

# Multiple Sclerosis

RTS 5

## Different Phenotypes:

Multiple sclerosis (MS) is a chronic inflammatory demyelinating disease of the central nervous system<sup>1</sup> and the history of clinical diagnostic criteria demonstrates the evolution from the rather tentative classifications of restricted value to a more elaborate scheme.<sup>2</sup> With that being said, there are four different types of MS that show the different ways in which it develops and presents itself: clinically isolated syndrome (CIS), relapsing-remitting MS (RRMS), secondary progressive MS (SPMS), and primary progressive MS (PPMS).

Clinically isolated syndrome (CIS) is a first episode of neurologic symptoms caused by inflammation and demyelination in the central nervous system. The episode, by definition must last for at least 24 hours, is characteristic of MS but does not yet meet the criteria for a diagnosis of MS. Relapsing-remitting MS (RRMS) is the most common disease course and is characterized by clearly defined attacks of new or increasing neurologic symptoms. These attacks (relapses or exacerbations) are followed by periods of partial or complete recovery (remissions). During remissions, all symptoms may disappear, or some symptoms may continue and become permanent. However, there is no apparent progression of the disease during the periods of remission. At different points in time, RRMS can be further characterized as either active (with relapses and/or evidence of new MRI activity) or not active, as well as worsening or not worsening (as seen in Figure 2).<sup>3</sup>

Secondary progressive (SPMS) follows an initial relapsing-remitting course. Most people who are diagnosed with RRMS will eventually transition to a secondary progressive course in which there is a progressive worsening of neurologic function and accumulation of disability. SPMS can be further characterized at different points in time as either active (with an occasional relapse and/or evidence of new MRI activity) or not active, as well as with progression (evidence of disease worsening on an objective measure of change over time, with or without relapse or new MRI activity) or without progression (as seen in Figure 2).<sup>3</sup> Primary progressive MS (PPMS) is characterized by worsening neurologic function or accumulation of disability from the onset of symptoms, without early relapses or remissions. PPMS can also be further characterized at different points in time as either active or not active, as well as with progression or without progression (as seen in Figure 2).<sup>3</sup>

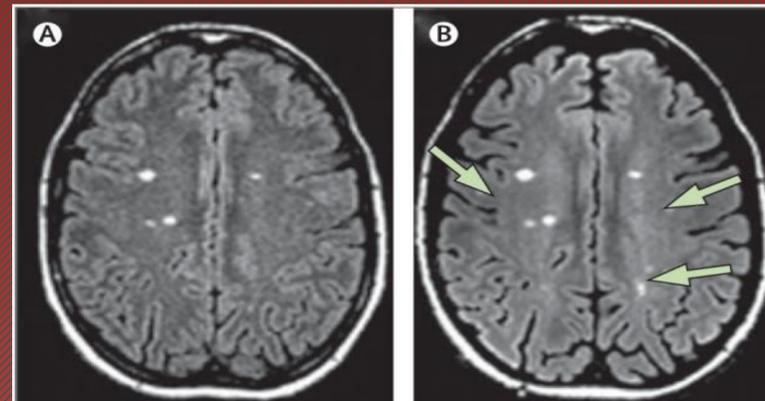


Figure 1. Axial FLAIR images from a 48 year-old woman with SPMS on a 1.5 tesla scanner (A) vs. a 3.0 tesla scanner (B).<sup>8</sup>

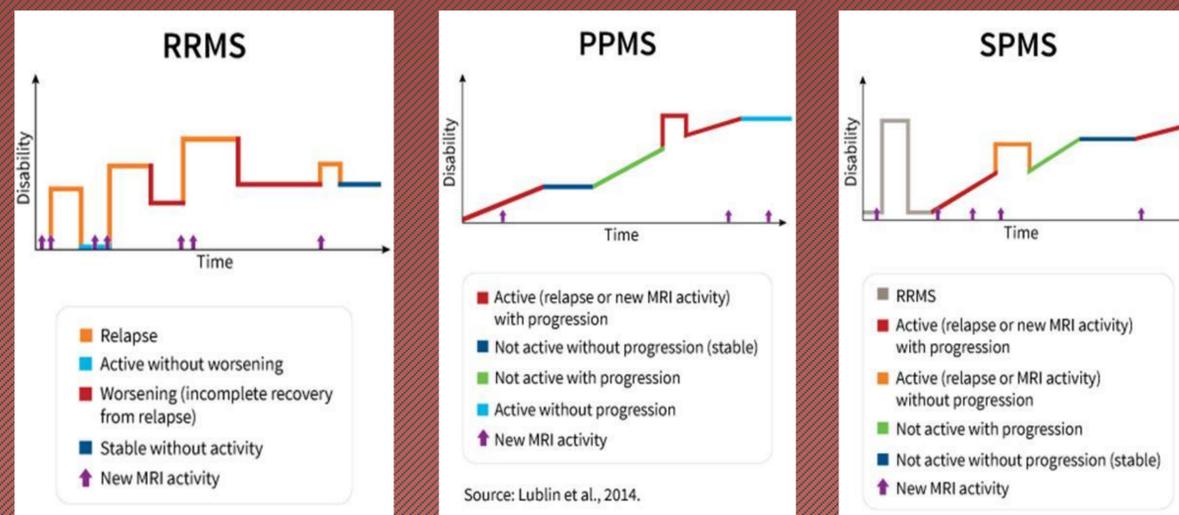


Figure 2. Graphical representation of relapsing-remitting MS, primary progressive MS, and secondary progressive MS in regards to disability and time.<sup>3</sup>

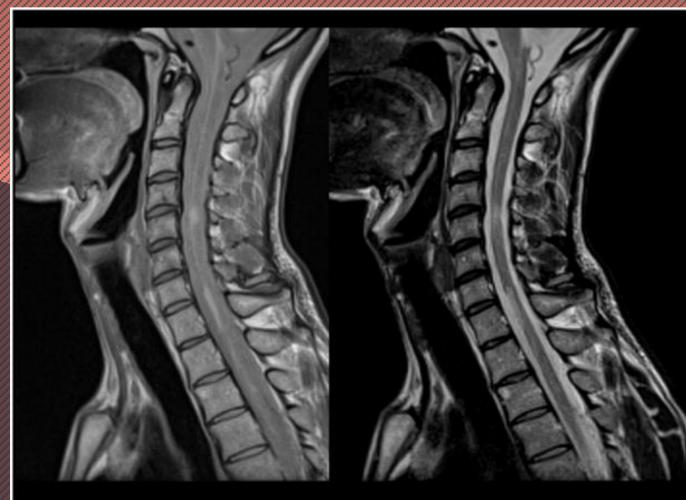


Figure 3. Sagittal intermediate and T2-weighted dual echo fast-spin echo images of the spinal cord in a patient with MS. Note the presence of abnormalities both at the cervical and thoracic level of the cord.<sup>7</sup>

## Causes and Risk Factors:

The etiology of MS remains elusive.<sup>4</sup> With that being said, scientists believe that it is triggered by a combination of immunologic, environmental, and genetic factors. Because of the lack of understanding of causation, all therapies are expected to be ongoing life-long therapies as long as they remain safe and effective.<sup>5</sup> Epidemiologists have been studying disease patterns in large groups of people and looking at the variations in geography, demographics, and migrations patterns of areas where MS is more frequently known to occur. They also look at other factors such as vitamin D, smoking, and obesity. In regards to genetics, MS is not an inherited disease and therefore cannot be passed down generations however, there is a genetic risk component that can be passed down and inherited.

## Imaging Technique:

Magnetic resonance imaging has been used to confirm the diagnosis and determine efficacy of disease-modifying treatments for MS. This is done through measurement of new lesion counts in which there is a strong correlation between the effect on new lesion formation and the effect on relapses.<sup>6</sup> A T1 weighted brain MRI will supply information about current disease activity by highlighting areas of active inflammation when injected with gadolinium. On the other hand, T2-weighted images give off information about disease burden or lesion load which is the total amount of lesion area, both old and new. These image weighting differences can be seen in Figure 3.<sup>7</sup> Fluid attenuated inversion recovery (FLAIR) images are used to better identify these brain lesions associated with MS (see Figure 1).<sup>8</sup>

## References:

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