

PATHOGENICITY OF MOUSE HEPATITIS VIRUS, MHV-2cc, FROM A
PERSISTENTLY INFECTED DBT CELL LINE

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Pathogenicity of a small plaque mutant of mouse hepatitis virus, MHV-2cc, from persistently infected DBT cell culture for nude mice (BALB/c) was studied. The mutant virus was purified by the same procedure as described previously¹ by serial cultures of resistant DBT cells carrying MHV-2.

After inoculation with 10^5 PFU of MHV-2cc, adult ICR mice, which were highly susceptible to the original MHV-2, showed no signs of illness, while suckling ICR mice died of fulminant hepatitis. Adult athymic nude mice, however, were found to have subacute or chronic hepatitis resulting in death between 18 and 90 days after inoculation. Grossly they showed remarkable nodular hyperplastic changes in the liver (Fig.1). By direct immunofluorescence MHV antigen was demonstrated within the cytoplasm of hepatocytes. Though the times-to-death were varied, changes of the liver were common to all cases until one week postinfection. The viral antigen was demonstrated as early as 48 hr postinoculation followed by production of many focal necrotic lesions. Specific fluorescence mostly faded at 7 days postinoculation when some inflammatory reactions appeared around the lesions. By electron microscopy, a small number of virions was seen outside of hepatocytes at 72 hr postinoculation but many virions still existed in the cytoplasm of degenerated hepatocytes (Fig.2). Some hepatocytes containing virions were phagocytized by macrophages, and recurrent inflammatory reactions as well as fibrosis were observed later.

Chronic active hepatitis has been experimentally produced in some nude mice² after infection with low virulent MHV, MHV-NuU, but the pathogenicity of this virus for nude mice is not uniform enough to be a model for subacute or chronic hepatitis. MHV-2cc virus seems to be of much lower virulence producing a

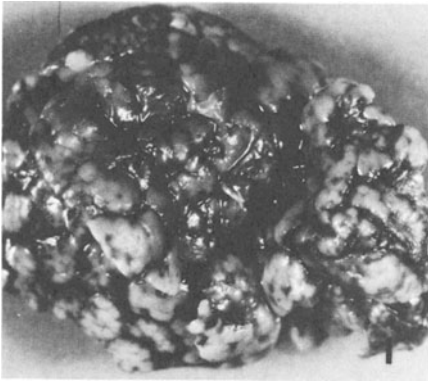


Fig.1. The liver of an MHV-2cc infected athymic nude mouse. 42 days post-inoculation.



Fig.2. MHV-2cc virions in the cytoplasm of a degenerated hepatocyte of an athymic nude mouse. 96 hr post-inoculation. Bar=1 μ

more typical chronic active hepatitis with recurrent inflammatory reactions. Such type of MHV mutant retaining high hepatotropism has never been reported, while various neurotropic mutants of MHV have been shown to cause persistent infection in the nervous system^{1,3}. The system of MHV-2cc and athymic nude mice may provide a good model for progressive hepatitis with virus persistence.

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