

Rotaviruses

The genus rotavirus is divided into a number of groups between which antigenicity is distinct (Bridger 1994)

Host species

- laboratory animals, particularly mice, rats, and rabbits (Sheridan & Vonderfecht 1986, Vonderfecht 1986, National Research Council 1991, Harkness & Wagner 1995)
- wide range of domestic and wild mammalian animals, birds, humans

Properties

- murine rotavirus is stable at -70°C but unstable at -24 , 4 , and 37°C ; not resistant to environmental conditions (Sheridan & Vonderfecht 1986, National Research Council 1991, Vonderfecht 1994)
- rotaviruses tend to be stable at low pH and labile at pH values above 10.0

Strain susceptibility

- naive BALB/c mice of all ages are susceptible to murine rotavirus; other strains of mice, such as C57BL/6, are much more resistant to infection with murine rotavirus as adults (Ward & McNeal 1999)
- Prkdcscid mice may become persistently infected with rotavirus (Riepenhoff-Talty et al. 1987, Franco & Greenberg 1999)

Organotropism

- fenterotropic
- hepatobiliarytropic in heterologously infected mice (Uhnnoo et al. 1990b, Petersen et al. 1998)

Clinical disease

- usually inapparent in adults
- major cause of acute diarrhea in infants and in the young of other mammalian and avian species
- the natural disease in mice is caused by group A rotaviruses and has been known as "epizootic diarrhea of infant mice" (EDIM); the susceptibility to EDIM is dependent on the immunological status and the age of the host, and peaks between 3-14

days of age (Sheridan & Vonderfecht 1986, National Research Council 1991, Harkness & Wagner 1995, Ball et al. 1996)

- the natural disease in rats has been named "infectious diarrhea of infant rats" (IDIR) and is caused by a group B rotavirus; the clinical course of IDIR is similar to that of EDIM (Vonderfecht 1986, National Research Council 1991, Harkness & Wagner 1995)
- rabbits ranging from 1-12 weeks of age may exhibit clinical signs of diarrhea following infection with group A rotaviruses (Thouless et al. 1988, Vonderfecht 1994)

Pathology

- histopathologic changes in the intestine are confined to the small intestine and most prominent at the tips of villi; lesions include swelling and vacuolation of epithelial cells, formation of epithelial syncytial cells, intracytoplasmic inclusion bodies in the epithelial cells, epithelial cell necrosis, sloughing of epithelial cells into the intestinal lumen, villus atrophy and blunting, edema and mild inflammation in the lamina propria of villi (Sheridan & Vonderfecht 1986, Vonderfecht 1986, National Research Council 1991, Salim et al. 1995, Ciarlet et al. 1998)
- hepatitis, cholangitis, and biliary atresia in infant Balb/c mice after experimental infection with rhesus rotavirus (Uhnnoo et al. 1990b, Petersen et al. 1998)
- Morbidity and mortality
- rotaviruses are highly contagious and infection is easily spread within a group (Kraft 1958)
- high morbidity (in the young) and low mortality; mortality is more common in infected rabbits (Vonderfecht 1994)

Zoonotic relevance

- animal-to-human transmission may occur (Nakagomi et al. 1992, Shirane & Nakagomi 1994) but does not appear to be common

Interference with research

Physiology

- rotaviruses bind to the neutral glycosphingolipid gangliotetraosylceramide (Willoughby et al. 1990) and to O-linked sialylglycoconjugates and sialomucins (Willoughby 1993)
- malnutrition and other dietary alterations may enhance murine rotavirus infection (Morrey et al. 1984, Noble et al. 1983, Uhnnoo et al. 1990a, Sagher et al. 1991)
- rotaviruses induce changes in the microcirculation of intestinal villi of neonatal mice (Osborne et al. 1991)
- rotavirus infection alters intestinal absorption (Davidsson et al. 1977, Graham et al. 1984, Heyman et al. 1987, Ijaz et al. 1987, Salim et al. 1995, Katyal et al. 1999) and intestinal enzyme profiles (Collins et al. 1988, 1990, Jourdan et al. 1998, Katyal et al. 1999)

- intestinal fluid and electrolyte secretion is enhanced through the effects of a viral enterotoxin NSP4 (Ball et al. 1996, Estes & Morris 1999) and by activation of the enteric nervous system (Lundgren et al. 2000)

Cell biology

- rotavirus infection causes alterations in the polarized sorting of neuronal proteins (Weclawicz et al. 1993)
- NSP4 increases intracellular calcium levels by release from the endoplasmic reticulum (Tian et al. 1994, 1995, Ball et al. 1996)
- NSP4 alters plasma membrane permeability and may facilitate cell death (Tian et al. 1996, Newton et al. 1997)

Immunology

- rotavirus infection causes recruitment and activation of CD4+ and CD8+ T cells (Offit & Dudzik 1989, Offit et al. 1992, McNeal et al. 1997, Rott et al. 1997) and a vigorous mucosal IgA response (Merchant et al. 1991, Coffin et al. 1995); resolution of rotavirus infection is due to both T (particularly CD8+ cells) and B cells, while protection against rotavirus is primarily dependent on antibodies (Ward 1996, Feng et al. 1997, McNeal et al. 1997, Franco & Greenberg 1999)
- rotavirus infection induces a mixed Th1/Th2 pattern of cytokine production (IFN- γ , IL-5, IL-10) by mouse spleen cells (Fromantin et al. 1998)
- rotavirus infection leads to increased mRNA for several C-C and C-X-C chemokines and interferon- β in the mouse small intestine (Rollo et al. 1999)
- Interactions with other infectious agents
- a synergistic pathogenic effect between rotavirus and *Escherichia coli* occurs in infant mice (Newsome & Coney 1985) and weanling rabbits (Thouless et al. 1996)
- infection of human enterocyte-like cells with rotavirus enhances invasiveness of *Yersinia enterocolitica* and *Y. pseudotuberculosis* (Di Biase et al. 2000)

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