Multiple Sclerosis acadeMe
Personalized medical education

MERCK MEDICAL GRAND ROUNDS

DIAGNOSING MS

Based on the 2024 McDonald criteria[1]

- Modifications to the use of DIS
- The optic nerve as a 5th anatomical location
- DIT is no longer required to diagnose MS
- kFLCs are now interchangeable with OCBs
- Addition of CVS and PRLs to increase specificity
- RIS is MS if specific criteria are met
- Additional requirements for diagnosis in special populations

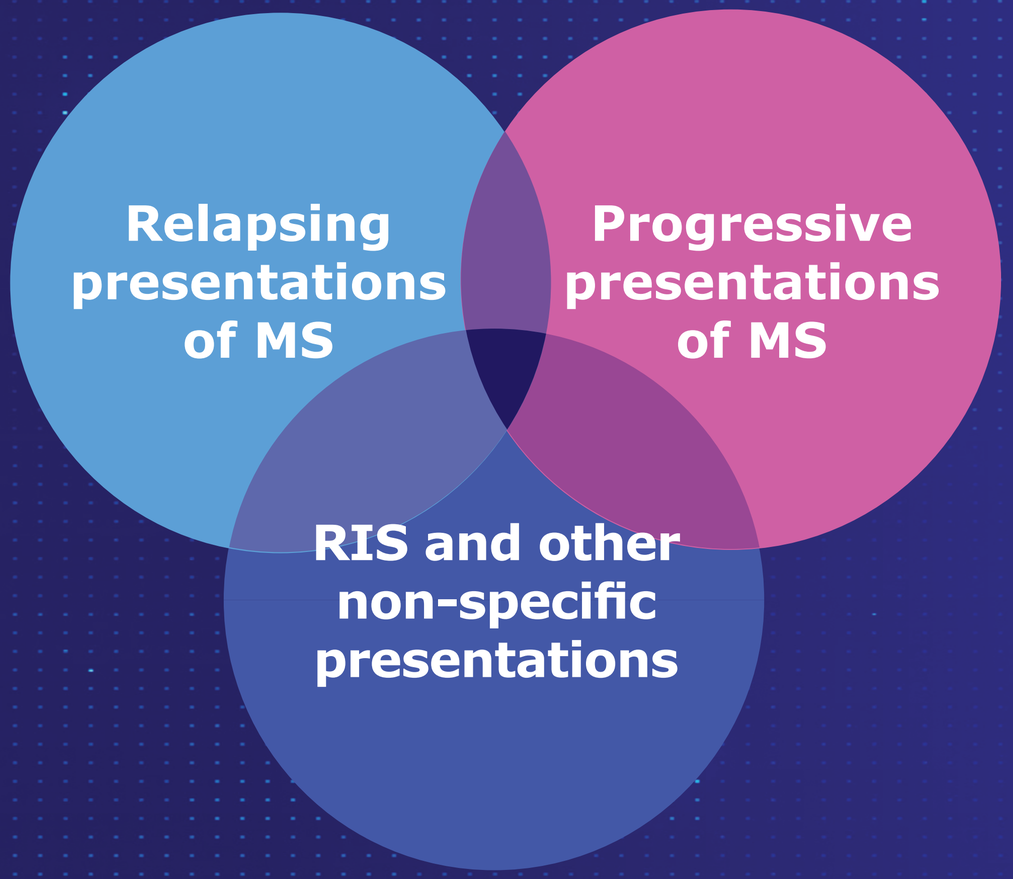
Fundamental principles for MS diagnosis

Essential role of paraclinical diagnostic tests[1,2]

While clinical history and examination remain fundamental, the diagnosis of MS should be corroborated by **paraclinical tests**

CVS, **kFLCs**, and **PRLs** can be used, when available, to support diagnosis and increase specificity

Modalities of presentation guide the acquisition of paraclinical evidence[1,2]



Global implementation of the diagnostic criteria[1,2]

Inclusion of paraclinical tools presents challenges for global implementation; however, the diagnostic framework is **flexible** and **can be adapted** to fit the **local availability of resources** and the **requirements of each patient**

Unified framework for MS diagnosis

A single diagnostic criteria framework should be applied to relapsing-onset and progressive-onset MS[2]

Initial clinical assessment

- Typical relapsing onset
- Typical progressive onset
- Incidental MRI findings (RIS)
- Non-specific symptoms

Exclude other diagnoses

Assess number of regions with lesions

Possible regions: juxtacortical/cortical, periventricular, infratentorial brain, spinal cord, and optic nerve

4–5 regions[a] | **2–3 regions** | **1 region**[a]

No paraclinical tools required

One tool required

Two tools required

Apply paraclinical tools

Positive CSF:
- OCBs and/or kFLCs

Further lesion characterization:
- CVS and/or PRLs[b]

Demonstration of other regions:
- Brain and/or spinal cord MRI[c] and/or
- Optic nerve MRI, VEP, OCT

DIT:
- MRI (Gd+) and/or clinical/MRI follow-up

Diagnosis of MS

Continue monitoring if inconclusive

Figure adapted from Moccia M et al. "Implementation of the 2024 revision of the McDonald criteria for multiple sclerosis", Nat Rev Neurol 2025; doi: 10.1038/s41582-025-01141-3, Springer Nature.

To be diagnosed with MS, individuals with RIS or other non-specific presentations should have MRI lesions in ≥2 anatomical locations and ≥1 additional feature among DIT or positive CSF or CVS.[1]

[a]Only for typical relapsing or progressive onset, and if no other region can be demonstrated, using CVS and/or PRLs and positive CSF and/or DIT; [b]PRLs apply only in cases in which only one region is affected; [c]Two spinal cord lesions are considered as two regions in typical progressive onset.

Recommendations for PPMS, older, and paediatric patients

PPMS[1]

- PPMS requires evidence of clinical progression extending at least 12 months
- ≥2 spinal cord lesions count as 2 regions for PPMS

Aged ≥50 years and/or with significant vascular disease/risk factors[1,a]

Additional features are strongly recommended to confirm diagnosis:

- ≥1 spinal cord lesion
- Presence of OCB/kFLCs
- CVS positivity (Select 6)[b]

Paediatric MS[1]

- A single diagnostic criteria framework should be applied to adult-onset and paediatric-onset MS
- For children aged <12 years with CNS demyelination, MOG-IgG testing using a cell-based assay is strongly recommended

[a]Hypertension, smoking, diabetes, hyperlipidaemia, or known macular disease; [b]CVS or PRLs may aid diagnosis but are not required.

Implementation of the revised McDonald criteria

OCT and VEPs in the 2024 McDonald criteria[1,3,a]

Provided no better explanation exists, the following support optic nerve injury:

OCT:
pRNFL inter-eye difference of ≥6 µm or composite GCIPL inter-eye difference of ≥4 µm

VEP:
P100 latency delay or asymmetric interocular VEP latencies (2.5 SD above the mean in both cases)[b]

Positive CSF in the 2024 McDonald criteria[4]

A positive CSF is defined by a kFLC index of ≥6.1 or by the presence of oligoclonal bands in CSF

- In the 2024 criteria, kFLCs in CSF are interchangeable with OCBs to demonstrate intrathecal IgG synthesis
- Where MS is strongly suspected but kFLCs are not elevated, CSF should be sent for OCB detection for confirmation and vice versa

2024 MAGNIMS-CMSC-NAIMS consensus recommendations on the use of MRI for the diagnosis of MS[5]

- Diagnostic imaging should always cover the brain and spinal cord and include susceptibility-sensitive sequences for assessment of CVS and PRLs
- T2-weighted FLAIR sequences (preferably in 3D) for identifying brain lesions
- Initial exam should include administration of intravenous Gd-based contrast agents
- Optic nerve MRI is recommended for initial presentation of optic neuritis
- Use of fat-saturated sequences is recommended for detecting symptomatic optic nerve lesions

Refer to paper for MRI protocols for the brain, optic nerve, and spinal cord

[a]OCT and VEP interpretation should be done according to the quality control criteria and other parameters outlined in the companion paper; [b]Exact numerical measures depend on technical and methodological factors and are centre and device dependent.

Abbreviations
CMSC, Consortium of Multiple Sclerosis Centers; CNS, central nervous system; CSF, cerebrospinal fluid; CVS, central vein sign; DIS, dissemination in space; DIT, dissemination in time; FLAIR, fluid-attenuated inversion recovery; GCIPL, ganglion cell and inner plexiform layer; Gd, gadolinium; Gd+, gadolinium-enhancing; IgG, immunoglobulin G; kFLC, kappa free light chain; MAGNIMS, Magnetic Resonance Imaging Network in Multiple Sclerosis; MOG-IgG, myelin oligodendrocyte glycoprotein immunoglobulin G; MRI, magnetic resonance imaging; NAIMS, North American Imaging in Multiple Sclerosis Cooperative; OCB, oligoclonal band; OCT, optical coherence tomography; PPMS, primary progressive MS; PRL, paramagnetic rim lesion; pRNFL, peripapillary retinal nerve fibre layer; RIS, radiologically isolated syndrome; RRMS, relapsing–remitting MS; SD, standard deviation; VEP, visual evoked potential.

References
1. Montalban X et al. Lancet Neurol 2025;24:850–65; **2.** Moccia M et al. Nat Rev Neurol 2025; doi: 10.1038/s41582-025-01141-3; **3.** Saidha S et al. Lancet Neurol 2025;24:880–92; **4.** Deisenhammer F et al. eBioMedicine 2025;120:105905; **5.** Barkhof F et al. Lancet Neurol 2025;24:866–79.

GL-NONNI-02573 | February 2026