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Parvovirus (mice – MVM and MVP, rats – KRV/RV, H-1, RPV, and RMV)

Prevalence

- Mice – subject to two different autonomously replicating types:
  - Minute virus of mice (MVM)
  - Mouse parvovirus (MPV-1, -2 and -3) - predominant
- Amongst the most prevalent viruses in contemporary laboratory mouse populations – due to persistence in infected animals and the environment
- Rats – naturally susceptible to 4 serotypes:
  - Kilham's rat virus (KRV/RV) – most pathogenic
  - Toolan's H-1 virus (H-1)
  - Rat parvovirus (RPV-1 and -2)
  - Rat Minute Virus (RMV)
- Subclinical infections common among laboratory rats

Significance

- Immune dysfunction is probable in mice and rats
- Mice and rat parvovirus are oncolytic and oncotropic – explored as potential anti-cancer agents
- Rat parvoviruses may affect studies involving fecal development

Disease

- Single stranded DNA viruses
- Clinical disease seldom present in immunocompetent mice, but virus has significant immunomodulatory effects and are refractory to effective eradication from contaminated mouse colonies
- Dependent upon the S phase of the cell cycle for virus replication – induce cytolytic disease only in dividing tissues (including lymphoid tissues undergoing antigenic stimulation)
- Replication limited to certain cell types that bear the appropriate viral receptors
- Following oral inoculation, mouse parvovirus initially replicates in intraepithelial lymphocytes, lamina propria, and endothelium of small intestine
- Disseminate into kidney, intestine, lymphoid tissues, liver, and lung
- Virus shedding documented in urine, faeces, and oropharynx
- Natural infection of immunocompetent is clinically silent
- Experimental infection of neonatal with MVM – mortality due to:
  - hemorrhage, hematopoietic involution, and renal papillary infarction
- Infection of pregnant animals - increased number of uterine resorption sites in dams, runting, ataxia, cerebellar hyperplasia and jaundice in pups
- Rat juveniles - dyspnea, ruffled hair coat, muscular weakness, and cyanotic scrotums
- Rat adults (mostly due to RV infections) - congestion of lymph nodes, loss of body fat, and scrotal hemorrhage, with peri-testicular fibrinous exudation (splenomegaly, icterus, and ascites are variable)

- Microscopic changes may be present in brain, liver, and testes

Transmission

- Through faeces and urine by oronasal exposure
- Contact with infected animals, contaminated fomites, and maternal milk
- Slow rate of cage-to-cage spread
- Known contaminant of transplantable tumors and cell lines
- Transplacental transmission demonstrated in pregnant rats inoculated with high doses – resulting in infertility and fetal resorption
- Neonatal mice protected from infection by seropositive maternal antibody in enzootically infected colonies
- Mice resist reinfection with homotypic virus, but are susceptible to heterotypic serotype – high frequency of dual MPV and MVM infections
- Requirements for dividing cells for replication – results in frequent contamination of tumor cell lines and tumor virus stocks

Diagnosis

- **Preferred** – Seroconversion
- Colony surveillance challenging due to inefficient cage-to-cage transmission
- There are specific assays for the structural antigens (VP – specific to each Parvovirus) as well as for non-structural antigens (NS- common for all Parvoviridae)
- ELISAs detect antibody to both MVM and MPV (rNS1 ELISA only used for rats – low sensitivity in mouse serum samples)
- PCR detection in tissues (MLN optimal) and faeces
- Serological assays prone to low level false positive if sample preparation is not optimal
- Differential diagnoses include – bacterial septicemias, chronic wasting due to agents such as Mycoplasma pulmonis, and trauma
- MAP test and virus isolation, including tissue explant cultures – more labour-intensive methods

Strains

- Total number unknown - more isolates and stains are likely to be discovered
- Antigenically distinct, although NS-1 protein highly conserved across all parvoviruses

Duration

- MVM infection is limited in duration, with recovery (infant and immunocompetent mice)
- MVP infection is typically persistent (mice of all ages) – juvenile may transmit virus more efficiently (may be present for up to 14 weeks)
- Persistence of parvovirus infections can occur in rats – depend on continuous availability of susceptible animals to permit propagation

Durability

- Extremely tough and resistant to heat (80°C 2 hours or 40°C 60 days), drying, pH 2-11, chloroform, ether, alcohol, and lipid solvents
- Inactivated by formalin, 13-propiolactone and oxidizing agents

Screening

- All colonies – quarterly
- Commercial breeding colonies – more frequently as pathogen becomes established in Australia

Prevention and Control

- Pathogen exclusion by:
    - regular health monitoring of supplier sub-populations, transport in filter boxes, quarantine at receiving institution with serology testing 2 weeks post arrival
- Post infection:
    - caesarean rederivation, embryo transfer, test and cull
- Strict husbandry protocols, decontamination procedures and efficient barrier conditions are essential for success

Reading

- Stephen W. Barthold, Stephen M. Griffey & Dean H. Percy. Pathology of Laboratory Rodents and Rabbits (Fourth Edition), 2016
- Laboratory Animal Science, 46(4):370 -380