AGE DEPENDENCE OF SENSITIVITY TO MHV3 INFECTION IN RESISTANT MICE. E. Levy-leblond, C. Leprevost and J.M. Dupuy, Lab. Immunology, U56, Hopital Parrot, Bicetre 94270. France.

Mechanisms of newborns susceptibility to viral infection was studied in A strain mice infected with mouse hepatitis virus type 3(MHV3). Virus was regularly passaged in susceptible adult DBA/2 mice, prepared by liver homogeneization and titered by LD50 determination. Normal adult A strain mice were always resistant to virus. Young isogenic mice however were highly susceptible and 100% of them died when infected during the first two weeks of age. Resistance to disease developed suddenly during the 3d week of life. Passive transfer of serum from immune A mice failed to protect young animals. When newborns from immunized A strain mothers were injected with MHV3 the mortality was similar to that of control groups. In addition A strain newborns were not protected against virus infection either by injection of isogenic spleen cells or by means of educated thymus cells. However when A strain mice were thymectomized at birth they failed to resist MHV3 infection when tested at adult age. Therefore, along with cell mediated immunity it appears that other mechanism(s), e.g. viral replication in susceptible target cells may play an important role in resistance of mice to MHV3. (Supported by INSERM ATP 5).

LATE ONSET GLOBOID CELL LEUCODYSTROPHY.
F. Hanefeld[1], L. Crome[2], D. Patrick[3], J. Wilson[4]

We present further evidence of the separate entity of a late onset form of globoid cell leucodystrophy which is clinically and perhaps genetically distinct from the infantile form of the disease with which the name of KRABBE is associated.
Clinical and biochemical features in three patients are presented together with the neuropathological findings in one of them. All three patients showed onset in late infancy of visual loss, walking difficulties and dementia. Pathological and enzymic studies established the diagnosis of globoid cell leucodystrophy. Histology demonstrated typical globoid cells in one case. Activity of Galactocerebroside-B-galactosidase in the white blood cells of 2 cases, and in the cerebral cortex of one case was reduced to less than 5 per cent of the mean activity of controls. A few similar cases have been recorded in the past, and it is suggested that all of these are instances of a late-onset variant of globoid cell leucodystrophy.

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NEUROLOGY

EVIDENCE FOR THE PARTICIPATION OF A GLYCOPROTEIN IN THE EARLY PROCESSES OF MYELINATION. J.-M. Matthieu, R.O. Brady and R.H. Quarles. Developmental and Metabolic Neurology Branch, NINDS, NIH, Bethesda, Md. 20014, USA.

The presence of a glycoprotein in myelin has been recently reported (Quarles et al. Biochem. biophys. Res. Commun. 47, 491, 1972). Since glycoproteins on the plasma membrane of cells are believed to be involved in specific cell-to-cell interactions, the myelin associated glycoprotein could be involved in contact relationships between axons and oligodendrocytes or between the different layers of myelin. Myelin-associated glycoproteins were investigated during myelination in normal rats and in normal and myelin-deficient mutant mice. Glycoproteins were labelled in vivo by injection of [^{3}H] or [^{14}C] fucose, and purified myelin fractions were prepared. Proteins were extracted with SDS, separated by polyacrylamide gel electrophoresis and stained with Fast Green or periodic acid-Schiff reagents. Radioactivity was measured in gel slices by liquid scintillation spectrometry. This study has shown anomalies of the myelin-associated glycoprotein in the myelin-deficient mutants which could impair the recognition between oligodendrocyte and axon, and consequently involve an arrest in myelinogenesis. These and other results from this laboratory suggest a role of this glycoprotein in the processes of myelination.

MUCOSULFATIDOSIS: MULTIPLE SULFATASE DEFICIENCY.
U. Wiesmann, Y. Eto, J. Carson and N. Herschkowitz.

In two cases of metachromatic leucodystrophy associated with mucopolysaccharidosis the biochemical defect has been investigated.
In the organs there was an accumulation of sulfatid, mucopolysaccharide (MPS) and cholesterolsulfate. This accumulation of different sulfate containing compounds was correlated with a deficiency of the activity, of several sulfatases: arylsulfatase A,B, C, cholesterolsulfate and dehydroepiandrosterone sulfatase. Mixing experiment did not show an inhibitory effect of the affected tissues. Isoelectric focusing column electrophoresis showed an abnormal isoelectric point of the arylsulfatase B. Both fibroblast lines demonstrated faulty degradation of $^{35}SO_4$-MPS. Mixing experiments between the patients fibroblasts and cells from different types of MPS-oses successfully corrected the faulty $^{35}SO_4$-MPS metabolism except for Hunter and Sanfilippo A fibroblasts, both disorders are suspected to be due to a single MPS-sulfatase deficiency. This suggests that MPS-sulfatases are deficient in mucosulfatidosis patients also. Possible explanations of these multiple enzyme deficiencies will be discussed.

PATHOGENETIC STUDIES OF LEUCODYSTROPHY
N. Herschkowitz and J. Carson

1. The pathogenetic mechanisms of most in the hereditary degenerative brain diseases are unknown. The possibility to study animal modes of these diseases is therefore a valuable help in pediatric research.
2. In the murine leucodystrophy, the animals show at the 12th postnatal day tremor and ataxia, convulsions appear at the 18th day and death occurs around the 22nd day.
3. In the central nervous system there is an almost complete absence of myelin. The sequential analysis of biochemical markers of brain structures (DNA, glycolipids, basic proteins) shows that this is not due to a defect of proliferation of oligodendrocytes but of the differentiation of these cells. These findings are confirmed by morphological studies on the histological and ultrastructural level.
4. Investigation of the turnover of the affected proteins indicates, that in this disease, the defect is not a decrease of the synthesis of the proteins, but an increase of their degradation.

MULIBREY NANISM. J. Perheentupa, S. Autio, S. Leisti, C. Raitta, L. Tuuteri, Children's Hosp., Univ. of Helsinki, Finland.

Mulibrey (muscle, liver, brain, eye) nanism is a previously unknown, probably autosomal recessive syndrome of prenatal onset growth failure with involvement of several tissues mostly of mesodermal origin. We've studied 24 patients, 0.3-24 yrs old. On average, the size at birth was 2 SD below mean for gestational age; present height 5 SD below mean for age and sex. General gracility was marked in the children; extremities were significantly short for length of trunk. Face was triangular with prominent forehead and low nasal bridge. Muscles were hypotonic in children. All had characteristic "small" voice. Most had elevated venous pressure and marked enlargement of liver; 6 had oedema and ascites. In contrast, heart was normal in size or only slightly enlarged. This is probably due to pericardial constriction, which has actually been demonstrated in 6 patients, at operation or autopsy. Cerebral ventricles and cisternas were enlarged in the 6, who were appropriately studied. All had characteristic long shallow sella turcica. Hypoplasia of choriocapillaris, pigment dispersion and yellowish dots in ocular fundi were observed in all but one. 7 had fibrous dysplasia of tibia, which had progressed to pseudarthrosis in 3. Most had cutaneous capillary haemangiomas. The 21 propositi had a total of 57 liveborn siblings. Of these, 3 were certainly and 10 probably or possibly affected with mulibrey nanism. In addition, the mothers had had a total of 17 spontaneous abortions.