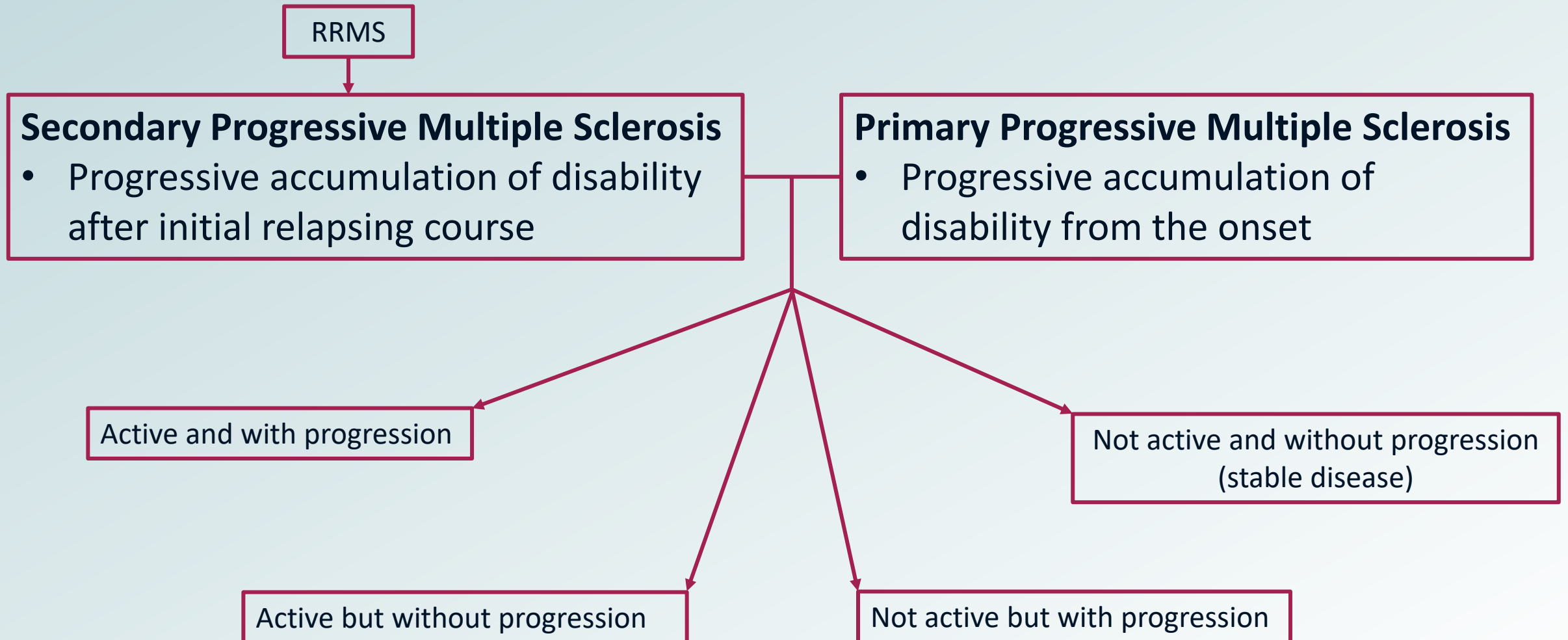


# Types of Progressive Multiple Sclerosis

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# Definitions of “Activity” and “Progression”

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**Activity** – defined by either clinical or MRI criteria

- Relapses, either acute or subacute episodes of new or increasing neurologic dysfunction, followed by full or partial recovery, in the absence of fever or infection
- and/or*
- Gadolinium-enhancing lesion or new or unequivocally enlarging T2 lesions

## **Progression**

- Accrual of disability, independent of any relapse activity, during the progressive phase of MS – either PPMS or SPMS

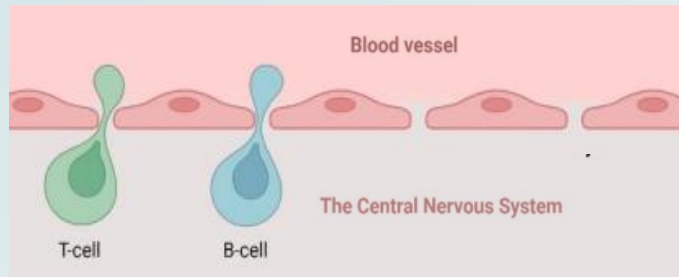
The definitions of “activity” or “progression” should include a specified time frame – typically of one year

# Different Pathology for Different Phenotypes?

- Overlapping pathologies underlying relapsing and progressive mechanisms
- Below is a simplified description of major differences

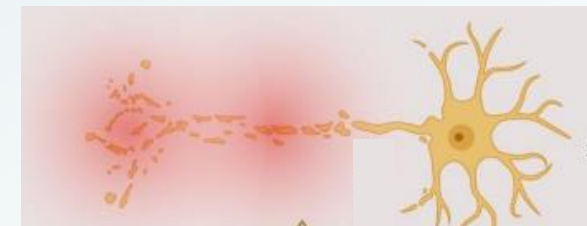
## Relapsing-Relmitting Disease

- Characterized by lymphocyte-mediated inflammation infiltration across damaged blood-brain barrier
- Blood-brain barrier damage is greatest in RRMS, allowing lymphocyte infiltration into CNS



## Progressive Disease

- Primarily due to widespread injury and loss of neurons (axons and cell bodies)
- Microglia and macrophage-mediated inflammation predominates
- Greater demyelination and meningeal inflammation than in RRMS
- PPMS: disease process begins much earlier than initial symptoms



CNS, central nervous system; PPMS, primary progressive multiple sclerosis; RRMS, relapsing-remitting multiple sclerosis.

Yong HYF et al. *Nat Rev Neurol*. 2022;18:40-55.

Illustration adapted from Sandi D et al. *Int J Mol Sci*. 2022;23:5162. ([CC BY 4.0](#)).