INFLUENCE OF THE IMMUNE SYSTEM ON THE COURSE OF
INFECTION WITH MURINE CORONAVIRUS JHM IN SUCKLING MICE

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INTRODUCTION

JHM-virus, a neurotropic strain of murine corona virus, has been shown to induce various diseases of the central nervous system in rats which are influenced by the age of the animals at the time of infection (1-3). Infection early in life always results in acute disease while sub-acute or chronic diseases develop when adult animals are infected. In this connection it appears to be of importance to analyze the factors determining the different reactions of young and adult animals to infection with JHM virus. It has been shown for various viruses, that resistance to infection can occur, based either on the genetics or on the age of the animal (4-11). In this study experiments were carried out to investigate age dependent resistance by analyzing the influence of components of a competent immune system on the course of JHM virus infection in suckling mice.

MATERIALS AND METHODS

VIRUS: JHM-virus, originally derived from suckling mouse brain (1) was propagated in the C3H mouse fibroblast cell line L 929 to titres of 1 -5 x 10^5 plaque forming units (PFU)/ml. The titre was evaluated by plaque assay on L 929 cells. Inactivation of JHM-virus...
was obtained by UV-irradiation of $2 \times 10^5$ PFU/ml with 30,000 erg/mm².

MICE: C3H mice were purchased from Bomholtgart (Ry, Denmark). The expression "baby mice" was used for mice younger than 25 days, "adult mice" for mice older than 2 months.

CELLS: Spleen and thymus cell suspensions were prepared in MEM containing 5% FCS, and injected intraperitoneally if not quoted otherwise. Normal spleen cells (NSC) were derived from non-immune adult C3H mice, immune spleen cells (ISC) from adult C3H mice, which were immunized i.p. once with $10^5$ PFU of JHM virus. Immune spleen cells were obtained 4 days, 14 - 30 days, or 50 - 100 days after immunization. All ISC populations were tested for the presence of infectious virus in vitro by plaque assay, and in vivo by injecting the cells into susceptible baby mice. Both assays always worked comparably: injection of cell samples which turned out to be positive in the plaque assay killed suckling mice.

DESIGN OF EXPERIMENTS: To circumvent maturation differences between different litters, experiments were set up in the following way: When differently treated groups were compared in an experiment, in which more than one litter was used, the animals of the different litters were dispensed in such a way that each experimental group was represented in each litter. The virus was injected intraperitoneally throughout the experiments.

RESULTS

Age Dependence of the Outcome of JHM-Virus Infection in C3H mice

The outcome of an infection with respect to the age of the animals was followed up by injecting virus into suckling mice at different intervals after birth. As shown in Table 1A it was found that intraperitoneal infection with 20 PFU per mouse was always lethal for mice up to the age of 20 days. The rate of mortality was reduced when mice were 21 or 22 days old. Older animals were resistant to infection. There was hardly any time shift when higher virus doses were given (Table 1B). Table 1A and 1B show the results of distinct representative sets of experiments. Comparing different sets, the occurrence of resistance was shifted by maximally 2 days.