Mouse Hepatitis Virus (MHV)

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Background: Mouse hepatitis virus is probably the most important pathogen of laboratory mice. Although the infection generally causes no overt clinical signs, it can cause profound changes in the immune system, affecting the interpretation of a wide variety of experimental results. It is a ssRNA virus of the family *Coronaviridae.* Approximately 25 strains or isolates of MHV have been described.

Transmission: MHV is extremely contagious and is transmitted primarily via aerosol, direct contact, fomites and, experimentally, via transplantable tumors and via the placenta.

Clinical Signs: Clinical infection occurs when the virus is introduced into a naïve colony. Adult infections are usually asymptomatic. Clinical signs depend on the strain of virus and are most evident in infant mice. Typically, these include diarrhea, poor growth, and death.

Eventually, the infection adults are asymptomatic, asymptomatically infected by inirnunity wanes at weaning.

Iminunodeficient mice, such as athymic nude mice, develop a wasting disease that eventually results in death.

Diagnosis: Diagnosis is usually based on serology, via ELISA or WA or both. The diagnosis can be strengthened by demonstration of typical lesions in clinically ill animals.

Effects on Research: Numerous reports document the effects of natural and experimental infection with MFIV on host physiology and research. In immunocompromised mice, these effects include the following:

- Necrotic changes in liver, lungs, spleen, intestines, brain, lymph nodes, and bone marrow.
- Differentiation of cells bearing T-lymphocyte markers
- Altered enzyme activities. bilirubin concentration, and antibody responses to sheep eiythrocvtes in serum.
- Enhanced phagocytic activity of macrophages.
  Rejection of xenograft tumors.
- Impaired liver regeneration.

In immunocompetent mice, these effects include the following:

- Transient immunostimulation followed by immunodepression.
- Thymic involution.
- Depletion of LDEV-pennissive macro-phages.
- Microcytic anemia and changes in ferrokinetics.
- Decreases in lymphocyte proliferative responses.
- Decreases in antibody secretion.
- Decrease in phagocytic activity.
- Decrease in liver regeneration.
- Decrease in blood cell production.
- Decrease in the number of hepatic sinusoidal endothelial cell fenestrae.
- Decreased incidence of diabetes mellitus in nonobese diabetic mice.
- Apoptotic changes of the thymus.
- Increased tumoricidal activity of peritoneal macrophages.
- Increased uptake of injected iron.
- Increased susceptibility or resistance to pathogens.
- Increased IL-12 and IFN production.
- Altered hepatic activity.
  Altered behavior of ascites myelomas.
- Altered expression of cell surface markers on splenic T lymphocytes.
- Molecular mimicry of the host Fc gamma receptor.
- Nerve demyelination.
- Impaired bone marrow pre-B and B cells
- Induced production of *a*-fetoprotein and antiretinal autoantibodies in serum.
- Induced macrophage procoagulant activity.

Prevention: To prevent this disease, obtain replacement stocks from sources that are known to be free of disease. Tumor lines should be assessed for infection using MAP tests or other appropriate tests. Personnel working with infected animals should not enter rooms that contain naïve animals.

Eradication: The most effective way to eradicate MHV infections is to cull the colony and obtain clean replacement stock. However, this is not always a feasible option when working with valuable mice.

Caesarian rederivation or embryo transfer can be used to produce offspring that have not been exposed to the virus. Repeated serological evaluations should be performed prior to reintroduction of the mice into a naïve population.

A breeding moratorium of at least 8 weeks can also be used to prevent the spread of the virus from young weanling animals to younger naïve animals. The animals should be housed in microisolator caging and handled with standard microisolator techniques. This method requires repeated serologic testing and strict adherence to a zero-tolerance for breeding policy. It is important to note that transgenic and knockout mice often have altered immune systems that may allow them to sustain the infection for longer periods of time or to develop a carrier state. In these cases, the breeding moratorium would not be the appropriate means of eradication.

References:

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