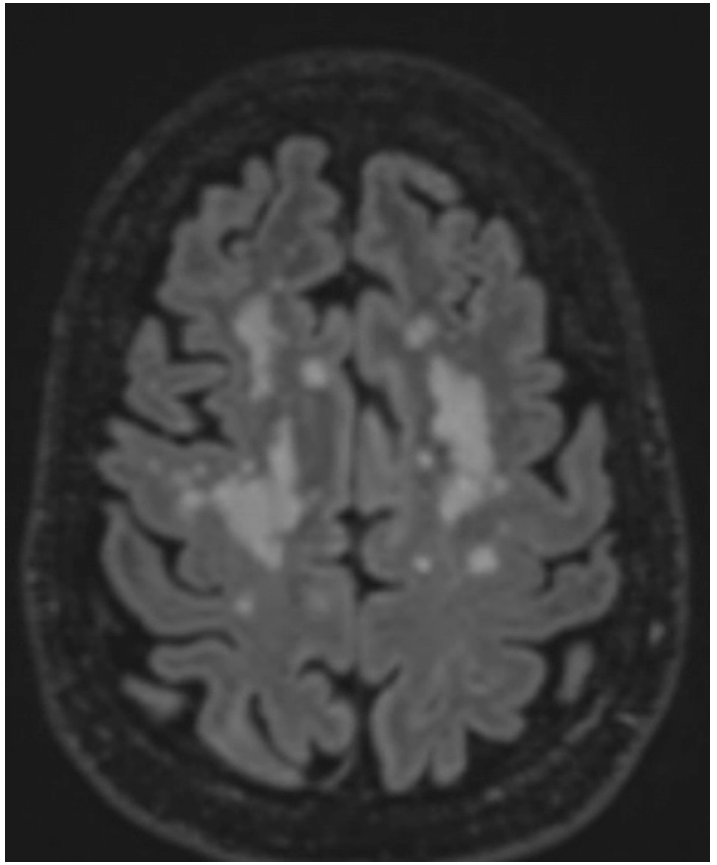
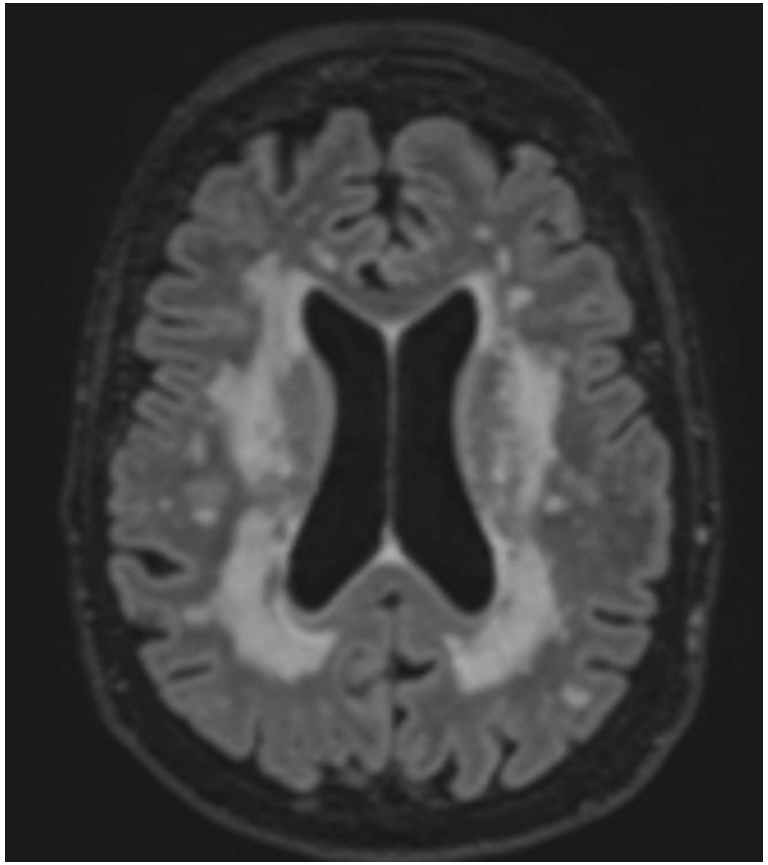


# Case 3

- Does patient have MS by:
  - 2017 McDonald criteria?
    - Yes – DIT met (CSF+) and DIS met (2 MS typical regions)
  - 2024 McDonald criteria?
    - Yes- satisfying 2017 still satisfies 2024 criteria

# Case 4

- 76 y/o woman with symptoms of tremor and abnormal MRI brain.
- Had five-minute episode of double vision in 2017, and a prolonged episode of vertigo lasting weeks 30 years ago.
- Reports symptoms of progressive gait disturbance
- Admits to deconditioning and orthopedic issues
- PMH: HTN, Hyperlipidemia, CKD, CAD
- EXAM: absent AJ bilaterally, esotropia decrease vibration in feet bil, slow walk
- B12 – 144 in 2025, other labs/mimics negative
- MRI- patchy and confluent WM abnormalities, no PV, no juxtacortical, no spinal cord lesions, no CVS

# Case 4

# Case 4

- Does patient have MS by:
  - 2017 McDonald criteria?
    - Unclear – atypical symptoms, diffuse white matter changes in multiple anatomic regions
  - 2024 McDonald criteria?
    - No
    - Caution – multiple vascular risk factors and age > 50
    - CSF pursued – negative kFLC

### *Panel 6:* Recommendations related to older age and comorbidities in the diagnosis of multiple sclerosis

- In patients being considered for a diagnosis of multiple sclerosis presenting at age 50 years and older, multiple sclerosis is more likely to be misdiagnosed
- Small vessel ischaemic disease, psychiatric disorders, and some autoimmune diseases are associated with an increased risk of misdiagnosed multiple sclerosis
- Headache disorders, particularly migraine, are associated with periventricular lesions and an increased risk of misdiagnosis of multiple sclerosis
- In patients who are being considered for a diagnosis of multiple sclerosis presenting at age 50 years and older or with significant vascular risk factors (eg, hypertension, smoking, diabetes, hyperlipidaemia, or known macrovascular disease), additional features are strongly recommended to confirm the diagnosis:
  - A spinal cord lesion
  - CSF positivity by demonstration of intrathecal antibody production with oligoclonal bands or kappa free-light chain index
  - Central vein sign positivity

# Summary of Major Changes – 2024 McDonald Criteria

- The optic nerve may serve a fifth anatomical location
- DIS is fulfilled when two of five anatomical locations show typical lesions, regardless of whether these lesions are symptomatic
- DIT is no longer mandatory for a diagnosis of MS
- The Central vein sign (CVS) on MRI can be used
- Paramagnetic rim lesions (PRLs) on MRI can be used
- The Kappa free-light chair index is interchangeable with OCB in CSF, and can replace it to diagnose MS
- Radiologically isolated syndrome and other non-specific clinical presentations can be MS when specific criteria are met
- Pediatric onset MS and adult onset have same diagnostic framework
- Progressive and relapsing MS represent a unified diagnosis and require unified diagnostic criteria
- Additional criteria are recommended when diagnosing MS in people over 50 years or with vascular comorbidities

# IMPACT of 2024 Revisions

- CIS now can be classified as MS right away in many cases
- RIS now can be diagnosed as MS in many cases
- Earlier diagnosis, earlier treatment, less disability
- One framework for all forms of MS (relapsing, progressive, pediatric, etc)
- CSF / LP less often necessary

Thank you!!!