105 ABNORMAL MYELIN SHEATHS IN MULTIPLE SCLEROSIS J.W. Prineas. Veterans Administration Hospital, East Orange, N.J. and New Jersey Medical School, Newark, N.J. (introduced by S.D. Cook*).

Thinly myelinated nerve fibers in which groups of superficial myelin lamellae terminate prematurely along the length of the internode - resulting in an unusual, stepwise reduction in myelin sheath thickness - have been observed by a number of investigators in MS lesions considered to be possibly actively demyelinating. To decide if this change represents a stage in myelin breakdown or an unusual or abnormal form of remyelination, typical, old plaques were studied in two brains fixed for electron microscopy by early in situ perfusion. Thinly myelinated fibers were common at the edges of most of the lesions examined. Numerous examples of the type of abnormal lateral loop arrangement just described were observed in these fibers both at nodes and at points along the outer surface of affected internodes. That this appearance was not due to detachment of lateral loops was suggested by the fact that nodal gaps remained narrow in the presence of quite gross changes of this type. In adjacent, totally demyelinated regions, transverse bar formation was observed between oligodendrocyte perikarya and demyelinated axons. It is concluded that the thin myelin sheaths referred to are probably remyelinating internodes and that remyelination in MS may lead to the formation of abnormal myelin internodes.

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106 ARE DEMYELINATING SERUM FACTORS IN MS AND EAE GAMMA GLOBULINS?

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Sera of patients with Multiple Sclerosis (MS) and animals with experimental allergic encephalomyelitis (EAE) cause demyelination in cultured mammalian central nervous system tissue. The demyelinating factor in guinea pigs and rabbits with EAE has been reported to be IgG (J. Immunol. 116:1439, 1976, J. Exp. Med. 119:303, 1964). The nature of this factor in sera of MS patients is not known. Immunochemical studies on the nature of the demyelinating factor were carried out. IgG1, 2 and 4 were absorbed from sera of MS patients in different clinical stages by treatment with Protein A coupled to Sepharose. Aliquots of the same sera treated with Sepharose alone served as controls. More than 90% of the total IgG was removed by the Protein A treatment, as determined with quantiative radial immunodiffusion. No significant decrease in the demyelinating activities of the IgG depleted sera as compared to the controls could be detected. The isolated IgG fraction had minimal demyelinating activity. In contrast, similar treatment of rabbit EAE sera which removed most of the IgG, resulted in the reduction of the rate of demyelination, and the isolated IgG fraction was actively demyelinating. Furthermore, depletion of IgG from EAE sera previously heated at 56°C for 30 min.abolished its ability to produce swelling of myelin, known to exist with the heated sera (Lab. Invest. 35:391, 1976). The IgG fraction prepared from the heated sera caused swelling of myelin. These studies suggest that unlike EAE, the major classes of IgG present in sera of MS patients does not appear to be responsible for in vitro demyelination. (Supported by Grant NS 11920).

107 MOLECULAR MECHANISMS OF NEUROTROPIC MURINE CORONAVIRUS DISEASE: (JHMV).

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The murine hepatoencephalitis group of coronaviruses produces panencephalitis, hepatitis and interstitial pneumonitis in weanling BALB/c mice. We have two goals: (1) to understand the molecular mechanisms underlying the pathogenesis and organ tropism of this group of viruses and (2) to develop a reproducible model of persistently infected oligodendrocytes with subsequent demyelination. We are characterizing the avirulent MHV-A59, the virulent JHMV, and temperature-sensitive mutants of JHMV in vitro and in vivo to achieve our goals. In Vitro: Radiolabeled intracellular and virion proteins are being characterized by two dimensional polyacrylamide gel electrophoresis and radioimmune precipitation. Radiolabeled intracellular and virion genomic RNA and intracellular mRNA are being characterized by sucrose density gradient ultracentrifugation and polyacrylamide slab gel electrophoresis. In Vivo: Four week old BALB/c mice are examined for JHMV-induced panencephalitis by immunofluorescence of paraffin embedded tissue, transmission electron microscopy, and recovery and characterization of infectious virus. The LD_{50} for JHMV by the intracerebral and intranasal routes is 3 and 300 infectious units, respectively. Intraperitoneal inoculations of 10,000 infectious units are not pathogenic. Differences between the MHV-A59 and JHMV ribonucleoproteins and proteins have been found and may be responsible for the lack of neuropathogenicity of MHV-A59. (Supported by Grant NS-12382 from NINCDS. J. Robb is recipient of RCDA #CA-70567 from the NCI).