# *Multiple Sclerosis*

"The Great Mimic"

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# *History of MS*

- Other clinical names-
- -disseminated sclerosis
- -encephalomyelitis disseminata

- First described by Jean-Martin Charcot in 1868
- Many anecdotal reports suggest the disease has been recognized since 1200.

# *Diagnosis*

- Auto-immune disease that affects the myelin sheath of axons (demyelination)
- Nerve cells of the brain, spinal cord are unable to communicate with one another.
- Young adults-predominantly females
- Incurable. A progressive complex of symptoms, findings, disability and death
- Treatment is designed to slow progression

# *Risk factors*

Ages between 20 to 40 years

Northern European descent

Female – women 3 to 1 ratio to men

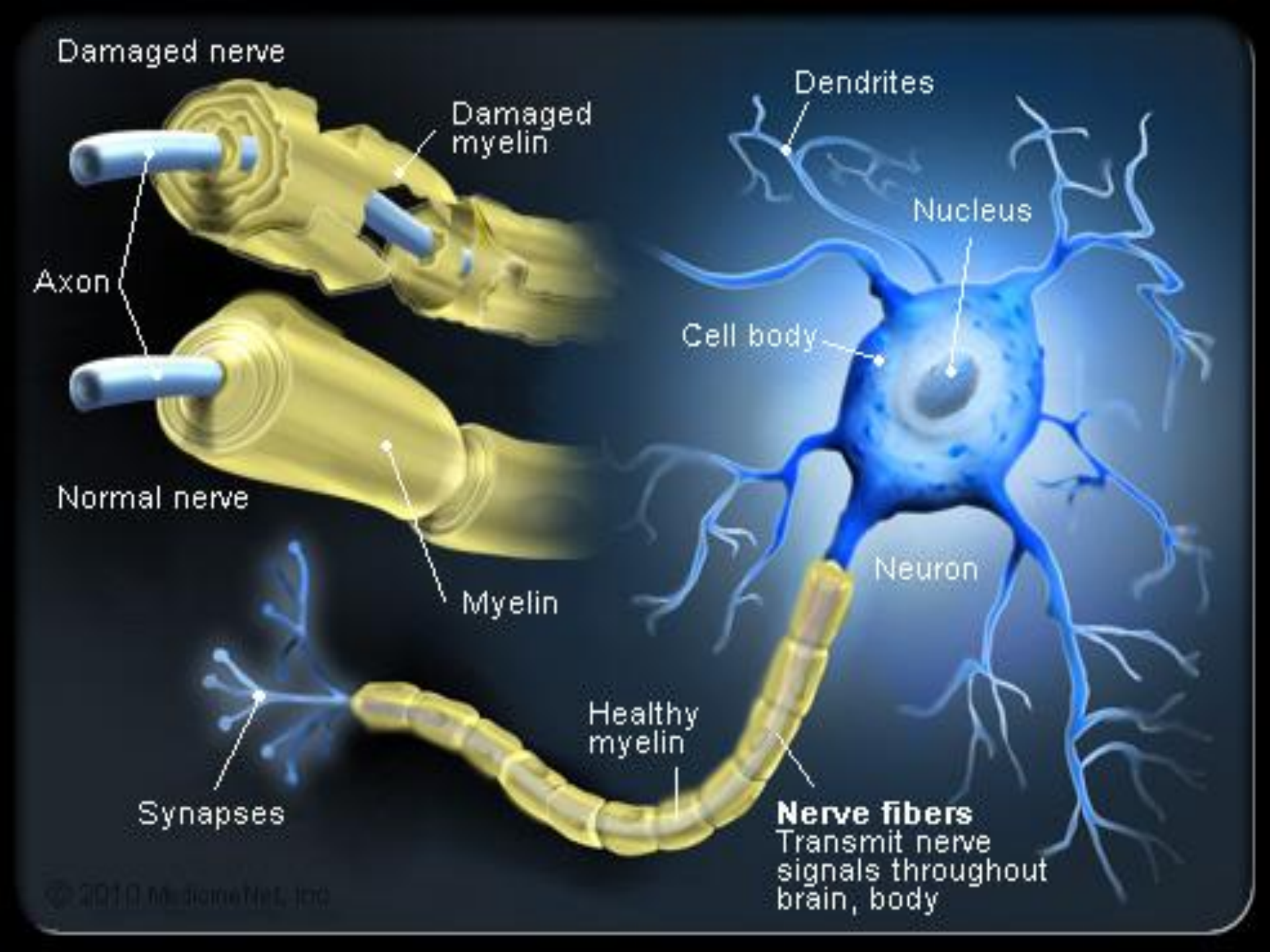
Low levels of Vitamin D

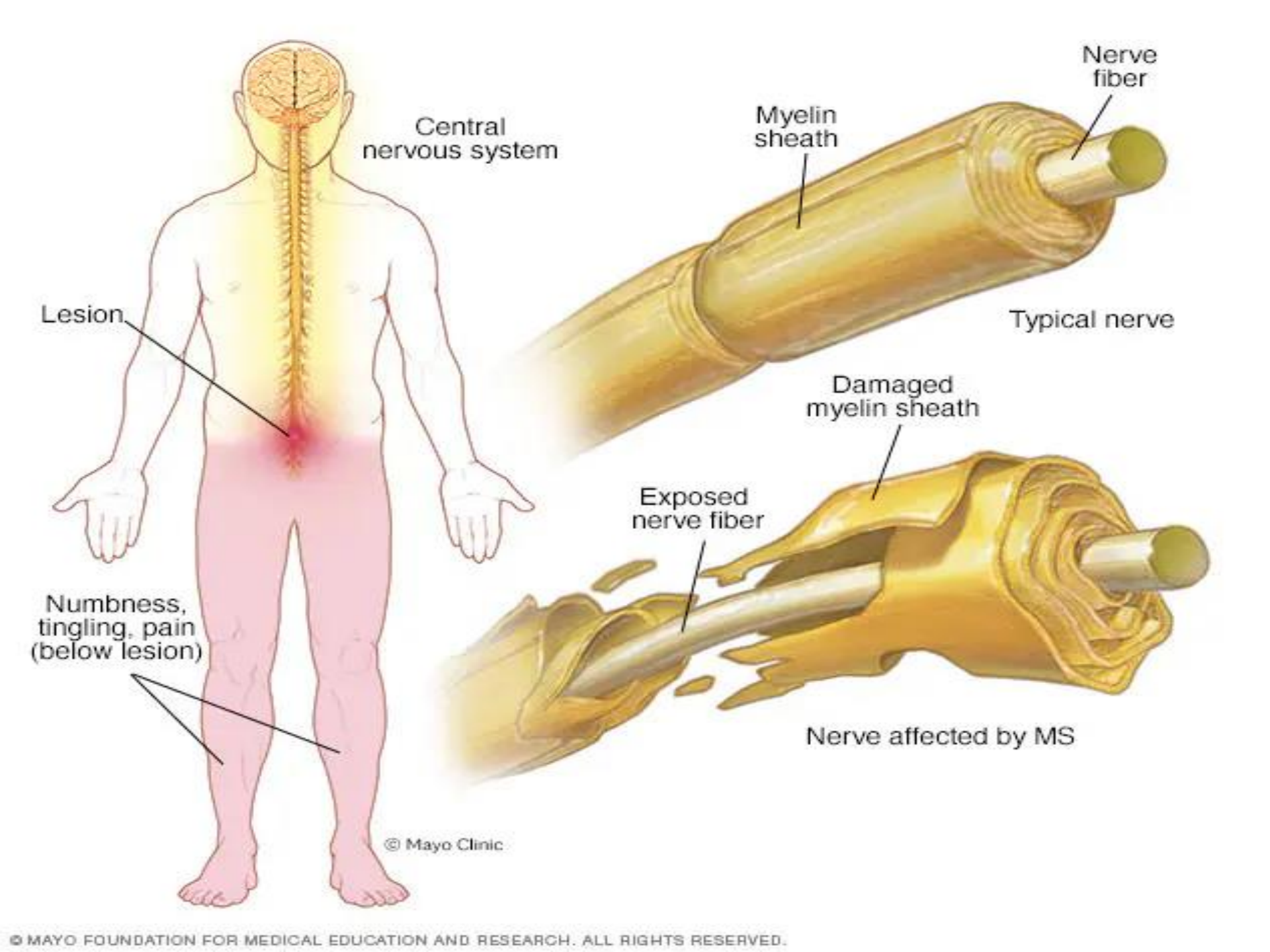
Genetic predisposition

Exposure to Epstein Barr Virus (EBV)

Childhood obesity

Toxin exposures including smoking


Damaged nerve
Damaged myelin
Axon
Normal nerve
Myelin
Dendrites
Nucleus
Cell body
Neuron
Synapses
Healthy myelin
Nerve fibers
Transmit nerve signals throughout brain, body



# *Great Mimic*

- The initial symptoms are varied, vague and extremely difficult to link to a specific cause
- Numbness, tingling, muscle weakness, changes in cognition, nystagmus, optic neuritis, diplopia, difficulty swallowing or speaking, unexplained fatigue or depression
- Early symptoms often increased with stress of increased heat (Uhthoff's phenomenon)

# Lhermitte's Sign

Patient may report an electrical shock-like sensation shooting down the spine and any combination of extremities with certain head movements or postures, especially active cervical flexion.

# Potential Triggers of Uhthoff's Phenomenon

Hot and humid weather

Direct sunlight

Using a hairdryer

Exercise

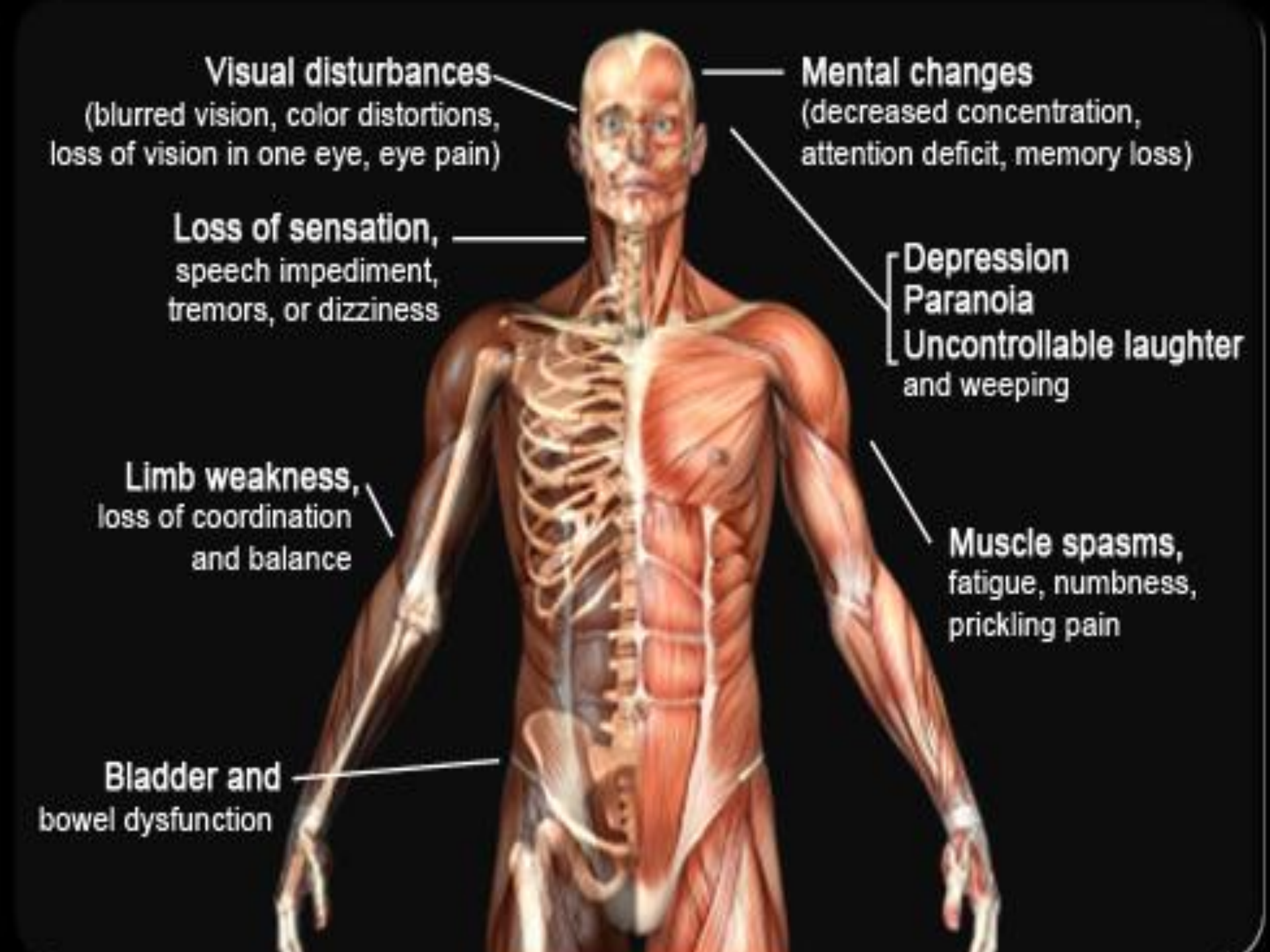
Saunas or hot tubs

Hot/warm showers or baths

A fever from an infectio

Hormonal fluctuations

well


Visual disturbances
(blurred vision, color distortions, loss of vision in one eye, eye pain)
Mental changes
(decreased concentration, attention deficit, memory loss)
Loss of sensation,
speech impediment, tremors, or dizziness
Depression
Paranoia
Uncontrollable laughter
and weeping
Limb weakness,
loss of coordination and balance
Muscle spasms,
fatigue, numbness, prickling pain
Bladder and
bowel dysfunction

# *Physical examination*

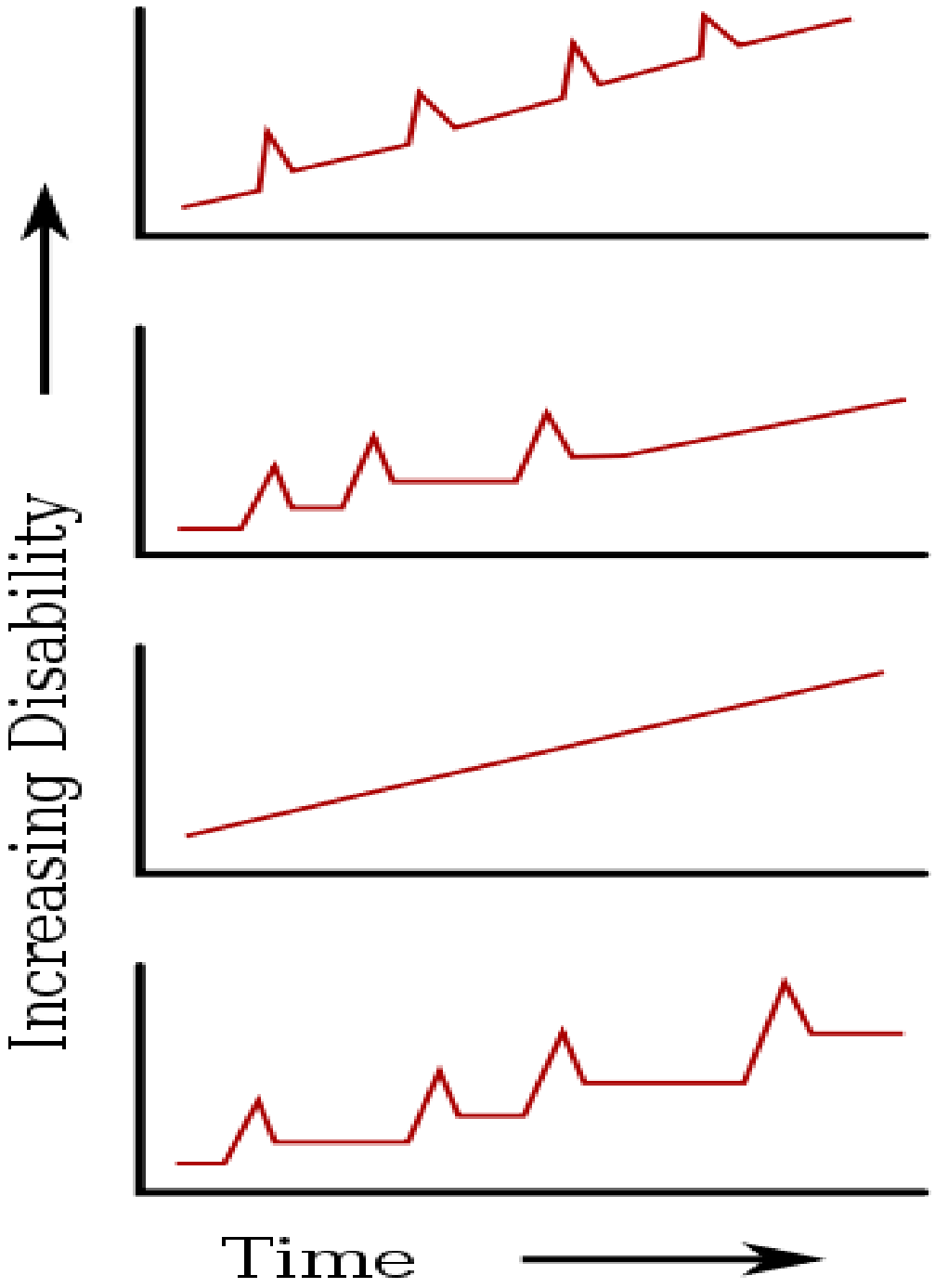
- Often very non-focal. Mild motor weakness. Non-dermatomal sensory loss
- Llhermitte's phenomenon
- Optic Neuritis
- INO-intranuclear ophthalmoplegia
- Myelopathy-seen with transverse myelitis
- Motor weakness. Fatigability of muscles with activity
- Spasticity
- Ataxia
- MMSE

# *Clinical testing*

- SSEP-somatosensory evoked potentials
- VEP- visual evoked potentials
- +CSF for increased IgG synthesis and oligoclonal bands
- MRI-brain/spinal cord w/gadolinium
- McDonald ‘s criteria-clinical, laboratory and radiographic evidence
- NPS
- Myelin Basic Protein- CSF

# *Classification of MS*

- Relapsing-remitting-periods of clinical worsening that resolves with time. However, baseline function is not restored
- Secondary progressive (galloping MS)
- Primary progressive-later onset w/minimal recovery
- Progressive relapsing-progressive decline with superimposed attacks (Devic's dz)




*Progressive-relapsing multiple sclerosis*

Steady decline since onset with super-imposed attacks.

*Secondary progressive multiple sclerosis*

Initial relapsing-remitting multiple sclerosis that suddenly begins to have decline without periods of remission.

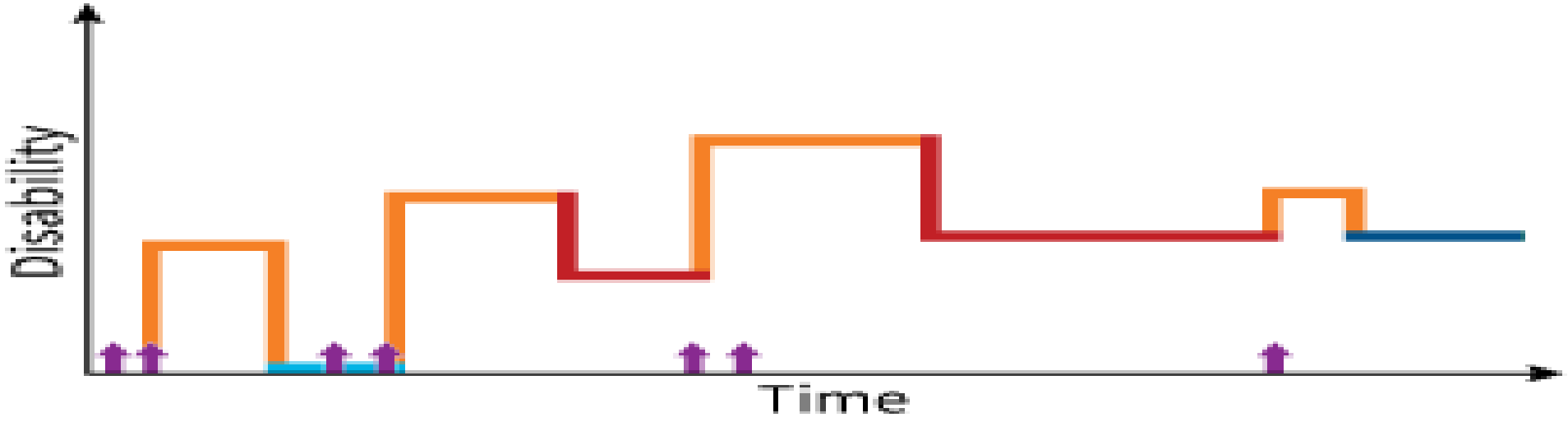
*Primary progressive multiple sclerosis*

Steady increase in disability without attacks.

*Relapsing-remitting multiple sclerosis*

Unpredictable attacks which may or may not leave permanent deficits followed by periods of remission.

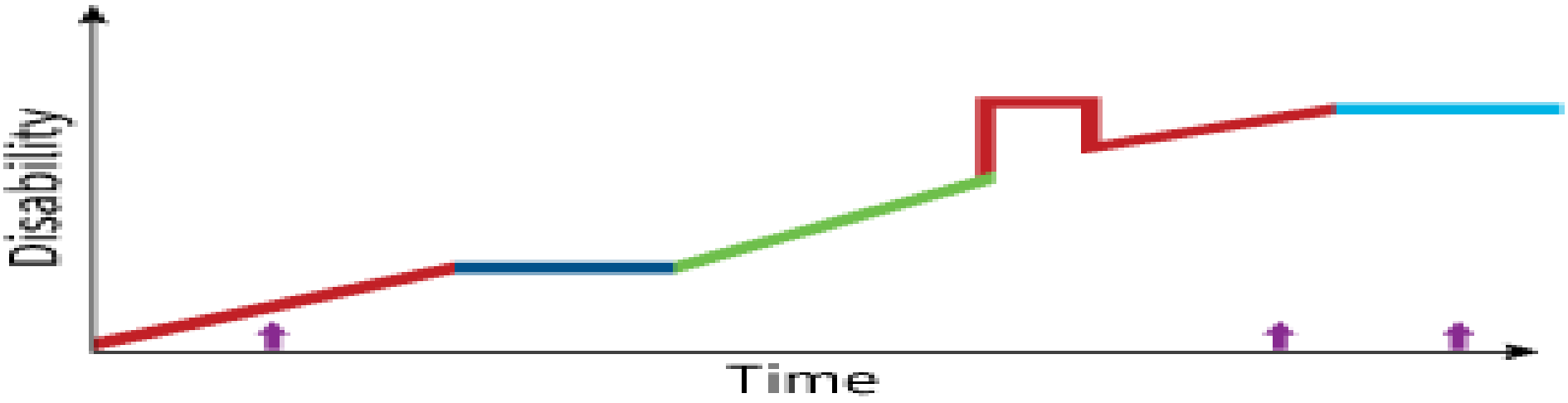
# RRMS




- Relapse
- Active without worsening
- Worsening (incomplete recovery from relapse)
- Stable without activity
- New MRI activity

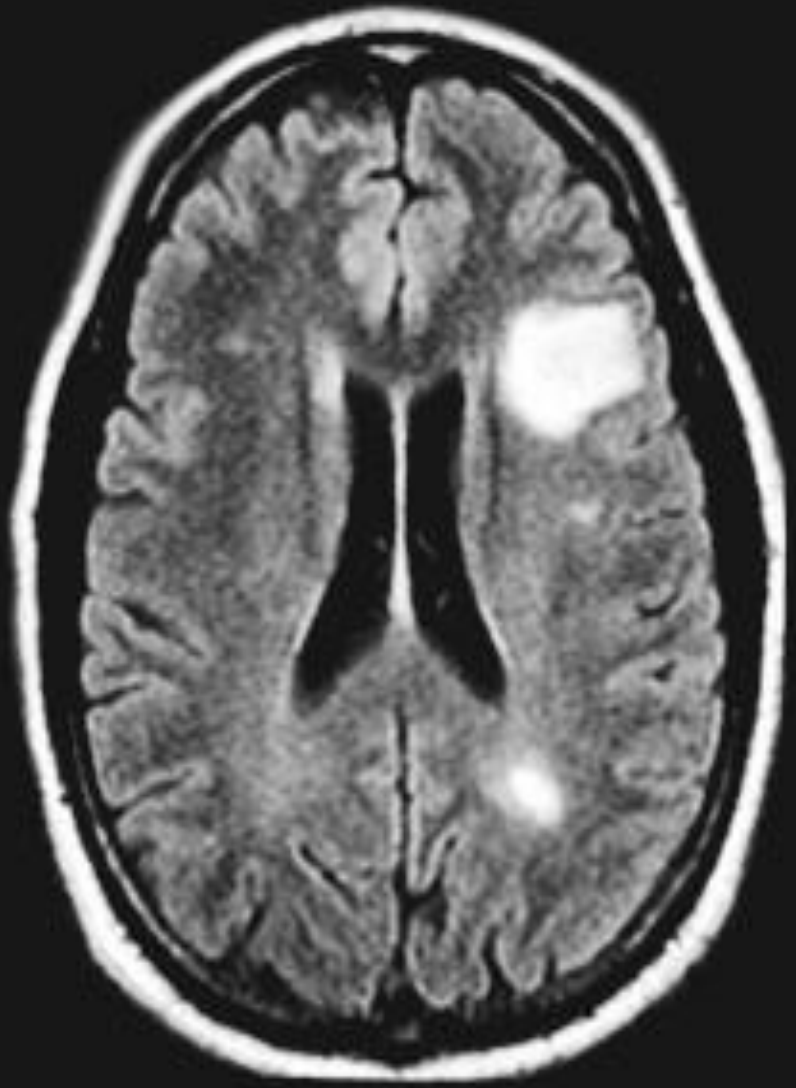
Source: Lublin et al., 2014.

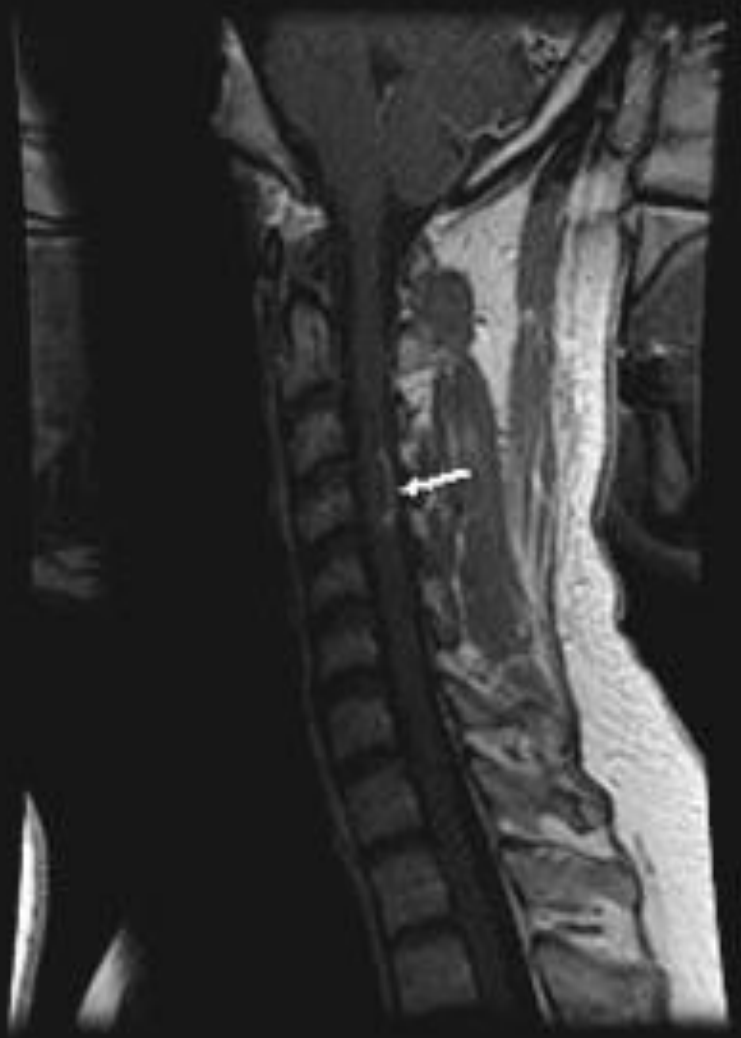
# PPMS

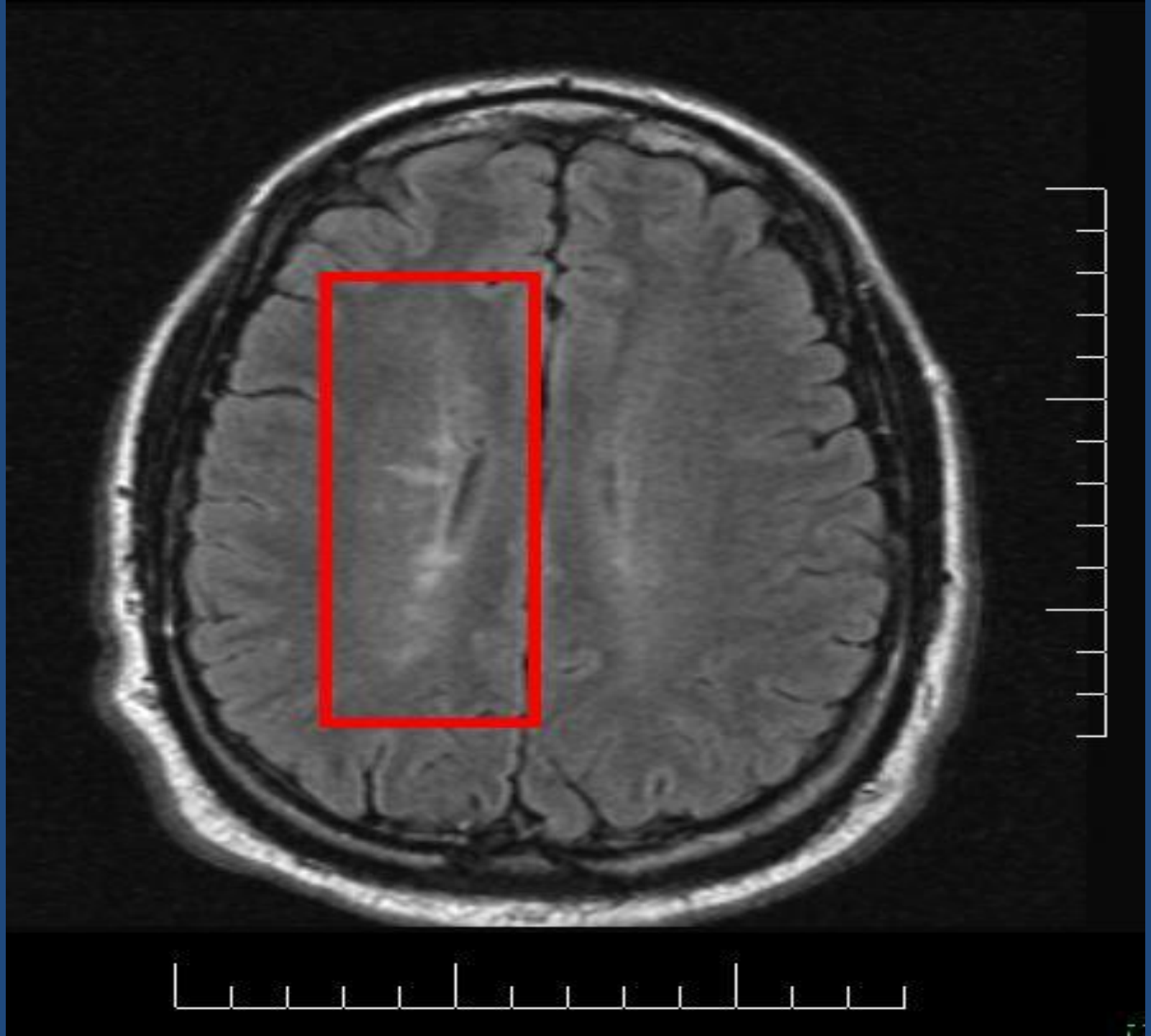


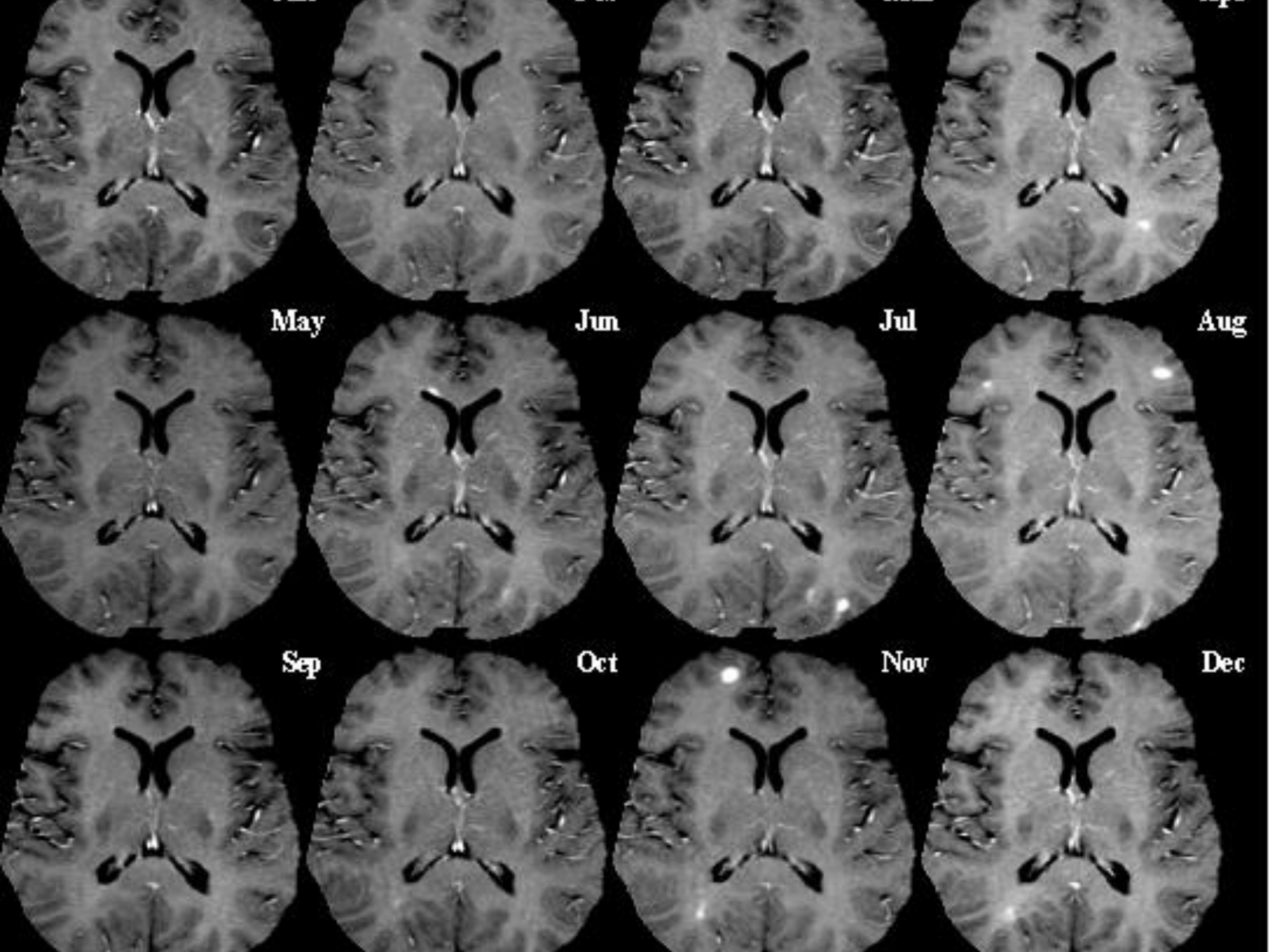

- Active (relapse or new MRI activity) with progression
- Not active without progression (stable)
- Not active with progression
- Active without progression
- New MRI activity

Source: Lublin et al., 2014.








May
Jun
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Aug
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Oct
Nov
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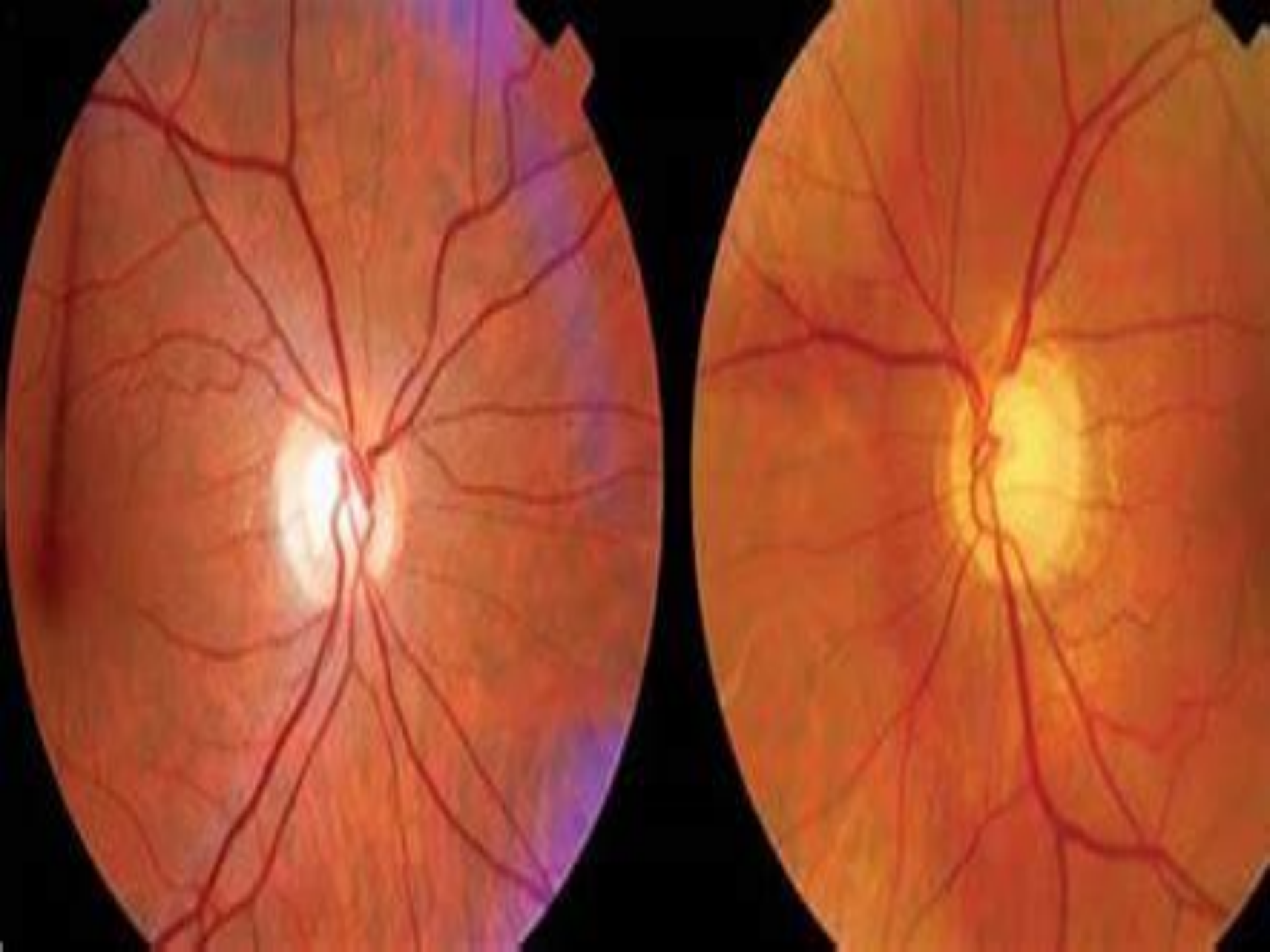
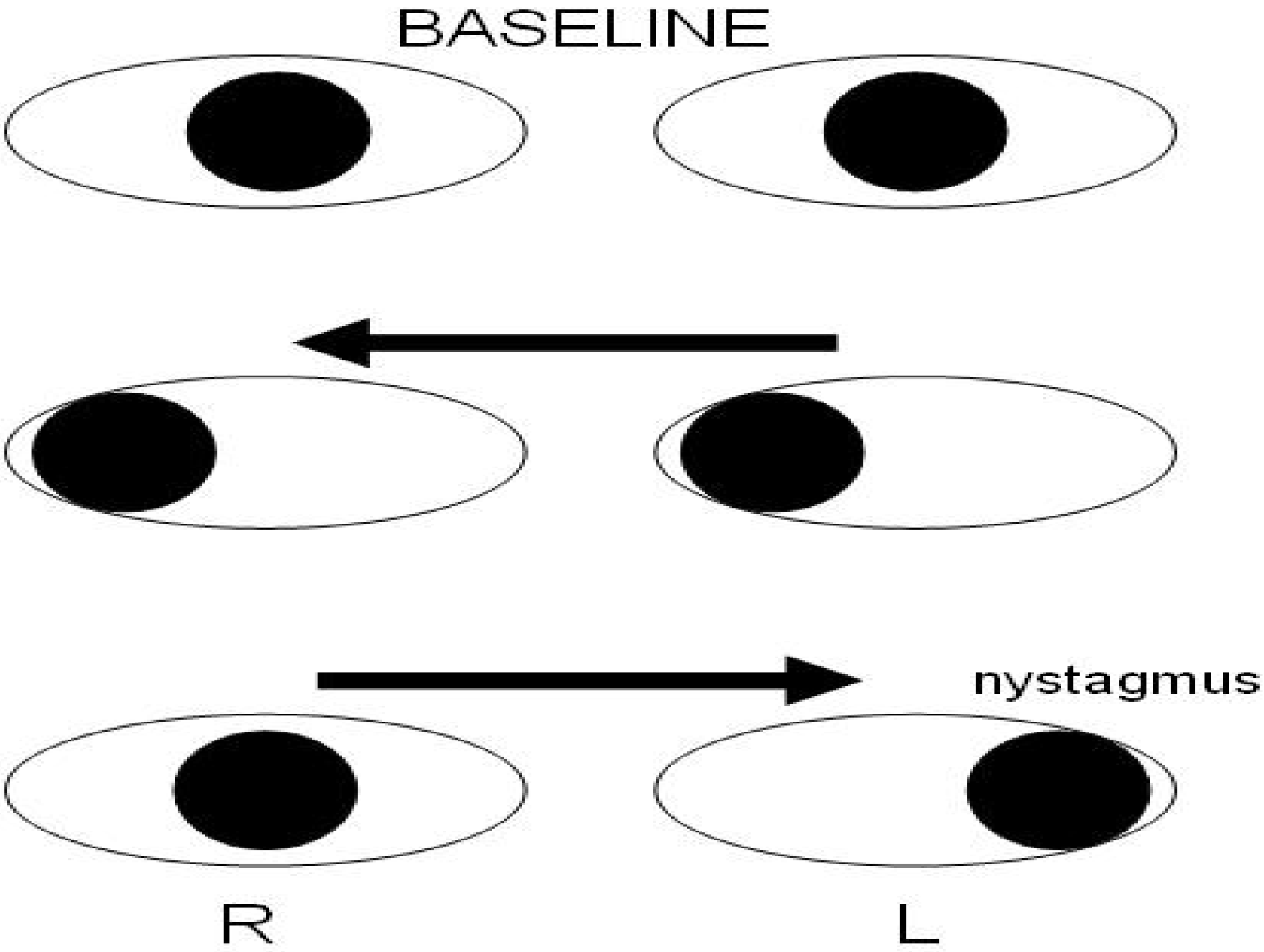
R15




BASELINE
nystagmus
R
L


ATAXIA

# *Disability*

- 25 foot walk test-

  normal- 5 seconds- men

  - 6 seconds- women

- EDSS-Expanded Disability Status Scale

  Steps from 0 to 10

  1.0-4.5 individuals - fully ambulatory

  5.0 – 9.5 - ambulatory impairment

  10.0 – death

  A claimant with an EDSS of 5.0 or > would typically be disabled.

# EXPANDED DISABILITY

## Status Scale


healthline

# *Treatment*

Fatigue- Amantadine, Provigil, Nuvigil, Ritalin, Amphetamine

Muscle spasm- Baclofen-sometimes given per continuous pump

Neurogenic bladder-Detrol, oxybutynin

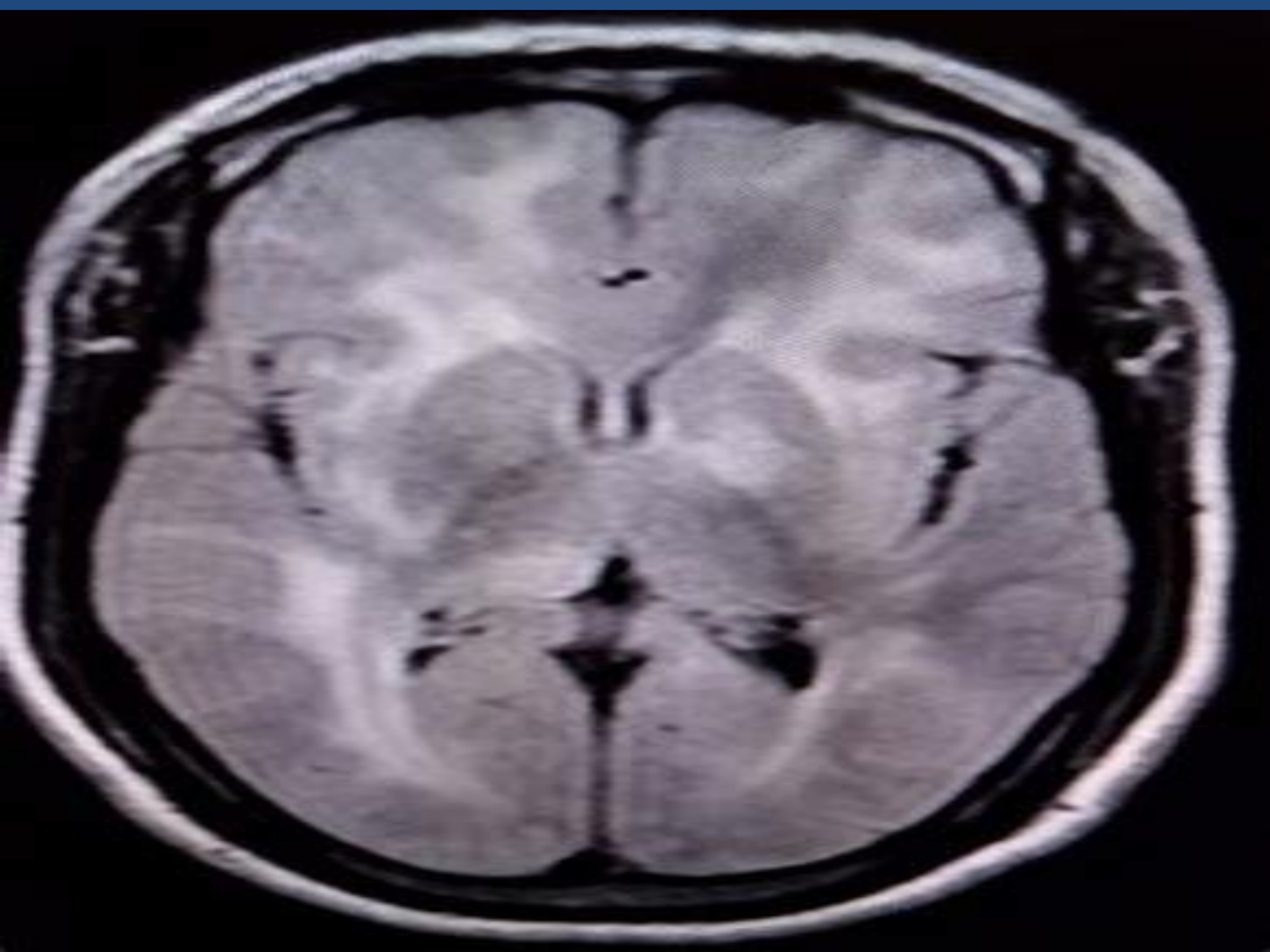
Acute flares- IV steroids- Solu-Medrol

Maintenance- IFN-Avonex, Betaseron, Rebif and Copaxone (no longer)

Progressive disease- Mitotraxone, Tysabri

# *New Treatments*

- Extavia- Interferon
- Cladribine- antineoplastic
- Rituximab- biologic agent-antineoplastic
- Myelin Basic Protein Supplement
- Oral therapies are being developed
- Tysabri(natalizumab) must screen for the presence of JC virus. Significant side effect PML



# *Oral therapies*

- Aubagia (teriflunomide) – 10000/month

-relapse rate of 30%

- Gilenya (fingolimod) – 11200/month

- both prevent T-cells from getting out of a LN into the bloodstream causing more inflammation and demyelination. (54%)

- Tecfidera (dimethyl fumarate) -4800/mo.

-anti-inflammatory and prevents immune cells from entering the brain and spinal cord

| | | | |
|---|---|---|---|
| Plegidry | - | IF B1a | SQ |
| Vumerity | - | Dimethyl fumarate | Oral |
| Gilenya | - | Fingolimod | Oral |
| Zeposia | - | Ozanimod | Oral |
| Kesimptra | - | Ofatumumab | SQ |
| Mavenclad | - | Cladribine | Oral |
| Lemtrada | - | Alemtuzumab | Oral |
| Ocrevus | - | Ocerlizumab | IV |
| Zunovo | | | |
| Trodelvy | - | Sacituzumab | IV |

- 11.09 *Multiple sclerosis,* characterized by A or B:
- **A.** Disorganization of motor function in **two** extremities (see 11.00D1), resulting in an **extreme** limitation (see 11.00D2) in the ability to stand up from a seated position, balance while standing or walking, or use the upper extremities; or

11.09 B – MARKED limitation in physical function (11.00 G3a) and in one of the following,

1. Understanding, remembering, or applying information (see 11.00G3b(i)); or
2. Interacting with others (see 11.00G3b(ii)); or
3. Concentrating, persisting, or maintaining pace (see 11.00G3b(iii)); or
4. Adapting or managing oneself (see 11.00G3b(iv)).

- B. Marked limitation (see 11.00G2) in physical functioning (see 11.00G3a), and in one of the following:

Clinical History:
10/2022: Was vacationing at Disneyland with her children when she noticed abrupt onset of right leg weakness; initially felt her symptoms were due to strain/overuse but symptoms continue to worsen; also reported concurrent right lower extremity numbness and tingling
3/2023: **MRI** of thoracic and lumbar spine with chronic degenerative changes; lower extremity **EMG** without evidence of significant radiculopathy or neuropathy; she was later seen by spine clinic who suggested PT for ongoing weakness, which did not help as prolonged walking, standing/activity exacerbated her weakness
6/2023: Sensation of right arm "locked up" intermittently and she was able to use her phone; has continued to have chronic issues with dexterity in her right hand, including dropping objects due to weakness; denies pain or sensory loss in her hand; was carrying a pot of hot water to the bathroom and her right leg buckled causing hot water to be splashed over multiple regions of her body and second-degree burns
9/2023: Repeat **MRI** lumbar spine ordered by her chiropractor was unchanged; spine clinic then referred her to pain clinic as well as neurology clinic

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10/13/2023: Seen in general neurology clinic for right lower extremity weakness in the setting of longstanding back pain associated with scoliosis
11/2023: Lumbar puncture with negative MBP, negative OCBs
12/2023: diagnosed with relapsing remitting multiple sclerosis
2/2024: started ocrelizumab infusions

MS **Diagnosis**:
2017 McDonald criteria met for **diagnosis** of multiple sclerosis, subtype is RRMS. **Diagnosis** year 2023.
Dissemination in space: Multiple bilateral periventricular greater than subcortical cerebral white matter and left thalamic T2/FLAIR lesions; presence of juxtacortical lesions
Dissemination in time: RLE weakness (October 2022), RUE weakness June 2023

Symptom onset: 10/2022
**Diagnosis** year: 12/2023

AQP4/MOG: not tested

MS DMT History:
Ocrelizumab (2/2024 - present): tolerating well with some flu-like sometimes afterwards

MS Relapse History:
10/2022: right leg weakness with paraethesia
6/2023: right arm feeling "locked up" intermittently, right arm weakness

2017 McDonald criteria met for **diagnosis** of multiple sclerosis, subtype is RRMS. **Diagnosis** year 2023.
Dissemination in space: Multiple bilateral periventricular greater than subcortical cerebral white matter and left thalamic T2/FLAIR lesions
Dissemination in time: RLE weakness (October 2022), RUE weakness June 2023
Workup for MS mimics: CSF
Progressive disability: Yes
Treatment/Disease modifying **therapy** (DMT): None prior
Activity: Last clinical relapse June 2023. Last radiographic progression - no active disease on November 2023 **MRI** .

Several of the left-sided - white matter periventicular T2/FLAIR lesions appear almost completely involuted c/w remote MS lesions. Large, left periventricular/corona radiata lesion is the lest-involuted (more recent) - although is no longer-enhancing/diffusion restriction on **MRI** -this would mostlikely localize to her right leg +/- recent right arm weakness in late 2022. CSF obtained November 2023 reassuringly bland with no OCBs and MBP < 4 - this can be artificially low/negative early in disease course; consider repeating if aberrant clinical trajectory.

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DMT is indicated for suspected RRMS (see disease criteria below). Given size and number of prior lesions, and recent clinical relapse ~ within 1 year) - intermittent vs high efficacy **therapy** is indicated. Studies have demonstrated that African American females are at high risk of both severity and frequency of relapse in RRMS which indicates her for higher-efficacy **therapy**. Pending screening labs, ocrelizumab would be indicated and likely appropriate choice.

Examination documented +4/5 motor weakness of the hip flexors and knee flexors.

+2/5 for the dorsiflexors. R foot drop with steppage gait. Knee mildly hyperextended.

RUE – 4/5 wrist extensor/wrist flexor. No RAM or assessment of motor function for the digits.

Decreased sensation to the R lower extremity.

Fatigue but does not take naps. No medications for fatigue

25’ walk – 10.6 seconds

Thank you for your kind attention!