PERIPHERAL NEUROPATHY ORCHESTRATED BY NONNEURAL-SPECIFIC T LYMPHOCYTES.

G.K. Harvey,2 R. Gold, K.V. Toyka and H.-P. Hartung
Neurologische Universitätsabteilung, Julius-Maximilians-Universität, Würzburg, Germany. *Institute of Clinical Neurosciences, University of Sydney, Australia.

Neural-specific T cells are held to play a pivotal role in the Guillain-Barré syndrome, and experimental allergic neuritis (EAN). Here, the effects of intranasal accumulation of nonneural-specific T cells on blood-nerve barrier permeability and on a peripheral nerve function were assessed. Rat ovalbumin (OA)-specific T cells were activated in vitro and on day 0 intranasally transferred to female adult Lewis rats. Rats were then given intranasal injections of OA or casin into left and right tibial nerves respectively. On days 3 and 4, selected rats also received intravenous purified immunoglobulin from rabbits with myelin-induced EAN.

Rapid accumulation of OA T cells and E1 + macrophages and marked increases in blood-nerve barrier permeability in OA but not casin injected nerves followed transfer of 2x10⁵ T cells. 5x10⁵ T cells induced decreases in proximal/distal CMAP amplitude ratios but also severe reductions in distal CMAF amplitudes and Wallerian degeneration in OA nerves. Depletion of T cells was occasionally observed in nerves proximal to sites of OA injection. 5x10⁵ T cells also induced decreases in amplitude ratio but with only minor axonal degeneration and reductions in distal amplitudes. Conduction block and demyelination were considered augmented in animals also receiving anti-myelin antibody.

Intranasal accumulation of nonneural-specific T cells can orchestrate demyelination, axonal degeneration, or both.

PERIPHERAL NEUROPATHY ORCHESTRATED BY NONNEURAL-SPECIFIC T LYMPHOCYTES.

A. Henneberg1, H. Imrich1, S. Faber2 and P. Heuser1

Department of Neurology, Heinrich-Heine-University Düsseldorf, Germany

Introduction: For the immunosuppressive treatment of multiple sclerosis (MS) an activity parameter is urgently needed. Since we had found antidiotypic antibodies in the sera of patients with chronic progressive, but not with relapsing-remitting form of MS, we were interested in confirming earlier results and in looking, whether the brain antibodies might be used as a tool for monitoring therapeutic effects. Here we report on antidiotypic antibodies in the sera of patients with chronic progressive, but not with relapsing-remitting form of MS.

Patients and Methods: Sera and cerebrospinal fluids (csf's) of 91 MS patients were tested on normal human pons tissue and other CNS tissues using an indirect immunofluorescence assay. The csf's were concentrated 1:40 before use.

Results: 1. Sera of patients with relapsing-remitting disease were antibody-negative also on other CNS tissues. 2. Sera of patients with chronic progressive MS were antibody-positive in about 80%, showing a tendency for antibody-increase before the symptoms worsened. 3. Csf's of patients with relapsing-remitting and chronic progressive MS were antibody-positive in about 50%. The binding was inhibited by IgG-antibodies (in the sera by IgG4). 4. Sera and csf's of the same patients showed differences in antibody-binding, after a "mix-up" of the cfs to the liposomal membranes becomes, relative like the sera of the same patient.

Conclusions: Chronic progressive MS patients show antibody binding to pons tissue, while relapsing-remitting patients do not. Those antibodies might be useful for being aware of a soon deterioration of the patient. These antibodies cannot be found in cfs of long untreated patients. After "crossing" the cfs' by several courses of lipomembranes, the antibodies suddenly appear in the cfs' of severe-positive patients. Lack of antibody might be wrong for getting an activity parameter in MS.

B CELL ACTIVITY IN IMMUNE-MEDIATED NEUROPATHIES: CELLULAR REQUIREMENTS AND CYTOKINE EFFECTS ON SYNTHESIS OF ANTI-GM1 ANTIBODIES

F. Hessendorf1 and P. Heuser2

Department of Neurology, Heinrich-Heine-University Düsseldorf, Germany

Introduction: We have previously reported on pokeweed mitogen (PWM) induced synthesis of anti-ganglioside GM1 antibodies (anti-GM1) by peripheral blood mononuclear cells (PBMC) from patients with the acute Guillain-Barré syndrome (GBS) and with multifocal motor neuropathy (MMN) (Hessendorf et al., 1994). We now aim to further characterize the immune mechanisms involved in the activation of GM1-specific B cells. Methods: PBMC were depleted of CD3+ T cells and CD5+ B cells by magnetic depletion of CD3+ T cells before infection. These animals were used by multiple clones from one, or a pair of individuals which are not found in any other reported split. By limiting dilution we have generated a panel of T cell clones specific for MBP (a.a. 84-102) and 65kD hsp (a.a. 3-13). All TCRs are limited within the V region repertoire. By limiting dilution we have generated a panel of T cell clones specific for either MBP (a.a. 84-102) or 65kD hsp (a.a. 3-13). The overall repertoire, but as well as within, individuals were diverse in the VJ region usage and the composition of the CDR3 regions. However, within particular individuals there appears to be some intra-individual limited restriction. This is illustrated by occurrence of the same V and J genes being used by multiple clones from one, or a pair of individuals which are not found or are very limited in the other pairs. On the whole, there was a limited conservation in the repertoire. A high frequency of Vβ2, 4, and 7 responded to MBP, whereas these V regions were not found in the hsp clones. Also, some similarities could be seen in the Vα region repertoire in the CD8+ T cell clones and in the CD3+ T cell clones, as well as with the CD4+ T cell clones. The CD4+ T cell clones, which are predominantly found in CD8+ T cell clones, but are also found in CD4+ T cell clones. The CD4+ T cell clones, which are predominantly found in CD8+ T cell clones, but are also found in CD4+ T cell clones. The CD4+ T cell clones, which are predominantly found in CD8+ T cell clones, but are also found in CD4+ T cell clones. The CD4+ T cell clones, which are predominantly found in CD8+ T cell clones, but are also found in CD4+ T cell clones. The CD4+ T cell clones, which are predominantly found in CD8+ T cell clones, but are also found in CD4+ T cell clones. The CD4+ T cell clones, which are predominantly found in CD8+ T cell clones, but are also found in CD4+ T cell clones. The CD4+ T cell clones, which are predominantly found in CD8+ T cell clones, but are also found in CD4+ T cell clones.

Conclusions: The CD4+ T cell clones are held to play a pivotal role in the Guillain-Barré syndrome, and experimental allergic neuritis (EAN). Here, the effects of intranasal accumulation of nonneural-specific T cells on blood-nerve barrier permeability and on a peripheral nerve function were assessed. Rat ovalbumin (OA)-specific T cells were activated in vitro and on day 0 intranasally transferred to female adult Lewis rats. Rats were then given intranasal injections of OA or casin into left and right tibial nerves respectively. On days 3 and 4, selected rats also received intravenous purified immunoglobulin from rabbits with myelin-induced EAN.