The immune-mediated diseases of the central nervous system (CNS) cover a wide range of clinical manifestations. Over the last years, considerable efforts have been made to establish a nosologic concept based upon distinctive pathophysiological characteristics of the single diseases. We describe the historically defined entities of immune-mediated diseases that primarily, but not exclusively, are affecting myelin structures. These include very rare entities as Schilder's, Balo's and Marburg's disease or the chronic and relapsing types of optic neuritis, for which evidence based paradigms still are virtually missing. In other, slightly more frequent diseases as neuromyelitis optica (NMO), advances in the concepts of specific biological features have been achieved and are beginning to transform into changes in clinical concepts. Acute disseminated encephalomyelitis (ADEM) and multiple sclerosis (MS) are by far the most frequent entities in this group and thus the only ones for which extensive empirical data on disease biology and evidence based clinical management strategies exist by now. For the most important entities, clinical features and therapeutic approaches are reviewed on the basis of current evidence. The results of basic science studies are assessed for their implications in nosological classification.