Survey of progress

Chronic relapsing experimental allergic encephalomyelitis: its value as an experimental model for multiple sclerosis

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Summary. Comparison of the pathohistology of chronic relapsing experimental allergic encephalomyelitis (CR-EAE) and multiple sclerosis (MS) reveals a close similarity. Thus, CR-EAE appears to be a valuable model for the study of pathogenetic factors leading to the formation of MS lesions, although the induction of the disease may be different (active sensitization with CNS antigens and adjuvant in CR-EAE versus unknown etiology in MS). CR-EAE furthermore mimicks the pathohistological patterns of other related human inflammatory demyelinating diseases (i.e., acute perivenous leukoencephalomyelitis and acute hemorrhagic leukoencephalomyelitis). The expression of an acute, predominantly inflammatory versus chronic inflammatory demyelinating disease in this model depends upon the time interval between sensitization and sampling of the animals. Recent evidence is discussed that a cooperation between cellular and humoral immune mechanisms, directed against multiple CNS antigens, is responsible for the formation of large demyelinated plaques in EAE and MS.

Key words: Multiple sclerosis – Experimental allergic encephalomyelitis


More than 100 years ago the first detailed description of the pathology of multiple sclerosis (MS) was published by Charcot [10]. This date can be regarded as the starting point of an intense and systematic research effort to clarify the pathogenesis of this disease and determine possible therapeutic approaches. These studies provided an enormous number of detailed results regarding clinical course, epidemiology, pathohistology, ultrastructure, immunology, neurochemistry, and virology, which are summarized in a large number of original articles, reviews, monographs, and symposia proceedings [3, 5, 62, 64, 75].

The major breakthrough in our understanding of MS pathogenesis is, however, still missing. This is at least partly due to the lack of a suitable animal model, which allows individual findings in this disease to be related to their pathogenetic significance.

Experimental allergic encephalomyelitis (EAE) has been regarded as a model for MS since the earliest description by Rivers et al. [57]. In these experiments, which were confirmed later by others [13, 14, 56], a chronic inflammatory demyelinating disease was induced by repeated challenge of susceptible animals with brain homogenate. The necessity for repeated sensitization was later overcome by the introduction of Freunds's adjuvant [22, 44]. EAE was further simplified by the discovery that myelin basic protein (MBP) is the factor responsible for induction of the disease [25, 58]. These two modifications of the sensitization procedure, however, produced an acute monophasic disease of the central nervous system (CNS) with only sparse demyelination, a disease more comparable to acute disseminated leukoencephalomyelitis than to MS [1].

A reproducible model of chronic, sometimes relapsing EAE was first induced by Stone and Lerner [66] in guinea pigs by single sensitization with CNS tissue. In the following years, it became evident that in addition to the inflammatory changes, demyelination and gliafibrillary sclerosis were pronounced in this model [53, 65]. By modification of the sensitization procedure Wisniewski and Keith [78] were able to induce a model of chronic EAE with regular and predictable remissions and relapses. This model will be compared with clinical, pathohistological, and immunological findings in MS.

Requirements for the induction of CR-EAE

Several models of chronic relapsing experimental allergic encephalomyelitis (CR-EAE) have been described. The detailed sensitization procedures are contained in the original publications [24, 42, 47, 66, 78]. There are several requirements for the induction of CR-EAE which differ from those necessary for the induction of acute EAE. One of the most important factors is the use of very high doses of antigen and adjuvant in the sensitization medium [66, 78]. Both the antigen and the adjuvant