MS is primarily an inflammatory disease with secondary neurodegeneration: con

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Multiple sclerosis is a heterogeneous demyelinating disease of the central nervous system (CNS), with inflammatory and neurodegenerative components, typically causing relapses and remissions of diverse neurological symptoms, followed by accumulation of disability in patients. The exact pathomechanism of MS is not known. The predominant hypothesis assumes that the disease is primarily driven by myelin-autoreactive T cells, which are abnormally activated by environmental factors in immunologically susceptible subjects. It was supported by animal models, which have obvious limitations in human translation of data. However, the primarily inflammatory hypothesis has several flaws. Firstly, while all currently approved MS therapies are directed at the inflammatory component, none of them are definitive cures and the response to therapy is variable across the patient population. Also, if one assumes that axonal degeneration is a result of multifocal inflammatory response, then in primary progressive MS, where brain lesions are typically scarce, it is not plausible. This suggests that there is another pathomechanism leading to disease progression, which may be either primary neurodegeneration, or failure of neuroregeneration strategies. The main evidence for primary role of degeneration in MS was provided by a neuropathological study by Barnett and Prineas (Annals of Neurology 2004). They showed that in newly forming symptomatic lesions there is extensive oligodendrocyte apoptosis with activation of microglia, but few or no lymphocytic infiltrates or myelin phagocytes. Oligodendrocyte degeneration could lead to liberation of autoantigens, resulting in a secondary immunological reaction, whose severity and course are dependent on individual immunological profile of the patient.