

Transcript Details

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MS: A Progressive Disease From the Start

Announcer:

Multiple Sclerosis (MS) is a chronic inflammatory and neurodegenerative disease of the central nervous system, or CNS.^{1,2}

Although the exact cause of MS is not clear¹, the pathogenic process involves the lymph nodes where T and B cells interact, initially outside the CNS, and later probably also in follicles inside the CNS.¹

B cells are critical for mounting healthy immune responses. They release cytokines to protect the body from infection, produce antibodies to capture and eliminate antigens, and present antigens to T cells.³ When T cells encounter B cells presenting antigen in the lymph node, T-cell differentiation and proliferation are triggered.⁴

In people with MS, B cells capture auto-antigens derived from neurons or their myelin sheaths and present peptides they generate from these auto-antigens to T cells within the lymph nodes, thereby promoting activation of pathogenic (encephalitogenic) T cells.⁴ In other words, B cells direct T cells to attack the body's CNS tissue.³

Homing signals—much like a GPS—help these autoreactive B cells and T cells navigate to the CNS, where they drive inflammation that damages the brain and/or spinal cord by inducing de-myelination, axonal damage and impaired transmission of nerve impulses.^{4,5} B cells may also produce pathogenic antibodies that contribute to the development of MS.³

MS is often characterized by relapses, disability progression, lesions and grey and white matter damage.⁶

Every person's MS journey is unique, but many diagnosed with relapsing-remitting MS advance to secondary progressive MS, or SPMS.^{7,8}

Inflammation and neurodegeneration damage myelin and axons from the start, though compensatory repair mechanisms may mask the initial clinical signs of this damage, making it difficult to identify progression early.^{6,9-12}

In relapsing-remitting MS, progression occurs alongside relapses,¹¹ driven by peripheral inflammation and lymphocyte infiltration of the CNS.^{10,13}

As MS progresses, central inflammation and neurodegeneration become more prominent; compensatory repair mechanisms become exhausted and irreversible gray and white matter damage occurs.^{6,11,14}

References:

1. Bittner S, Ruck T, Wiendl H, Grauer OM, Meuth SG. Targeting B cells in relapsing-remitting multiple sclerosis: from pathophysiology to optimal clinical management. *Ther Adv Neurol Disord*. 2017;10(1):51-66.
2. Haider L, Zrzavy T, Hametner S, et al. The topography of demyelination and neurodegeneration in the multiple sclerosis brain. *Brain*. 2016;139(Pt 3):807-815.
3. Archelos JJ, Storch MK, Hartung HP. The role of B cells and autoantibodies in multiple sclerosis. *Ann Neurol*. 2000;47(6):694-706.
4. Fletcher JM, Lalor SJ, Sweeney CM, Tubridy N, Mills KH. T cells in multiple sclerosis and experimental autoimmune

- encephalomyelitis. *Clin Exp Immunol.* 2010;162(1):1-11.
5. Pender MP, Greer JM. Immunology of multiple sclerosis. *Curr Allergy Asthma Rep.* 2007;7(4):285-292.
 6. Mahad DH, Trapp BD, Lassmann H. Pathological mechanisms in progressive multiple sclerosis. *Lancet Neurol.* 2015;14(2):183-193.
 7. Ontaneda D, Thompson AJ, Fox RJ, Cohen JA. Progressive multiple sclerosis: prospects for disease therapy, repair, and restoration of function. *Lancet.* 2017;389(10076):1357-1366.
 8. Larochelle C, Uphaus T, Prat A, Zipp F. Secondary Progression in Multiple Sclerosis: Neuronal Exhaustion or Distinct Pathology? *Trends Neurosci.* 2016;39(5):325-339.
 9. Cree BAC, Hollenbach JA, et al. Silent progression in disease activity-free relapsing multiple sclerosis. *Ann Neurol.* 2019;85(5):653-666.
 10. Dendrou CA, Fugger L, Friese MA. Immunopathology of multiple sclerosis. *Nat Rev Immunol.* 2015;15(9):545-558.
 11. Pérez-Cerdá F, Sánchez-Gómez MV, Matute C. The link of inflammation and neurodegeneration in progressive multiple sclerosis. *Mult SclerDemyelinating Disord.* 2016;1(9).
 12. Lassmann H, van Horssen J, Mahad D. Progressive multiple sclerosis: pathology and pathogenesis. *Nat Rev Neurol.* 2012;8(11):647-656.
 13. Bradl M, Lassmann H. Progressive multiple sclerosis. *Semin Immunopathol.* 2009;31(4):455-465.
 14. Lassmann H. Targets of therapy in progressive MS. *Mult Scler.* 2017;23(12):1593-1599.