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# Mouse Hepatitis Virus
(MHV)

## Classification
RNA virus, enveloped

## Family
Coronaviridae

## Affected species
Mice

## Frequency
Common in both wild and laboratory mice.

## Transmission
MHV may be transmitted through aerosols, fomites, and direct contact. The virus is highly contagious, although not persistent in the environment. MHV may also contaminate cell cultures, and transplantable tumors.

## Clinical Signs and Lesions
In general, MHV infection in immunocompetent mice is asymptomatic. Expression of the disease depends on the age, genotype, sanitary status, and experimental status of the mouse and the tropism and virulence of the infecting strain of the virus.

If a mild strain of MHV exists in enzootic form in a colony, the adults are immunized by a previous infection. Young mice are protected by maternal antibodies up to weaning. The infection survives amongst the newly weaned animals with few or no clinical appearances. Epizootic MHV is generally observed in young mice, in populations with no previous contact with MHV. Young mice may show clinical signs, depending on the tropism of the virus. The epizootic quickly spreads to the entire population. In immunocompetent adults, it is usually asymptomatic.

MHV has two types of tropism in the initial infection. Respiratory-tropic strains, also known as polytropic strains, are uncommon and replicate first in the nasal mucosa, then may disseminate to other organs via the bloodstream. The classic lesion in disseminated respiratory MHV is white foci found on the liver. Histopathologic examination reveals the presence of focal necrotizing hepatitis with syncytial cells. These lesions may be found in lymphoid organs as well. Polytropic strains of MHV are the strains that commonly contaminate cell lines, tumors, and other material of mouse origin. Infection of naïve neonates with polytropic strains of MHV can result in disseminated infection.

Most strains of MHV in animal houses are enterotropic strains. These have a primary tropism for the intestine and are excreted in feces. Enterotropic strains tend to spread quickly from mouse to mouse, as the high level of excretion in feces will result in significant environmental contamination. In an entrotropic MHV infection, the lesions are limited to the intestine in immunocompetent mice. Variable levels of epithelial cell lysis and atrophy of villi may be noted in the terminal small intestine. Giant multinucleated syncytial cells appear in the crypts and the intestinal villi. Similar lesions may be seen in the caecum and the ascending colon.

With either viral tropism, disease is more severe in immunodeficient mice. Polytropic strains of MHV cause severe disease in immunodeficient mice, as the ability of the virus to replicate in many tissues leads to necrosis and syncytial cell formation in the liver, spleen, lymph nodes, and bone marrow. If animals are infected as neonates, similar lesions may also be seen in the brain. Enterotropic MHV strains cause similar lesions in immunodeficient mice as in immunocompetent mice. Immunodeficient mice may become chronic carriers of MHV, serving as a source of infection for other colonies.

## Diagnosis
MHV infection in immunocompetent animals is commonly diagnosed through the use of serology, either MFIA™/ELISA or IFA. In immunodeficient animals, diagnosis is best accomplished through PCR on feces or serologic examination of sentinel mice. Occasionally, diagnosis is made via histopathology after the observation of characteristic intestinal lesions, but histology should not be considered diagnostic without PCR or immunohistochemistry confirmation.

## Interference with Research

The effects of MHV on research are too numerous to list here, especially when infection of immunodeficient animals is considered. Of significant interest, however, is the fact that MHV infects the lymphatic tissue and therefore has significant and prolonged effects on the immune system, even in immunocompentent mice. Co-infection with MHV can modulate the course of several viral, bacterial, and parasitic infections, resulting in a more severe infection, resistance to infection, or a more or less severe course of infection, depending on the particular agent. MHV may also modify the activity of hepatic enzymes, reduce liver regeneration after partial hepatectomy, produce anaemia, leukopenia, and thrombocytopenia, and decrease the incidence of diabetes in some susceptible strains of mice.

## Prevention and Treatment

MHV is extremely contagious and is one of the most frequent viral infections found in modern research facilities. Strict control of movement of animals, materials, and people into the animal house is necessary to prevent contamination with MHV. Animals should be tested regularly and frequently to detect contamination. All biological products of animal origin should be tested via MAP (mouse antibody production) test or PCR for the presence of MHV before being inoculated into mice.

If an MHV infection is detected in an animal facility, depopulation, thorough cleaning, and restocking is recommended. If animals must be kept, euthanasia of all non-essential animals and a strict quarantine (negative pressure isolators work well in this case) is recommended until the animals can be rederived. Hysterectomy rederivation or embryo transfer are recommended to rederive infected colonies. “Burn out” of an MHV infection through cessation of breeding is not generally recommended.

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