Rotavirus diarrhea in bovines and other domestic animals

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Abstract Rotavirus diarrhea is the major cause of death of millions of children in developing countries besides causing economically significant malady in neonates of many domestic animals. In neonates, the infection is non-viremic, have very short incubation period, and manifests profuse diarrhea and severe dehydration. Concurrent infection with secondary pathogens may augment the disease severity. Diarrhea occurs due to virus-mediated destruction of absorption efficient enterocytes, activation of enteric nervous system, or due to a rotavirus enterotoxin. Diagnosis of the infection relies on conventional techniques like isolation in MA 104 cell lines, electron microscopy, electro-pherotyping, and various serological tests. Presently, diagnosis and molecular typing is performed using serotype specific RT-PCR, sequencing or genomic hybridization techniques. As the rotaviruses are known to exhibit extreme genetic diversity and outplay disinfection procedures, eradication of the pathogen is often difficult. Hence, for prevention, good management practices coupled with vaccination of dam for protecting young ones, has to be practiced. Recently, new generation prophylactic strategies including DNA vaccines, subunit vaccines, virus-like particles (VLPs) and edible vaccines have been found to induce sufficient levels of passive immunity. Aside to the infection in animals, zoonotic significance of the animal rotaviruses has to be further unearthed. In this review, efforts have been made to highlight the importance and prevalence of the disease in bovines, its pathogenesis along with preventive measures, salient features of rotaviruses and their inter-

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species transmission abilities, zoonotic implications, and a concise account of the infection in various domestic animals and poultry.

Keywords Bovine rotavirus · Neonatal diarrhea · Viral enteritis · Rotavirus · Viral diarrhea

Abbreviations

VP	viral protein/polypeptide
SNT	serum neutralization test
EM	electron microscopy
BRV	bovine rotavirus
HA	hemagglutination
MDBK	Madin Darby bovine kidney
PK	porcine kidney
NSP	non-structural protein
G	glycoprotein
P	protease sensitive protein

Introduction

Since earlier days, it has been observed that young ones of animals succumb to infectious agents at neonatal period, thus adversely affecting the economic stability of many animal-farming ventures. Among the infectious diseases of calves, neonatal diarrhea is a matter of major concern, and multiple etiological agents that include *Escherichia coli, Salmonella* species, *Clostridium perferingens*, rotavirus, coronavirus, *Cryptosporidium* and *Coccidia* have been suggested (Holland, 1990; Steele *et al*. 2004; Gumusova *et al*. 2007). Among these agents, bovine rotaviruses (BRV) are contributing significantly to enteritis and diarrhea in intensively reared neonatal calves (Malik *et al*. 1995; Chauhan and Singh 1996; Murphy *et al*. 1999; Pisanelli *et al*. 2005; Rathi *et al*. 2007). The disease is usually seen in young calves of 2–8 weeks of age and the susceptibility decreases as the age progresses. Besides affecting cattle and buffalo calves, rotaviruses also affect piglets, foals, lambs, kids, and young ones of pet animals and poultry (Holland 1990; Kaminjolo and Adesiyun 1994; Malik *et al*. 1995; Dodet *et al*. 1997; Murphy *et al*. 1999; Steele *et al*. 2004). The clinical signs and the outcome of the disease are similar in most species, and severity may range from an asymptomatic or subclinical condition to severe enteritis. Pertaining to domestic animals and humans, rotavirus diarrhea is a major cause of death of millions of infants in developing countries while inflicting severe losses to the livestock sector. The virus etiology of neonatal calf diarrhea (NCD) was first documented in USA in the year 1969, when reo-like viruses were first identified in diarrheic feces (Mebus *et al*. 1969), and it was in 1974, the term 'reo-like virus' has been replaced by 'rotavirus' as the virus exhibited a 'wheel-like' appearance (*Rota*-in Latin means wheel). Initially, electron microscopy (EM) based detection of rotaviruses in faeces has been popular due to the difficulty of isolating the virus in cell cultures.

Numerous reports of bovine rotavirus (BRV) causing calf diarrhea have appeared in literature, since its first description almost four decades ago, suggesting a worldwide distribution (Woode 1976; Kharalambiev *et al*. 1983; Castrucci *et al*. 1988b; Chauhan and Singh 1996; Vende *et al*. 1999; Pisanelli *et al*. 2005; Alfieri *et al*. 2006; Ghosh *et al*. 2007a). The BRV is ubiquitous and cause localized infection in small intestine of neonatal calves by disrupting the efficient absorptive surfaces to produce diarrhea (Muniappa *et al*.

1987; Chauhan and Singh 1996; Malik et al. 2005). They were among the earliest rotaviruses to be successfully adapted in tissue culture (Mebus et al. 1971a). The rotaviruses, being mostly species-specific and existing as geno-groups, have multiple gene segments of double-stranded (ds) RNA, and exhibit considerable genetic diversity as a result of genetic shift, gene rearrangements or interchange of segments (Schroeder et al. 1982; Shen et al. 1994; Murphy et al. 1999; Steele et al. 2004). Besides, inter-species transmission and close relationship between human and animal rotaviruses have been reported (Nakagomi and Nakagomi 1991; Adah et al. 2003). But it is suggested that rotaviruses isolated from animals, even those indistinguishable from human viruses, rarely cause natural infection in infants (Murphy et al. 1999).

For identification of rotaviruses, isolation in primary calf kidney cells or cell lines like MA104, MDBK or PK-15, and various diagnostic methods like electron microscopy, polyacrylamide gel electrophoresis (PAGE)-based electro-pherotyping, enzyme linked immunosorbent assay (ELISA), dot-immunoblotting, immuno-fluorescence test, immuno-peroxidase test, passive HA, latex agglutination test and dot blot hybridization, are employed (Hammami et al. 1990; Chauhan and Singh 1992a; Murphy et al. 1999; Malik et al. 2005). Presently, the diagnosis as well as molecular typing is performed using serotype-specific reverse transcription-polymerase chain reaction (RT-PCR), nested/multiplex RT-PCR and restriction fragment length polymorphism (RFLP) (Chinsangaram et al. 1995; Alfieri et al. 2004; Steele et al. 2004). Methods like sequencing and oligonucleotide microarray hybridization that are sensitive and capable of vividly discriminating mixed rotavirus infections are also being developed. For an effective prevention of rotaviral diarrhea, good management practices coupled with vaccination of the dam, a few weeks before parturition, has been practiced globally. The vaccinated dam will transfer the specific antibodies passively through the colostrum to their young ones to provide sufficient immunity at the intestinal level (Agrawal et al. 2002; Steele et al. 2004). The high incidence of rotavirus diarrhea in calves and other domestic animals has prompted scientific fraternity to focus on developing new generation vaccines as well as rapid diagnostic tools. As a result of the advances made in the field of recombinant DNA technology, DNA and subunit vaccines, virus-like particles (VLPs) and plant-based edible vaccines are being attempted (Kim et al. 2002a; Wigdorovitz et al. 2004; Graham et al. 2006; Herrmann 2006; Dhama et al. 2008). Further, the recombinant techniques may provide suitable antigens of diagnostic value for upgrading the conventional detection tools.

Keeping in mind the significance of rotavirus diarrhea to the livestock sector, in this review, the authors have made substantial efforts to highlight the features of the disease, global prevalence and their pathogenic potential in bovines. Inter-species transmission and zoonotic significance of the animal rotaviruses, novel diagnostic and preventive strategies, and a concise purview regarding the infection in various domestic animals and poultry are also discussed.

The etiological agent

In 1974, the name 'rotavirus' was assigned for reo-like viral agents, after analyzing the viral morphology using transmission electron microscopy. Later, the International Committee on Taxonomy of Viruses (ICTV) placed these viruses, having a diameter of 65–70 nm, in genus Rotavirus within the family Reoviridae. Rotaviruses are icosahedral and non-enveloped, with 32 capsomers and 11 segments of ds RNA (16–21 kbp), well protected by an inner and outer capsid layer (Murphy et al. 1999; Desselberger et al. 2005). The virus

has structural proteins located in the core (VP1, VP2, and VP3), inner capsid (VP6) and the outer capsid layer (VP4 and VP7). VP4 and VP7 proteins generate neutralizing antibodies that protect animals from infections; VP6 is a group specific antigen that is common to all rotaviruses; and VP1, VP2 and VP3, along with other non-structural proteins (NSP), play a key role in viral transcription (Paul and Lyoo 1993; Steele *et al*. 2004; Desselberger *et al*. 2005). The functions of major structural and non-structural proteins of rotaviruses have been identified (Murphy *et al*. 1999; Desselberger *et al*. 2005). VP1 is a RNA-dependent RNA polymerase; VP2 produces a protein needed for the proper functioning of the VP1; VP3 forms complex with VP1 and have an important role in transcription; VP4, seen in outer capsid as spikes helps the virus to attach to host cells and forms a major virulence factor; VP6, the group specific antigen, have a role in transcription and VP7 provides the protective outer capsid layer. NSP3, a non-structural protein, has major role in translation and the NSP4 functions as viral enterotoxin and virulence factor to increase the intracellular Ca^{2+} concentration and disturb the cellular homeostasis of the host (Estes 2003).

Besides, antigenic specificities of rotaviruses have been assessed and they are classified into groups, subgroups and serotypes; immune responses to rotavirus are essentially serotype-specific. The group and sub-group specificity is conferred by VP6 protein, which differentiate the rotaviruses into 7 groups (A to G) and into two subgroups (mainly subgroup I or II) (Steele *et al*. 2004; Desselberger *et al*. 2005). Group A rotaviruses comprises of important pathogens of human beings, cattle and other animals; Group B rarely affect calves, lambs, piglets and human beings; Group C may affect swine and occasionally humans; Group D, F and G can affect poultry and Group E may affect swine (Steele *et al*. 2004; Villarreal *et al*. 2006). However, group A viruses are the major cause of rotaviral infections in domestic animals, even though atypical rotaviruses (belonging to other groups) have also been isolated in some instances (Snodgrass *et al*. 1984; Steele *et al*. 2004; Ghosh *et al*. 2007b). Exploiting the RNA-PAGE technique, all the 11 segments of rotaviruses can be easily separated, and a characteristic visual pattern known as RNA electropherotype is generated (Chauhan and Singh 1993b; Steele *et al*. 2004). Based on this, group A has a 4–2–3–2 pattern; group B has 4–2–2–3 pattern and group C viruses show a 4–3–2–2-segment migration (Snodgrass *et al*. 1984; Steele *et al*. 2004). Besides, group B rotaviruses are known to have short electropherotypes when compared to the longer electropherotype pattern of group A viruses. Also, it is suggested that detection of different electropherotypes during an outbreak could be an indicative of novel or emerging virus strains. Similarly, there is a serotype-based classification scheme for rotaviruses based on outer capsid proteins VP7 (designated as 'G' as it is glycoprotein) and VP4 (designated as 'P', being a protease sensitive protein) (Steele *et al*. 2004; Desselberger *et al*. 2005). Based on this, rotaviruses affecting domestic animals have been reported to belong to 16 G types and 27 P types (Rao *et al.* 2000; Steele *et al*. 2004; Desselberger *et al*. 2005; Khamrin *et al*. 2007; Gulati *et al.* 2007; Martella *et al*. 2007b). Further, Fukai *et al.* (2007) have demonstrated that there exist group A BRV having novel G and P type specificity, which has not yet been reported among group A rotaviruses. The group A rotaviruses affecting bovines come under G1, G6, G8, G10 and G15 serotypes, and among these G6 and G10 serotypes are most prevalent (Snodgrass *et al*. 1990; Ciarlet *et al*. 1997; Rao *et al.* 2000; Steele *et al*. 2004). It has been found that the G6 serotype has been mostly seen in beef herds and G10 in dairy herds. In India, the G10 serotypes predominated in contrast to the G6 serotypes reported from other countries (Varshney *et al*. 2002). Also, periodic changes in the circulating serotype viz. G10 (1995), G8 (1996) and G6 (1997) have been reported from Japan (Fukai *et al*. 2002). Very recently, novel serotypes like G3 and G5 have been isolated from bovines, strongly suggesting them to be natural reassortants of bovine and

porcine rotaviruses (Park *et al.* 2006; Ghosh *et al.* 2007a). The serotypes affecting other domestic animals are discussed later.

Besides a thorough study on the biological characteristics, researchers have also analyzed the physical and chemical features of rotaviruses. They are known to survive in fecal material for long periods and remain a source of infection to susceptible population (Chauhan and Singh 1996; Steele *et al.* 2004). They are stable at low and high relative humidity, at pH range 3–9; and exhibit a reduction in infectivity at higher temperatures (Murphy *et al.* 1999; Steele *et al.* 2004). Further, the rotaviruses are not inactivated in presence of ether, chloroform, quaternary ammonium disinfectants and sodium hypochlorite (Steele *et al.* 2004). But, ethanol, phenol, formalin and lysol are suitable disinfectants; and 37% formaldehyde (1:10), 0.75% hexachlorophene (1:3) and 67% chloramine-T (1:5) can effectively destroy rotaviruses (Tan and Schnagl 1981; Steele *et al.* 2004).

Virus replication and pathogenesis

Rotaviruses, being stable at a wide range of pH and due to buffering action of milk in the gut of young ones, survive the inclemencies of gastro-intestinal tract, to further invade the intestinal epithelial cells (Hall *et al.* 1993; Murphy *et al.* 1999). The virus replicates in the cytoplasm of epithelial cells of small intestinal villi (Holland 1990; Murphy *et al.* 1999). Its inability to multiply outside the intestinal tract or to invade deeper tissues for causing systemic disease may be an evolutionary mechanism that maximizes shedding capacity and transmissibility without producing harmful effects in host. However, this hypothesis has been challenged recently, and it is suggested that rotaviruses may also infect the neonates, systemically (Ramig 2004; Blutt and Conner 2007).

After entry through oral route, rotaviruses have been found to replicate in the mature villous epithelial cells (enterocytes). For their efficient colonization and infectivity, viruses need their outer capsid to be cleaved and removed, which is facilitated by intestinal proteases like chymotrypsin (Ramig 2004; Desselberger *et al.* 2005). This has been proven by trypsin treatment-based enhanced infectivity of the viruses, seen in cell cultures (Chauhan and Singh 1992e; Steele *et al.* 2004). The epithelial cells of the villi in duodenum are the first to become infected and they releases significant number of virions, to favor more severe attack on enterocytes of mid and distal portion of small intestine (Holland 1990; Ramig 2004; Chauhan *et al.* 2008). The hypothesis of the rotavirus receptors has not yet been proved and it is assumed that the virus may gain entry into the absorptive enterocytes by pinocytosis or direct penetration (Hall *et al.* 1993; Desselberger *et al.* 2005). However, it is suggested that sialic acid or galactose-based receptors may have some role in endocytosis, along with co-receptors like integrins (Murphy *et al.* 1999; Sugiyama *et al.* 2004; Desselberger *et al.* 2005). The pathogenesis commences soon after the virus starts replication in the epithelial cells of the small intestine.

The viral replication occurs after the removal of outer capsid proteins, which lead to activation of RNA-dependent RNA polymerase (VP1). Then the VP1-VP3 transcriptional complex generates the positive strand RNA molecules that act as mRNAs, and get translated in the cytoplasm or serve as template for replication (Murphy *et al.* 1999; Desselberger *et al.* 2005). Later, the proteins VP1, VP2, VP3 and VP6 along with other NSP are added, and finally, budding occurs through the endoplasmic reticulum where VP4 and VP7 proteins are attached to the particles to form the outer capsid layer; and later the virions get released via cell lysis (Desselberger *et al.* 2005). As the multiplication progresses, the mature enterocytes are sloughed off and immature cells from crypts take

over to cover the villus surface, creating a sudden change in the ratio of absorption and secretion, and this result in the accumulation of fluid in the lumen of intestine (Holland 1990; Chauhan and Singh 1992d; Hall et al. 1993; Murphy et al. 1999; Ramig 2004); as the substituted cells are of cuboidal or squamous type that lack functional activities like absorption, glucose coupled sodium transport and secretion of lactase (Holland 1990; Chauhan and Singh 1992d; Steele et al. 2004). The loss of mature enterocytes also results in depletion of bicarbonates, sodium, potassium, chloride and water, eventually leading to acidosis (Holland 1990; Chauhan and Singh 1992d). Microbial fermentation of undigested milk is another key factor responsible for development of acidosis (Mebus et al. 1977). Also, ingestion of milk by neonates having reduced intestinal lactase may further exacerbates the osmotic dysregulation (Chauhan and Singh 1992d; Hall et al. 1993; Steele et al. 2004). All these factors, together with inflammatory changes in the intestinal epithelium, contribute to hypermotility to generate bouts of diarrhea in young animals (Woode and Crouch 1978; Hall et al. 1993; Steele et al. 2004).

Currently, it has been proposed that rotaviral diarrhea may be caused by mechanisms like malabsorption due to destruction of mature enterocytes, activation of the enteric nervous system by vasoactive agents from damaged cells, or by the secretion of a viral enterotoxin, NSP4, which alters calcium-dependent cell permeability and elevates the chloride secretion (Estes 2003; Desselberger et al. 2005; Chauhan et al. 2008). It has been suggested that after cell lysis, the viral NSP4 is released to extracellular area where it binds to adjacent cells in a paracellular fashion (Desselberger et al. 2005). The role of NSP4 as a major determinant of pathogenesis has been ascertained by using the NSP4-specific antibodies to block or reduce the severity of rotavirus induced diarrhea in experimental animals (Estes 2001; Desselberger et al. 2005; Chauhan et al. 2008). Recent reports, based on gene expression profiling using microarrays, also suggest an immune evasion mechanism by rotaviruses, mediated by down regulation of interferons and other cytokines (Aich et al. 2007).

During later stages of disease progression, enterocytes are regenerated along with recovery of the villi; hence the rotavirus infection is considered a self-limiting one, provided the dehydration is not so significant to cause death of young ones (Holland 1990; Steele et al. 2004). The infected ones that recover from diarrhea may return to normal body weight within 10–28 days after infection. It is suggested that the CD8+cytotoxic T lymphocytes (CTL) have crucial roles in clearing the rotavirus infection (Dharakul et al. 1990; Chauhan and Singh 1992b; Chauhan et al. 2008). CD4+helper T cells (T_H) also play a vital role in the successful clearance of rotavirus by inducing B cell response (Malik et al. 2005). Thus both B and T lymphocytes are involved in immune generation against rotaviruses for which B cells secrete rotavirus specific IgA and IgG antibodies, while CTL directly clear the virus from the host. Also, the primary infection in neonates generates rotavirus-specific memory B and T cells which will help to reduce the severity during subsequent infections. Besides, the mature enterocytes also secrete antibacterial compounds, which are important to prevent the bacterial invasion (Chauhan and Singh 1992d; Chauhan et al. 2008). The antiviral activity of the collectins (CL-43) against rotaviruses has been reported which indicate their potential role in host defense against the infection (Reading et al. 1998).

Disease in bovines

Rotaviruses induce diarrhea in neonatal calves that have been exposed to virus contaminated milk, water and feed materials (Holland 1990; Chauhan and Singh 1996; Steele et al. 2004; Malik et al. 2005). As the infected animals shed a high concentration of

virus via feces, and the infectious dose needed is less, the minimal environmental contamination can cause widespread infection in calves (Holland 1990; Chauhan and Singh 1996). Also, aggregation of calves can hasten the transmission through direct contact (Chauhan and Singh 1996) and cows or buffaloes may excrete virus in feces during late stages of pregnancy, thus providing a source of infection to their offsprings. But it has been suggested that the major mode of virus spread is from infected calves to other susceptible ones. Calves are known to excrete the virus through feces by the second day of infection, which continues for 7–8 days; and susceptible calves of 2–3 weeks age may get contracted (Holland 1990; Murphy *et al*. 1999; Bendali *et al*. 1999; Steele *et al*. 2004). After 3 months of age, calves are not usually infected (Dodet *et al*. 1997). However, in buffalo calves, the infection has been recorded up to an age of six months (Muniappa *et al*. 1987).

Rotavirus diarrhea in calves presents an acute disease having very short incubation period of 12–24 hours or at times ranging from 18–96 hours (Chauhan and Singh 1996; Steele *et al*. 2004). It is usually a non-febrile disease, unless complicated by secondary pathogens and the rotaviruses causing disease in calves in the first week of life should be described as of having low virulence and those viruses that cause disease in higher age groups, as highly virulent ones (Bridger 1994). In neonatal calves, the mortality rate due to rotavirus diarrhea may go up to 80%, but majority of reports suggest it to be around 5–20% (Chauhan and Singh 1996). However, the mortality could be higher in calves, which have received insufficient amount of colostrum and are under stressful conditions. As part of inflicting the disease in host, the virus rapidly grows and generates higher yields of virions, which is aimed at completing the transmission cycle before host immune mechanisms may intervene. The affected calves manifest severe diarrhea, dehydration and inappetance, apart from exhibiting a disinclination to move (Woode and Bridger 1975; Woode and Crouch 1978; Holland 1990; Murphy *et al*. 1999; Swain and Dhama 1999). The diarrheic feces are often devoid of blood or mucus, unless there is secondary bacterial infection (Steele *et al*. 2004). Repeated bouts of diarrhea often cause a failure to thrive and death occurs due to severe dehydration; the new born calves having less fluid reserve, becomes more vulnerable (Murphy *et al*. 1999). Usually the gross lesions are not prominent but may be often seen due to the secondary bacterial infections in the intestinal tract. The microscopic changes are quite typical of viral enteritis evincing blunt and short villi in small intestine, loss of brush bordered columnar epithelial cells, substitution by cuboidal or squamous cells from crypts, and infiltration of mononuclear inflammatory cells in lamina propria (Mebus *et al*. 1971b; Holland 1990).

Epidemiology Rotavirus infections are widespread in nature and inflicts diarrhea (scour) in young ones of bovines (Holland 1990; Chauhan and Singh 1996; Malik *et al*. 2005; Steele *et al*. 2004) and the group A rotaviruses account for majority of the infection in bovine species (Snodgrass *et al*. 1984; Steele *et al*. 2004; Ghosh *et al*. 2007b). The virus survives in faeces for several months in rearing pens and barns; and being resistant to many disinfectants, contribute to the persistence of infection (Chauhan and Singh 1996; Steele *et al*. 2004). Further, rotaviral infections are found to have a complex epidemiology because of co-circulation of different serotypes of the virus in a geographical area, primarily due to genetic shift or genomic rearrangements (Shen *et al*. 1994; Murphy *et al*. 1999; Steele *et al*. 2004). In the environment, as per hypothesis, reassortment of two different rotaviruses may generate 2^{11} different progeny viruses, which is much more when compared to avian influenza viruses having only 8 segments (Desselberger *et al*. 2005; Dhama *et al*. 2005). Futher, many researchers have described the incidence and prevalence of the infection in calves ranging from 7–98% even though the average rate should be considered as 30–40%.

In USA (1979), the prevalence rate as high as 98% has been reported while Italy (1988) recorded a prevalence rate of 90% (Schlafer and Scott 1979; Castrucci et al. 1988b). The incidence of bovine rotavirus infection (prevalence rate and method of detection are given in square brackets) has been reported from different countries like Italy [90%, SNT] (Castrucci et al. 1988b), [16.8%, ELISA] (Pisanelli et al. 2005); England [66–67%, Isolation] (Woode 1976); Canada [26.4%, ELISA] (Hussein et al. 1995); France [45.1%, ELISA] (Vende et al. 1999); Japan [16.7%, RT-PCR] (Fukai et al. 1998); Ireland [91%, ELISA] (Reidy et al. 2006); India [46.2%, ELISA, PAGE] (Chauhan and Singh 1996); Netherlands [46%, ELISA] (De Leeuw et al. 1980); USA [98.1%, SNT] (Schlafer and Scott 1979), [44%, RT-PCR] (Chinsangaram et al. 1995); Turkey [41.2%, ELISA] (Gumusova et al. 2007); Bangladesh [7%, PAGE] (Selim et al. 1991); Bulgaria [42%, ELISA] (Kharalambiev et al. 1983); Australia [49%, PAGE] (Tzipori 1985), [48.7%, ELISA] (Huang et al. 1992); Sweden [43.8%, ELISA, PAGE] (de Verdier Klingenberg and Svensson 1998); Brazil [17%, ELISA] (Barbosa et al. 1998), [19.4%, ELISA] (Alfieri et al. 2006); Argentina [62.5%, RT-PCR] (Garaicoechea et al. 2006); Srilanka [68.5%, ELISA] (Sunil-Chandra and Mahalingam 1994); Venezuela [11.7%, ELISA] (Ciarlet et al. 1997) and Switzerland [46%, ELISA] (Luginbuhl et al. 2005).

Factors affecting disease severity The factors that influence the severity of the disease as well as pathogenesis are reduced intake of colostrum, age and health status of the calves, immune status of the dam, degree of exposure and virulence of virus, and the presence of secondary pathogens (Holland 1990; Bridger 1994; Chauhan and Singh 1996; Steele et al. 2004). If rotavirus infection occurs in combination with *E. coli* or corona virus, the mortality rate could be high. Several other factors like dehydration, unhygienic environment, temperature variations or chilling during winter and high population density in farms may also enhance disease severity (Woode 1976; Chauhan and Singh 1996). However, the major stress factors that potentiate the infection have been found to be cold climate and marked fluctuations in the ambient temperature between day and night (Chauhan and Singh 1996). An age-related resistance has also been observed. As there is competition between the rate of replication of rotavirus and replacement of enterocytes in older animals; highly virulent strains can only cause diarrhea in adult calves (Bridger 1994; Dodet et al. 1997). In another interesting observation, the BRV infection seemed to occur more frequently in female calves of both cattle and buffaloes (Hasso and Pandey 1986).

Diagnosis Rapid and accurate detection of the etiological agent is important to further contain the spread of infection in animals. Generally, the diagnosis of rotavirus is based on isolation and identification of the virus in intestinal contents or feces (Holland 1990; Chauhan and Singh 1996; Steele et al. 2004). Isolation of BRV has been performed in rotavirus specific cell line MA 104 (Simian origin), and direct detection has been facilitated by electron microscopy (Mebus et al. 1969; Chauhan and Singh 1992e; 1993a; Steele et al. 2004). Immunofluorescence test (IFT), immunoperoxidase test (IPT) and viral RNA-based PAGE have also been employed to detect the infectious agent (Hall et al. 1985; Chauhan and Singh 1992c; 1993b; 1999; 2001; Steele et al. 2004). Latex agglutination test (LAT) has also been used for the rapid detection of rotavirus antigens (Hammami et al. 1990; Reidy et al. 2006). ELISA, being a highly sensitive and specific test, has been developed by many workers and used for the identification of rotaviruses (Holland 1990; Barbosa et al. 1998; de Verdier Klingenberg and Svensson 1998; Murphy et al. 1999). Also, a rapid dot-immunobinding assay has been developed by direct application of antigen to nitrocellulose membrane followed by the detection of antigen-antibody complex, within few hours

(Chauhan and Singh 1992a). Efforts have been made to improve the specificity of ELISAs by using type-specific antibodies in antigen-capture assays. Regarding the molecular detection tools, initially, hybridization tests were developed using labeled cDNA probe (Palombo 2002). Such probes, based on hypervariable regions of outer capsid genes of rotaviruses, could be used in hybridization assays to characterize animal rotavirus strains. More rapid detection tools like PCR have caught the attention of researchers in recent years. Presently, RT-PCR, using the VP4 or VP7 gene primers, is much widely used for detection of animal rotaviruses (Ellis and Daniels 1988; Chinsangaram *et al.* 1995; Alfieri *et al.* 2004; Garaicoechea *et al.* 2006). Also, improvisations of RT-PCR like semi-nested or multiplex RT-PCR are being developed (Luan *et al.* 2006). Such novelties have greatly assisted in the G-typing of animal rotaviruses. Further, the sequencing of the outer capsid genes has also helped in differentiating various BRV isolates (Reidy *et al.* 2006). Very recently, genotype characterization using microarrays, capable of identifying the G and P serotypes in a most sensitive and specific manner, is also being suggested (Aich *et al.* 2007).

Prevention and control Good management and hygienic practices can help to reduce the incidence of rotaviral diarrhea in farm animals (Holland 1990; Chauhan and Singh 1996; Steele *et al.* 2004). Antibiotics to control secondary bacterial infection and fluid and electrolyte therapy to restore the fluid reserve, has to be given due importance so that the mortality rate in calves could be minimized (Murphy *et al.* 1999; Steele *et al.* 2004). For preventing infection, the local or mucosal immunity has to be enhanced, as they are more crucial in providing resistance to the infection. The rotavirus antibodies transmitted through colostrum is a key factor in protecting the neonates (Saif and Fernandez 1996; Dodet *et al.* 1997; Agrawal *et al.* 2002). Even though colostral antibodies enter the circulation, they are often considered less effective in protecting young ones when compared to those present in the intestinal lumen (Saif and Fernandez 1996); however, the antibody titer in calf serum could be considered as an indicator of protection against rotavirus diarrhea (Kohara and Tsunemitsu 2000). To boost the maternal antibody levels, the dam has to be immunized with rotavirus vaccines few weeks prior to parturition, which could enhance the level of protection in neonates (Holland 1990; Saif and Fernandez 1996; Barrandeguy *et al.* 1998; Agrawal *et al.* 2002; Steele *et al.* 2004). In calves, the protection against disease is primarily dependent on the presence of rotavirus-specific antibodies in the intestinal lumen (Castrucci *et al.* 1984a; Agrawal *et al.* 2002; Steele *et al.* 2004). This has been further ascertained when calves given pooled colostrum from vaccinated dams have been found to be devoid of diarrhea and virus shedding. Also, newborn calves fed for 5 consecutive days with colostrum obtained from vaccinated cows, have been refractory to rotavirus infections (Castrucci *et al.* 1988a). But, the passive immunity, which is conferrable to calves through rotavirus specific-antibodies in colostrum, may decline after calving and could be inadequate against a large quantum of the virus (Kohara and Tsunemitsu 2000). Hence, by vaccination, if serum antibodies are generated at high levels in dam, the colostrum should exert sufficient protective effect in neonates. Further, in bovines, while vaccination, if intramuscular and intra-mammary routes are combined, it could significantly enhance serum and colostrum antibody titers (Saif and Fernandez 1996). The feeding of artificial colostrum, containing BRV-specific immunoglobulins, whey and vegetable oils, are also being looked upon as an alternative strategy (Murakami *et al.* 1986). There are also reports of chicken egg yolk immunoglobulins being highly efficient in protecting neonatal calves from rotavirus diarrhea. Recently, it has been described that provision of one hyper-immune egg per day to newborn calves can reduce the severity of diarrhea (Bilbao *et al.* 2006). Also, supplementation of probiotics can prevent rotavirus-induced diarrhea in young ones (Gill and Prasad 2008).

Since the inactivated rotavirus vaccines used to vaccinate dams have not been occassionally found safe, researchers have been trying to develop new generation vaccines that are highly efficacious and regarded as much safer during administration (Kim *et al.* 2002a; 2002b; Garcia-Diaz *et al.* 2004; Komoto *et al.* 2006). Among these, plasmid DNA vaccines, virus like particles (VLPs), subunit vaccines and plant based edible vaccines are the front-runners. Immunization using plasmid DNA encoding the VP4 gene of rotaviruses has been found to induce humoral and cell-mediated immune response while a DNA vaccine encoding the VP6 gene has been reported to induce the anti-VP6 IgA antibodies by the intestinal lymphoid cells (Garcia-Diaz *et al.* 2004). In another experiment, it has been observed that orally administered plasmid DNAs encapsulated in polymeric microparticles may be of much higher utility against rotavirus infections (Herrmann 2006). Similarly, subunit vaccines based on the VP4 protein of rotaviruses, expressed in prokaryotic system, have been found useful in developing mucosal immunity in animals. Likewise, virus-like particles (VLPs), containing rotavirus capsid proteins, produced in baculovirus expression system, can be used as effective vaccines. It has been noticed that the colostrum from VLP vaccinated cows could ably provide passive protection against diarrhea and reduce the shedding of virus to the environment (Ciarlet *et al.* 1998; Fernandez *et al.* 1998). However, it has been observed that at least proteins from two different serotypes are needed to confer maximum efficacy while developing VLP-based vaccines (Kim *et al.* 2002a).

Researchers are also trying to exploit subunits of VP4 protein, for outplaying the alpha-2 beta-1 integrin-based attachment of rotaviruses, and this strategy may potentially block the rotavirus infections (Graham *et al.* 2006). Also, reverse genetics, a powerful and ideal methodology for generating an infectious clone of rotaviruses containing desirable gene segments, has been suggested for vaccine development (Komoto *et al.* 2006). Similarly, much research is focused on for developing plant-based edible vaccines that are capable of expressing rotavirus antigens, for prevention of rotavirus diarrhea in animals (Wigdorovitz *et al.* 2004). Recently, the utility of recombinant BCG vaccines, expressing rotavirus VP6 protein, has been explored using mouse models (Dennehy *et al.* 2007). Based on the current progress achieved, these novel vaccines and strategies coupled with the conventional vaccination programs are expected to make significant strides towards maintaining a bovine population free of rotaviral infections.

Disease in other domestic animals

Apart from bovines, rotavirus diarrhea has been considered a major infectious disease that cause enteritis and associated digestive disorders in young ones of many domestic animals as well as poultry (Holland 1990; Malik *et al.* 1995; Dodet *et al.* 1997; McNulty 2003; Wani *et al.* 2004; Fukai *et al.* 2006). In many domestic animals, the features of the infection, the intestinal involvement and the pathogenesis are similar to bovines, even though considerable serotype differences exist among animal rotaviruses of different geno-groups. A brief account of the rotavirus infection in equines, swine, ovine, caprine, canines, felines and poultry has been discussed further.

Equines In equines, enteritis and diarrhea poses a great challenge for professionals who are involved in intensive horse breeding programs, and the most commonly diagnosed etiological agent of foal diarrhea is Group A rotavirus (Imagawa *et al.* 1994; Fukai *et al.* 2006). However, diarrhea in foals may also be caused by *Salmonella spp., Rhodococcus equi, Clostridium difficile, C. perfringens, Strongyloides spp.* and *Cryptosporidium spp.*

(Netherwood *et al*. 1996; Fukai *et al*. 2006). Serotypes G3, G5, G10, G13 and G14 have been commonly found among equine rotavirus (ERV) isolates (Imagawa *et al*. 1994; Tsunemitsu *et al*. 2001). Majority of the strains belong to G3 or G14 with a P[12] serotype (Tsunemitsu *et al*. 2001; Fukai *et al*. 2006). Recently, Gulati *et al.* (2007) have reported a G16 serotype among equine group A rotavirus.

For diagnosis and characterization of ERV, RT-PCR, ELISA or PAGE pherotyping are being used (Tsunemitsu *et al*. 2001; Gulati *et al*. 2007). Nucleotide sequencing, coupled with DNA probing or RNA-RNA hybridization, has helped in characterizing the ERVs at genomic level and also to detect the interspecies relatedness (Fukai *et al*. 2006; Gulati *et al*. 2007). For prevention and control of the rotavirus diarrhea in foals, commercially available inactivated vaccines have proven to be quite effective for vaccinating dam, for dwindling down the infection in foals (Barrandeguy *et al*. 1998; Fukai *et al*. 2006). In addition, it has been observed that foals given bovine colostral immunoglobulins for 3 to 5 days have shown reduced morbidity due to viral diarrhea (Watanabe *et al*. 1993). Besides effective prophylactic strategies, management practices like quarantine, disinfection, and strict hygiene are essential for preventing the disease in foals. Altogether, assisted by a thorough understanding of the disease epidemiology as well as serotypes of the virus, prevention and control strategies have to be revised, for keeping the thoroughbred foals away from this economically important disease.

Swine Swine also suffers from rotavirus-associated diarrhea, and the infection is commonly seen in 1 to 4 week old or weaned piglets. The porcine rotaviruses (PRV) have been considered to have a worldwide distribution (Holland 1990; Teodoroff *et al*. 2005). PRV belong to groups A, B, C, and E, but similar to other animals, group A rotaviruses are the most prevalent ones (Holland 1990; Steele *et al*. 2004; Martella *et al*. 2007a). Rotaviral diarrhea has to be differentially diagnosed from infectious diarrhea of piglets caused by *E. coli*, *C. perferingens*, calici, corona or astroviruses (Holland, 1990). In mature herd or in piglets of above one month of age, the PRV may not cause clinical disease, unless complicated by secondary pathogens.

For detection, the virus has to be isolated in MA104 cell lines, similar to most of the mammalian rotaviruses. Diagonsis has also been facilitated by electron microscopy of diarrheic feces or immunofluorescence testing of tissue specimens (Terrett *et al*. 1987). For differential diagnosis, recently, a multiplex RT-PCR has been developed which could ably differentiate porcine epidemic diarrhea virus, transmissible gastroenteritis virus and porcine group A rotavirus (Song *et al*. 2006). For serotyping PRVs, virus neutralization tests or cross-protection assays have been performed and reports of emergence of novel serotypes have been documented (Holland 1990). However, due to the ease of analysis, characterization has largely depended on sequencing of VP4 or VP7 genes, and serotypes such as G1, G2, G3, G4 and G5, with P serotypes ranging from P[21–27] have been reported (Holland 1990; Khamrin *et al*. 2007; Steyer *et al*. 2007; Martella *et al*. 2007b). By phylogenetic analysis, group A PRVs belonging to G9 serotype with P serotypes P[13] and P[23], have been reported to predominate in young pigs, especially in countries like Japan (Teodoroff *et al*. 2005). Besides, the role of PRV in generating reassortants with a wide variety of other mammalian rotaviruses including the human rotaviruses has been suggested (Ciarlet *et al*. 2001; Varghese *et al*. 2006; Mascarenhas *et al*. 2007; Parra *et al*. 2008). For an effective prevention of rotavirus diarrhea in piglets, environmental stress factors have to be kept minimal and they have to be provided with colostrum from vaccinated dams (Holland 1990). Likewise, all-in all-out procedures and cleaning and disinfection of sty, has to be followed as the PRV have high environmental resistance. Currently, researchers are

trying to develop novel immunization strategies to tackle the problem of rotavirus diarrhea in swine. A recombinant VP6-microsphere (MS) based subunit vaccine has been developed which provided mucosal immunity by inducing high levels of VP6-specific IgA antibodies (Kim et al. 2002b). Also, live rotavirus prime/DNA boost vaccine regimen can be formulated, which exploits the use of plasmid DNA vaccine encoding VP6 gene of PRV.

Ovines In ovines, the rotaviruses are known to cause enteritis and diarrhea, especially in neonatal lambs (Theil et al. 1996, Wani et al. 2004). Other infectious agents that may cause neonatal diarrhea in lambs are *E. coli* and *Cryptosporidium* (Tzipori et al. 1981; Ellis and Daniels 1988). Besides the commonly seen group A ovine rotaviruses (ORV), atypical group B viruses may also cause the infection in ovines (Holland 1990; Theil et al. 1996). Group A ORV strains isolated from lambs belong to serotypes G1, G3, G5, G6, G8, G9, and G10, among which G3, G6, and G10, with P types belonging to P[1], P[11] or P[14], are often encountered (Holland 1990; Munoz et al. 1995a). ORV, isolated in MA104 cell lines can agglutinate chicken, sheep, rabbit, guinea pig and human erythrocytes (Chasey and Banks 1986). During earlier times, the detection of ORV depended on immunofluorescence or immuno-peroxidase test, and electron microscopy (Chasey and Banks 1986; Ellis and Daniels 1988), and by electron microscopy giant multinucleate syncytia composed of fused epithelial cells along with intracytoplasmic virus particles, are observed [Chasey and Banks 1986]. Latex agglutination test and ELISA have also been used to detect the presence of ORV in lambs (Ellis and Daniels 1988). Nowadays, nested reverse transcriptase-polymerase chain reaction (RT-PCR) are being developed for the detection, which is based on a target region in the sixth gene segment of ORV. For characterization of ORV at genomic level, PAGE pherotyping and gene sequencing are being commonly employed (Chasey and Banks 1986; Holland 1990). For prevention of the disease, the best option is feeding colostrum to the neonates so that passive immunity is transferred from dam to the young lambs. Vaccinating the adult animals prior to parturition has to be practiced, for which vaccines based on circulating serotypes have to be used. For evincing much higher protection, an immunostimulating complex (ISCOM) vaccine has been prepared from recombinant ORV proteins that could induce both cellular and humoral immune responses (Van Pinxteren et al. 1999).

Caprines The prevalence of caprine rotavirus (CRV) causing diarrhea in 2–3 days old kids has been widely reported (Mendes et al. 1994; Munoz et al. 1995b). The CRV is known to cause severe diarrhea along with dehydration, anorexia and prostration in neonatal kids (Munoz et al. 1995b). *Cryptosporidium parvum*, *Clostridium perfringens* and enterotoxigenic *Escherichia coli* (ETEC) are other agents responsible for diarrhea in kids (Munoz et al. 1995b). Mainly, CRV isolates belong to group A rotaviruses, as assessed by antigenic reactivity with group A monoclonal antibody (MAb) or by the migration patterns in PAGE (Legrottaglie et al. 1993; Mendes et al. 1994). Analysis with MAbs to the subgroup-specific VP6 antigen showed that they belong to subgroup I, like majority of the animal rotaviruses (Mendes et al. 1994). Also, some isolates of CRV have been found to show characteristic electropherotypes of group B rotaviruses (Munoz et al. 1995b). Based on hybridizations with cDNA chemi-luminescent probes, kids have also been shown to be getting infection from group B CRVs (Gueguen et al. 1996). Further, the majority of isolates belonging to group A CRVs when characterized by RT-PCR assay, have been identified to belong to G6 and P[5] serotypes. Even though, the relatedness of ORVs with simian and lapine rotaviruses has been suggested earlier, genetic analysis by RNA-RNA hybridization revealed the genomic RNA constellation of the CRV isolates to be unique among rotavirus genogroups, suggesting a separate status for the CRV (Lee et al. 2003).

Canines and felines Similar to the domestic livestock, pet animals like dogs and cats, also suffer from rotavirus induced diarrhea and such infections have been reported by many workers (McNulty *et al*. 1978; Hoshino *et al*. 1981, Hoshino *et al*. 1982; Nakagomi *et al*. 1989; Mochizuki *et al*. 1997; Martella *et al*. 2001a; 2001b; Kang *et al*. 2007). Adult dogs may get asymptomatic infection and in young pups of less than 3 months of age, the canine rotaviruses cause acute enteritis manifested by diarrhea, lack of appetite and lethargy (Hoshino *et al*. 1982; Martella *et al*. 2001a; Kang *et al*. 2007). The infection in susceptible pups can lead to acute diarrhea within 20–24 hours. The virus is known to produce ultrastructural changes that include swollen and hypertrophied epithelial cells, in jejunal and ileal regions. The group A rotaviruses detected in the diarrheal feces can be subsequently isolated by using either MA104 or Madin Darby canine kidney (MDCK) cell lines (Fulton *et al*. 1981; Martella *et al*. 2001a). Using indirect immunofluorescence test, the virus in cell cultures or its presence in tissue specimens has been studied (Fulton *et al*. 1981). Besides, many workers have tried to characterize the canine rotaviruses to classify them under a separate geno-group. By neutralization assay, more antigenic relationship between canine and simian rotaviruses and much lesser relationship with feline, bovine and porcine rotaviruses have been suggested (Hoshino *et al*. 1982). Also some canine strains were found related to human rotavirus serotypes (Hoshino *et al*. 1983). However, most of the isolates belonged to subgroup I during hybridization assays, and showed high degree of homology with other canine strains, suggesting a distinct geno-group (Nakagomi *et al*. 1989). Presently, based on RT-PCR assay and restriction endonuclease analysis, it has been established that majority of canine strains belong to group A rotaviruses, with serotype G3 in combination with P[5] or P[3] (Martella *et al*. 2001a; 2001b; Kang *et al*. 2007). For the control of disease in canines, vaccines are not commercially popular; however it is recommended that the affected pups have to be given adequate fluid therapy to prevent dehydration caused by intermittent diarrhea. Since, the canine rotaviruses have been shown to lose its virulence during attenuation in cell cultures, geno-group specific live vaccines should be developed to prevent rotavirus diarrhea in pups (Martella *et al*. 2001a).

In felines, there are only few published reports on rotavirus diarrhea, probably due to the subclinical infections often observed in this species. Diarrhea, which is mild and transient, is likely to be seen in kittens, but the severity may be enhanced due to secondary infections. Rotavirus has been reported to cause both symptomatic and asymptomatic infections in cats, especially in colostrum-deprived neonates (McNulty *et al*. 1978; Hoshino *et al*. 1981). The feline rotaviruses (FRV) belong to group A, and the serotype G3 has been found to be the most significant serotype (Hoshino *et al*. 1981; Nakagomi *et al*. 1990). Electron microscopy of feces, isolation of the FRV and PAGE analysis of viral RNA have been described to be useful for diagnosing rotavirus infections in felines. FRVs, like canine and simian rotaviruses, have been found less dependent on trypsin when compared to human, bovine, porcine and avian rotaviruses (Hoshino *et al*. 1981). Also, it has been reported that two genogroups are present within feline rotaviruses, one resembling the feline strains and the other resembling the canine rotavirus strains (Nakagomi *et al*. 1990). Some evidences, based on the epidemiological investigations of rotavirus excretion in cats in conjunction with human surveillance have suggested that felines might act as a source of infection to humans. But, the comparison of feline and human electropherotypes could not provide any measure of the degree of relatedness, hence ruling out this possibility (Birch *et al*. 1985). However, in another study, FRV strains have been found similar in their genomic constellation to human rotavirus G3 serotype, lending support to the earlier view that similar rotaviruses have been circulating in both human and feline population (Mochizuki *et al*. 1997).

Poultry Similar to domestic animals, rotaviruses have been identified as one of the major etiological agents of diarrhea and enteritis in avian species (McNulty 2003; Jackwood *et al*. 2007). In poultry, both in layer and broiler birds, rotavirus has established a pathogen that manifests diarrhea, dehydration, anorexia, and loss of weight gain and nutrient malabsorption. Cumulatively, all these can lead to huge economic losses to poultry production systems (McNulty 2003; Villarreal *et al*. 2006). Rotavirus infection is commonly observed in chickens and turkeys, but ARVs have been isolated from other birds also (Yason and Schat 1985; McNulty 2003). Recently, it has been suggested that ARVs can also cause runting and stunting syndrome in poultry (Otto *et al*. 2006). Typically, the ARV belongs to groups D, F, and G (McNulty 2003; Villarreal *et al*. 2006) but those belonging to group A have been considered a major threat (Brussow *et al*. 1992; Sugiyama *et al*. 2004; Villarreal *et al*. 2006). In contrast to the disease in domestic animals, the older birds can also be susceptible like the young ones, and turkeys have been the major sufferers when compared to chickens (Yason and Schat 1987). In birds, the *in vitro* cytotoxic activity studies have suggested a prominent role for natural killer (NK) cell activity against rotavirus infections (Myers and Schat 1990). Also, the role of maternally derived immunoglobulins in protecting the intestinal mucosa during early life has been documented (Shawky *et al*. 1993; McNulty 2003). For detection of ARV, isolation in MA104 cell line, PAGE, EM or ELISA has to be performed (Yason and Schat 1985; McNulty 2003; Villarreal *et al*. 2006). Recently, a multiplex RT-PCR assay for differentiating astroviruses and avian rotaviruses has been developed to use in poultry flocks (Day *et al*. 2007). For genomic characterization of ARVs, PAGE, northern hybridization or sequencing of VP4 and VP7 genes are being followed, and limited informations exist regarding the serotypes; even though there are reports of presence of serotype G7 in birds (McNulty 2003). For control of infection, secondary bacterial enteritis has to be checked, for which antimicrobial medication is essential, and dehydration has to be countered by implementing fluid and electrolyte therapy.

Inter-species transmission of rotaviruses

The inter-species transmission abilities of mammalian rotaviruses have been demonstrated by assessing the presence of non-genogroup-specific antibodies or by challenge studies with different rotaviruses (Sato *et al*. 1981; Heinrich *et al*. 1983; Castrucci *et al*. 1984b; Castrucci *et al*. 1985). Calves inoculated with equine or human rotaviruses have been protected against BRV challenge, showing their close relationship (Woode *et al*. 1978). It has also been suggested that porcine, murine, simian and equine rotaviruses are antigenically related (Mebus *et al*. 1977; Castrucci *et al*. 1985). The capability of human rotaviruses (HRV) to affect calves or piglets has been reported, and it has been found that piglets excreted the virus without clinical signs while calves produced intestinal lesions (Bridger *et al*. 1975; Mebus *et al*. 1977). Further, the presence of HRV antibodies has been detected in milk of cows (Yolken *et al*. 1985). In another study, calves were reported to be susceptible to rabbit rotaviruses and the rabbits also became infected, when inoculated with a BRV strain (Castrucci *et al*. 1984b). Also, it has been suggested that infection can occur in calves from rotaviruses of simian, porcine or lapine origin (Castrucci *et al*. 1985). Similarly, pet animals like cats and dogs may also excrete BRV, and are thought of having role in propagation of BRV (Schwers *et al*. 1982). Much later, in an interesting observation, a BRV isolate has been noticed to differ from other mammalian isolates during probe analysis, but got hybridized to genome of an ARV strain, thus representing a classical

candidate for a natural interspecies transmission between different classes of vertebrates (Brussow *et al*. 1992). Apart from bovines, interspecies transmission of ARVs to experimental animals has also been reported (Rohwedder *et al*. 1995; Mori *et al*. 2001). Similarly, instances of transmission of mammalian rotaviruses to avian species have also been documented (Wani *et al*. 2003).

Similarly equine rotaviruses may also have close serological and genomic relations with HRV and porcine rotaviruses. On sequence comparison of NSP4 of the rotavirus strains belonging to equine and swine, it has been observed that the ERV strains may represent an excellent example of interspecies transmission from swine to equines (Ciarlet *et al*. 2001). Further, hybridization experiments with probes prepared from different geno-groups and sequence analysis have given ample evidence for interspecies transmission during the evolutionary process of rotaviruses (Palombo 2002). It has also been suggested that rotaviruses circulating in one animal species can pose a risk to another by re-emerging as a reassortant virus (Khamrin *et al*. 2006). Very recently, the porcine G4&G5, G6 and G8 serotypes have been found closely related to rotaviruses circulating in humans, cattle and camelids, respectively; and this could suggest that swine might play a crucial role as reservoir and generator of newly adapted emerging strains for human beings and other animal species (Duan *et al*. 2007; Parra *et al*. 2008).

Zoonotic significance of animal rotaviruses

Animal rotaviruses could be considered as a potential threat to humans due to the possibility of genetic reassortment, materialized by exchange of gene segments. Infections by bovine-human reassortants and the presence of several unusual strains in cases of infant diarrhea suggest that animal rotaviruses could be considered of having significant zoonotic impact (Ramani and Kang 2007). Increasing evidences have been obtained regarding direct transmission; or animal rotaviruses contributing one or several genes to make animal-human reassortant viruses (Nakagomi and Nakagomi 1991; Adah *et al*. 2003; Malik *et al*. 2005; Muller and Johne 2007; Ramani and Kang 2007). Further, the surveillance of circulating rotaviruses in the human population has revealed the presence of uncommon serotypes that are commonly found in domestic animals (Cook *et al*. 2004; Malik *et al*. 2005).

In infants, generally the rotavirus infection is characterized by watery diarrhea and severe dehydration while the infection in adults is often subclinical (Malik *et al*. 2005; Ramani and Kang 2007). The main reason for a zoonotic transmission is the close contact between humans and domestic animals, promoting exposure to rotaviruses, especially in geographical regions where there may be intermittent floods or torrential rains. Potential also exists for contamination of water bodies and food crops with animal rotaviruses, via animal excreta. Similarly, animal rotaviruses could also be transmitted by food materials which are eaten raw, especially vegetables (Svensson 2000; Malik *et al*. 2005). Further, rotavirus strains such as G3 (commonly seen in cats, dogs, pigs and horse), G5 (pigs and horses), G6 and G8 (cattle), G9 (pigs and lambs) and G10 (cattle) have been isolated from the human population from different parts of the world (Desselberger *et al*. 2001; Malik *et al*. 2005; Ramani and Kang 2007).

Studies have also given numerous clues regarding human rotaviruses (HRV) deriving the surface proteins from animal rotaviruses. To further understand the epidemiological and genetic basis for the origin of human rotavirus (HRV) strains, relative frequencies of different serotypes of BRVs have been analyzed (Varshney *et al*. 2002). Based on the sequence analysis of VP4 and VP7 genes, it is presumed that there is predominant

association of BRV G10 serotype-derived reassortant strains causing asymptomatic infections in newborn infants. It has now been well proven that the HRV can acquire genomic segments from BRV strains by the phenomenon of gene reassortment (Adah *et al.* 2003). Similarly, hybridization experiments with HRV have provided the evidence for the close relationship with feline and canine rotaviruses (Nakagomi *et al.* 1990). In Italy, the sequence analysis of VP6, VP7, VP4 and NSP4 genes of human rotaviruses has given vital clues regarding the role of canine rotaviruses in contributing gene segments for rearrangement with human viruses (De Grazia *et al.* 2007). Also, existence of relatedness have been identified in case of porcine rotaviruses, when VP1, VP2, VP3, VP4, VP7 and NSP4 genes were analyzed with those of recent HRV strains (Teodoroff *et al.* 2005; Varghese *et al.* 2006; Mascarenhas *et al.* 2007). Cumulatively, all these research findings are pointing to the fact that such events may lead to evolution of novel reassortant human viruses during mixed infections that could further complicate the infection in infants. To conclude, the rapid evolution often seen with rotaviruses and the emergence of novel strains warrants an intensive serotype-specific surveillance before implementing any vaccination program to control the infection in human beings.

Conclusion

Considering the animal species and humans together, rotavirus diarrhea have to be considered as the proximal cause of enteritis and diarrhea in infants and young ones of domestic animals. Rotaviruses have extreme genetic diversty and are resistant to many common disinfection methods, thus adding to the difficulty of implementing suitable preventive measures against the infection. Gene reassortment or rearrangements has paved way for evolution of quasi-species that differ antigenically, and cause failure of vaccination programs. However, to prevent the losses due to rotavirus infections, multivariate approaches including good management, sanitation and hygiene together with vaccinating the dam in order to confer protection to neonates, has to be strictly followed. Since the local or mucosal immunity in the intestinal tract is crucial for protection, the intake of rotavirus-specific antibodies via colostrum is of paramount importance in reducing the incidence of the infection in young ones. As concurrent infections with other pathogens like *E. coli* can potentiate the effects of rotavirus infection, prime importance has to be given for eradicating such pathogens from intensive farming systems. Also, research should target to analyze the role of NSP4 is augmenting the severity of the diarrhea in neonates of domestic animals. The receptor based blocking of rotaviruses using viral protein subunits should also be considered a strong candidate for future research. Further, it is important to analyze the animal rotavirus genome, by serotype specific-RT-PCR or gene sequencing, for assessing the interspecies transmission of these viruses between other mammalian species including human beings. Currently, based on the novel techniques evolved in the field of vaccinology, there is a trend for the development of new generation efficacious vaccines. DNA vaccines and subunit vaccines have been reported to develop sufficient levels of serum antibody titres in dam. Similarly, the recombinant proteins expressed in baculovirus system has to be utilized for developing VLP-based vaccines, which could stimulate the production of desirable quantities of specific antibodies in serum as well as colostrum. Research also needs to be focused on for developing plant-based edible vaccines that may provide a simple and inexpensive method of immunoprophylaxis against this economically important pathogen of domestic animals; and all such novel efforts cumulatively may help to dwindle down the zoonotic risk to a susceptible human population.

References

Adah, M.I., Nagashima, S., Wakuda, M. and Taniguchi, K., 2003. Close relationship between G8-serotype bovine and human rotaviruses isolated in Nigeria. *Journal of Clinical Microbiology*, 41, 3945–3950

Agrawal, D.K., Singh, N.P. and Chauhan, R.S., 2002. Colostral antibodies against rotavirus infection in neonatal calves. *Journal of Immunology and Immunopathology*, 4, 107–109

Aich, P., Wilson, H.L., Kaushik, R.S., Potter, A.A., Babiuk, L.A. and Griebel, P., 2007. Comparative analysis of innate immune responses following infection of newborn calves with bovine rotavirus and bovine coronavirus. *Journal of General Virology*, 88, 2749–2761

Alfieri, A.F., Alfieri, A.A., Barreiros, M.A., Leite, J.P. and Richtzenhain, L.J., 2004. G and P genotypes of group A rotavirus strains circulating in calves in Brazil, 1996–1999. *Veterinary Microbiology*, 99, 167–173

Alfieri, A.A., Parazzi, M.E., Takiuchi, E., Medici, K.C. and Alfieri, A.F., 2006. Frequency of group A rotavirus in diarrhoeic calves in Brazilian cattle herds, 1998–2002. *Tropical Animal Health and Production*, 38, 521–526

Barbosa, E.F., Figueiredo, H.C.P., Garcia, A.M., Lobato, Z.I.P. and Lage, A.P., 1998. Group A rotavirus in calves in Minas Gerais State, Brazil. *Ciencia Rural*, 28, 435–439

Barrandeguy, M., Parreno, V., Lagos Marmol, M., Pont Lezica, F., Rivas, C., Valle, C. and Fernandez, F., 1998. Prevention of rotavirus diarrhoea in foals by parenteral vaccination of the mares: field trial. *Development of Biological Standards*, 92, 253–257

Bendali, F., Bichet, H., Schelcher, F. and Sanaa, M., 1999. Pattern of diarrhea in newborn beef calves in south-west France. *Veterinary Research*, 30, 61–74

Bilbao, G.N., Chacana, P.A., Mendiburu, A., Rodriguez, E., Blackhall, J.O. and Terzolo, H.R., 2006. Prophylaxis of neonatal diarrhoea in dairy calves using egg yolk immunoglobulins (IgY). *Revue Medicinia Veterinaria Buenos Aires*, 87, 135–139

Birch, C.J., Heath, R.L., Marshall, J.A., Liu, S. and Gust, I.D., 1985. Isolation of feline rotaviruses and their relationship to human and simian isolates by electropherotype and serotype. *Journal of General Virology*, 66, 2731–2735

Blutt, S.E. and Conner, M.E., 2007. Rotavirus: to the gut and beyond! *Current Opinions in Gastroenterology*, 23, 39–43

Bridger, J.C., 1994. A definition of bovine rotavirus virulence. *Journal of General Virology*, 75, 2807–2812

Bridger, J.C., Woode, G.N., Jones, J.M., Flewett, T.H., Bryden, A.S. and Davies, H., 1975. Transmission of human rotaviruses to gnotobiotic piglets. *Journal of Medical Microbiology*, 8, 565–569

Brussow, H., Nakagomi, O., Gerna, G. and Eichhorn, W., 1992. Isolation of an avianlike group A rotavirus from a calf with diarrhea. *Journal of Clinical Microbiology*, 30, 67–73

Castrucci, G., Frigeri, F., Ferrari, M., Cilli, V., Caleffi, F., Aldrovandi, V. and Nigrelli, A., 1984a. The efficacy of colostrum from cows vaccinated with rotavirus in protecting calves to experimentally induced rotavirus infection. *Comparative Immunology and Microbiology*, 7, 11–18

Castrucci, G., Frigeri, F., Ferrari, M., Cilli, V., Aldrovandi, V., Caleffi, F. and Gatti, R., 1984b. Comparative study of rotavirus strains of bovine and rabbit origin. *Comparative Immunology and Microbiology*, 7, 171–178

Castrucci, G., Frigeri, F., Ferrari, M., Cilli, V., Aldronvandi, V., Gatti, R. and Rampichini, L., 1985. A comparison of rotavirus strains of bovine, simian and porcine origin. *European Journal of Epidemiology*, 1, 274–280

Castrucci, G., Frigeri, F., Ferrari, M., Aldrovandi, V., Tassini, F. and Gatti, R., 1988a. The protection of newborn calves against experimental rotavirus infection by feeding mammary secretions from vaccinated cows. *Microbiologica*, 11, 379–385

Castrucci, G., Frigeri, F., Ferrari, M., Cilli, V., Gualandi, G.L. and Aldrovandi, V., 1988b. Neonatal calf diarrhea induced by rotavirus. *Comparative Immunology and Microbiology*, 11, 71–84

Chasey, D. and Banks, J., 1986. Replication of atypical ovine rotavirus in small intestine and cell culture. *Journal of General Virology*, 67, 567–576

Chauhan, R.S. and Singh, N.P., 1992a. Rapid diagnosis of rotavirus infection in calves by dot immunobinding assay. *Veterinary Record*, 130, 381

Chauhan, R.S. and Singh, N.P., 1992b. Cell-mediated immune response in rotavirus-infected calves: leucocyte migration inhibition assay. *Journal of Comparative Pathology*, 107, 115–118

Chauhan, R.S. and Singh, N.P., 1992c. Detection of rotavirus infection in calves employing immunofluorescence. *Journal of Applied Animal Research*, 1, 51–55

Chauhan, R.S. and Singh, N.P., 1992d. Assessment of intestinal damage in rotavirus infected calves by D-xylose malabsorption test. *Indian Journal of Veterinary Pathology*, 16, 13–16

Chauhan, R.S. and Singh, N.P., 1992e. Cytopathology induced by rotavirus in fetal rhesus monkey kidney cells (MA104). *Indian Journal of Veterinary Pathology*, 16, 76–78

Chauhan, R.S. and Singh, N.P., 1993a. Rotavirus infection in calves-electron microscopic studies. *Israel Journal of Veterinary Research*, 48, 110–112

Chauhan, R.S. and Singh, N.P., 1993b. Rotavirus infection in calves- Diagnosis by polyacrylamide gel electrophoresis. *Indian Journal of Animal Sciences*, 63, 1–3

Chauhan, R.S. and Singh, N.P., 1996. Epidemiology of rotavirus infection in calves in India. *International Journal of Animal Sciences*, 11, 221–223

Chauhan, R.S. and Singh, N.P., 1999. Detection of rotavirus in experimentally infected calves using immunoperoxidase technique. *Indian Journal of Animal Sciences*, 69, 239–291

Chauhan, R.S. and Singh, N.P., 2001. Demonstration of antirotavirus antibody producing cells in intestine of calves using immunoperoxidase technique. *Journal of Immunology and Immunopathology*, 3, 41–44

Chauhan, R.S., Dhama, K. and Mahendran, M., 2008. Pathobiology of rotaviral diarrhea in calves and its diagnosis and control: A review. *Journal of Immunology and Immunopathology*, 10, 1–13

Chinsangaram, J., Schore, C.E., Guterbock, W., Weaver, L.D. and Osburn, B.I., 1995. Prevalence of group A and group B rotaviruses in the feces of neonatal dairy calves from California. *Comparative Immunology and Microbiology*, 18, 93–103

Ciarlet, M., Pina, C.I., Garcia, O. and Liprandi, F., 1997. Identification of bovine rotaviruses in Venezuela: antigenic and molecular characterization of a bovine rotavirus strain. *Research in Virology*, 148, 289–297

Ciarlet, M., Crawford, S.E., Barone, C., Bertolotti-Ciarlet, A., Ramig, R.F., Estes, M.K. and Conner, M.E., 1998. Subunit rotavirus vaccine administered parenterally to rabbits induces active protective immunity. *Journal of Virology*, 72, 9233–9246

Ciarlet, M., Ia, P., Conner, M.E. and Liprandi, F., 2001. Antigenic and molecular analyses reveal that the equine rotavirus strain H-1 is closely related to porcine, but not equine, rotaviruses: interspecies transmission from pigs to horses? *Virus Genes*, 22, 5–20

Cook, N., Bridger, J., Kendall, K., Gomara, M.I., El-Attar, L. and Gray, J., 2004. The zoonotic potential of rotavirus. *Journal of Infection*, 48, 289–302

Day, J.M., Spackman, E. and Pantin-Jackwood, M., 2007. A multiplex RT-PCR test for the differential identification of turkey astrovirus type 1, turkey astrovirus type 2, chicken astrovirus, avian nephritis virus, and avian rotavirus. *Avian Diseases*, 51, 681–684

De Grazia, S., Martella, V., Giammanco, G.M., Gomara, M.I., Ramirez, S., Cascio, A., Colomba, C. and Arista, S., 2007. Canine-origin G3P[3] rotavirus strain in child with acute gastroenteritis. *Emerging Infectious Diseases*, 13, 1091–1093

De Leeuw, P.W., Ellens, D.J., Straver, P.J., Balken, J.A.M., Meerman, A. and Baanvinger, T., 1980. Rotavirus infections in calves in dairy herds. *Research in Veterinary Science*, 29, 135–141

de Verdier Klingenberg, K. and Svensson, L., 1998. Group A rotavirus as a cause of neonatal calf enteritis in Sweden. *Acta Veterinaria Scandinavia*, 39, 195–199

Dennehy, M., Bourn, W., Steele, D. and Williamson, A.L., 2007. Evaluation of recombinant BCG expressing rotavirus VP6 as an anti-rotavirus vaccine. *Vaccine*, 25, 3646–3657

Desselberger, U., Iturriza-Gomara, M. and Gray, J.J., 2001. Rotavirus epidemiology and surveillance. In: Chadwick D., Goode J.A., (eds), Gastroenteritis viruses, Wiley, New York, USA, 82–100.

Desselberger, U., Gray, J. and Estes, M.K., 2005. Rotaviruses. In: B.W.J. Mahy and V.T. Meulen (eds), Topley and Wilson's Microbiology and Microbial infections, ASM press, USA, 946–958

Dhama, K., Chauhan, R.S., Kataria, J.M., Mahendran, M. and Tomar, S., 2005. Avian Influenza: The current perspectives. *Journal of Immunology and Immunopathology*, 7, 1–33

Dhama, K., Mahendran, M., Gupta, P.K. and Rai A., 2008. DNA vaccines and their applications in veterinary practice: current perspectives. *Veterinary Research Communications 32*, 341–356

Dharakul, T., Rott, L. and Greenberg, H.B., 1990. Recovery from chronic rotavirus infection in mice with severe combined immunodeficiency: virus clearance mediated by adoptive transfer of immune CD8+T lymphocytes. *Journal of Virology*, 64, 4375–4382

Dodet, B., Heseltine, E., Mary, C. and Saliou, P., 1997. Rotaviruses in human and veterinary medicine. *Sante*, 7, 195–199

Duan, Z., Li, D., Zhang, Q., Liu, N., Huang, C., Jiang, X., Jiang, B., Glass, R., Steele, D., Tang, J., Wang, Z. and Fang, Z., 2007. Novel human rotavirus of genotype G5P[6] identified in a stool specimen from a Chinese girl with diarrhea. *Journal of Clinical Microbiology*, 45, 1614–1617

Ellis, G.R. and Daniels, E., 1988. Comparison of direct electron microscopy and enzyme immunoassay for the detection of rotaviruses in calves, lambs, piglets and foals. *Australian Veterinary Journal*, 65, 133–135

Estes, M.K., 2001. Rotaviruses and their replication. In: Knipe, D.M., Howley, P.M., (eds), Field's Virology, Lippincott Williams and Wilkins, Philadelphia, USA, 1747–1785.

Estes, M.K., 2003. The rotavirus NSP4 enterotoxin: current status and challenges, In: Desselberger, U., Gray, J., (eds), Viral Gastroenteritis, Elsevier Science, Amsterdam, Netherlands, 207–224.

Fernandez, F.M., Conner, M.E., Hodgins, D.C., Parwani, A.V., Nielsen, P.R., Crawford, S.E., Estes, M.K. and Saif, L.J., 1998. Passive immunity to bovine rotavirus in newborn calves fed colostrum supplements from cows immunized with recombinant SA11 rotavirus core-like particle (CLP) or virus-like particle (VLP) vaccines. *Vaccine*, 16, 507–516

Fukai, K., Sakai, T. and Kamata, H., 1998. Distribution of G serotypes and P genotypes of bovine group A rotavirus isolated in Japan. *Australian Veterinary Journal*, 76, 418–422

Fukai K., Maeda Y., Fujimoto K., Itou T. and Sakai T., 2002. Changes in the prevalence of rotavirus G and P types in diarrheic calves from the Kagoshima prefecture in Japan. *Veterinary Microbiology*, 86, 343–349

Fukai, K., Saito, T., Fukuda, O., Hagiwara, A., Inoue, K. and Sato, M., 2006. Molecular characterization of equine group A rotavirus, Nasuno, isolated in Tochigi Prefecture, Japan. *Veterinary Journal*, 172, 369–373

Fukai, K., Takahashi, T., Tajima, K., Koike, S., Iwane, K. and Inoue, K., 2007. Molecular characterization of a novel bovine group A rotavirus. *Veterinary Microbiology*, 123, 217–224

Fulton, R.W., Johnson, C.A., Pearson, J. and Woode, G.N., 1981. Isolation of a rotavirus from a newborn dog with diarrhea. *American Journal of Veterinary Research*, 42, 841–843

Garaicoechea, L., Bok, K., Jones, L.R., Combessies, G., Odeon, A., Fernandez, F. and Parreno, V., 2006. Molecular characterization of bovine rotavirus circulating in beef and dairy herds in Argentina during a 10-year period (1994–2003). *Veterinary Microbiology*, 118, 1–11

Garcia-Diaz, A., Lopez-Andujar, P., Rodriguez Diaz, J., Montava, R., Torres Barcelo, C., Ribes, J.M. and Buesa, J., 2004. Nasal immunization of mice with a rotavirus DNA vaccine that induces protective intestinal IgA antibodies. *Vaccine*, 23, 489–498

Ghosh, S., Varghese, V., Samajdar, S., Sinha, M., Kobayashi, N. and Naik, T.N., 2007a. Molecular characterization of bovine group A rotavirus G3P[3] strains. *Archives of Virology*, 152, 1935–1940

Ghosh, S., Varghese, V., Sinha, M., Kobayashi, N. and Naik, T.N., 2007b. Evidence for interstate transmission and increase in prevalence of bovine group B rotavirus strains with a novel VP7 genotype among diarrhoeic calves in Eastern and Northern states of India. *Epidemiology of Infections*, 135, 1324–1330

Gill, H. and Prasad, J., 2008. Probiotics, immunomodulation, and health benefits. *Advances in Eperimental and Medical Biology*, 606, 423–454

Graham, K.L., Takada, Y. and Coulson, B.S., 2006. Rotavirus spike protein VP5* binds alpha 2 beta 1 integrin on the cell surface and competes with virus for cell binding and infectivity. *Journal of General Virology*, 87, 1275–1283

Gueguen, C., Maga, A., McCrae, M.A. and Bataillon, G., 1996. Caprine and bovine B rotaviruses in western France: group identification by Northern hybridization. *Veterinary Research*, 27, 171–176

Gulati, B.R., Deepa, R., Singh, B.K. and Rao, C.D., 2007. Diversity in Indian equine rotaviruses: identification of genotype G10,P6[1] and G1 strains and a new VP7 genotype (G16) strain in specimens from diarrheic foals in India. *Journal of Clinical Microbiology*, 45, 972–978

Gumusova, S.O., Yazici, Z., Albayrak, H. and Meral, Y., 2007. Rotavirus and coronavirus prevalence in healthy calves and calves with diarrhea. *Medycnya Weterinaria*, 63, 62–64

Hall, G.A., Parsons, K.R., Reynolds, D.J. and Morgan, J.H., 1985. Detection of enteropathogenic viruses in paraffin embedded intestinal tissue of calves by immunoperoxidase. *Journal of Medical Microbiology*, 19, 14

Hall, G.A., Bridger, J.C., Parson, K.R. and Cook, R., 1993. Variation in rotavirus virulence: a comparison of pathogenesis in calves between two rotavirus of different virulence. *Veterinary Pathology*, 30, 223–233

Hammami, S., Castro, A.E. and Osburn, B.I., 1990. Comparison of polyacrylamide gel electrophoresis, an enzyme-linked-immunosorbent assay, and an agglutination test for the direct identification of bovine rotavirus from feces and coelectrophoresis of viral RNAs. *Journal of Veterinary Diagnostic Investigation*, 2, 184–190

Hasso, S.A. and Pandey, R., 1986. Possible sex differences in the susceptibility of calves to rotavirus infection. *Canadian Journal of Veterinary Research*, 50, 287–288

Heinrich, H.W., Schirrmeier, H., Lange, E. and Granzow, H., 1983. Cross infection with rotavirus of different species. *Archives Experimental Veterinamedicine*, 37, 55–60

Herrmann, J.E., 2006. DNA vaccines against enteric infections. *Vaccine*, 24, 3705–3708

Holland, R.E., 1990. Some infectious causes of diarrhea in young farm animals. *Clinical Microbiological Reviews*, 3, 345–375

Hoshino, Y., Baldwin, C.A. and Scott, F.W., 1981. Isolation and characterization of feline rotavirus. *Journal of General Virology*, 54, 313–323

Hoshino, Y., Wyatt, R.G., Scott, F.W. and Appel, M.J., 1982. Isolation and characterization of a canine rotavirus. *Archives of Virology*, 72, 113–125

Hoshino, Y., Wyatt, R.G., Greenberg, H.B., Kalica, A.R., Flores, J. and Kapikian, A.Z., 1983. Serological comparison of canine rotavirus with various simian and human rotaviruses by plaque reduction neutralization and hemagglutination inhibition tests. *Infection and Immunity*, 41, 169–173

Huang, J.A., Nagesha, H.S., Snodgrass, D.R. and Holmes, I.H., 1992. Molecular and serological analyses of two bovine rotaviruses (B-11 and B-60) causing calf scours in Australia. *Journal of Clinical Microbiology*, 30, 85–92

Hussein, A.H., Cornaglia, E., Saber, M.S. and el-Azhary, Y., 1995. Prevalence of serotypes G6 and G10 group A rotaviruses in dairy calves in Quebec. *Canadian Journal of Veterinary Research*, 59, 235–237

Imagawa, H., Ishida, S., Uesugi, S., Masanobu, K., Fukunaga, Y. and Nakagomi, O., 1994. Genetic analysis of equine rotavirus by RNA-RNA hybridization. *Journal of Clinical Microbiology*, 32, 2009–2012

Jackwood, P.M.J., Spackman, E., Day, J.M. and Rives, D., 2007. Periodic monitoring of commercial turkeys for enteric viruses indicates continuous presence of astrovirus and rotavirus on the farms. *Avian Diseases*, 51, 674–680

Kaminjolo, J.S. and Adesiyun, A.A., 1994. Rotavirus infection in calves, piglets, lambs and goat kids in Trinidad. *British Veterinary Journal*, 150, 293–299

Kang, B.K., Song, D.S., Jung, K.I., Lee, C.S., Park, S.J., Oh, J.S., An, D.J., Yang, J.S., Moon, H.J., Lee, S.S., Yoon, Y.D. and Park, B.K., 2007. Genetic characterization of canine rotavirus isolated from a puppy in Korea and experimental reproduction of disease. *Journal of Veterinary Diagnostic Investigation*, 19, 78–83

Khamrin, P., Maneekarn, N., Peerakome, S., Yagyu, F., Okitsu, S. and Ushijima, H., 2006. Molecular characterization of a rare G3P[3] human rotavirus reassortant strain reveals evidence for multiple human-animal interspecies transmissions. *Journal of Medical Virology*, 78, 986–994

Khamrin, P., Maneekarn, N., Peerakome, S., Chan-it, W., Yagyu, F., Okitsu, S. and Ushijima, H., 2007. Novel porcine rotavirus of genotype P[27] shares new phylogenetic lineage with G2 porcine rotavirus strain. *Virology*, 361, 243–252

Kharalambiev, K.H., Georgiev, G.K. and Mitov, B., 1983. Enzyme linked immunosorbent assay (ELISA) for detecting rotavirus. *Veterinary Bulletin*, 53, 5274

Kim, Y., Nielsen, P.R., Hodgins, D., Chang, K.O. and Saif, L.J., 2002a. Lactogenic antibody responses in cows vaccinated with recombinant bovine rotavirus-like particles (VLPs) of two serotypes or inactivated bovine rotavirus vaccines. *Vaccine*, 20, 1248–1258

Kim, B., Bowersock, T., Griebel, P., Kidane, A., Babiuk, L.A., Sanchez, M., Attah-Poku, S., Kaushik, R.S. and Mutwiri, G.K., 2002b. Mucosal immune responses following oral immunization with rotavirus antigens encapsulated in alginate microspheres. *Journal of Controlled Release*, 85, 191–202

Kohara, J. and Tsunemitsu, H., 2000. Correlation between maternal serum antibodies and protection against bovine rotavirus diarrhea in calves. *Journal of Veterinary Medical Science*, 62, 219–221

Komoto, S., Sasaki, J. and Taniguchi, K., 2006. Reverse genetics system for introduction of site-specific mutations into the double-stranded RNA genome of infectious rotavirus. *Proceedings of the National Academy of Science, USA*, 103, 4646–4651

Lee, J.B., Youn, S.J., Nakagomi, T., Park, S.Y., Kim, T.J., Song, C.S., Jang, H.K., Kim, B.S. and Nakagomi, O., 2003. Isolation, serologic and molecular characterization of the first G3 caprine rotavirus. *Archives of Virology*, 148, 643–657

Legrottaglie, R., Volpe, A., Rizzi, V. and Agrimi, P., 1993. Isolation and identification of rotaviruses as aetiological agents of neonatal diarrhoea in kids. Electro-phoretical characterization by PAGE. *New Microbiology*, 16, 227–235

Luan, J.J., Yang, S.H., Zhang, W.J., Gao, Y.D., Zhong, J.F. and Zhao, H.K., 2006. Rapid detection of bovine rotavirus with semi-nested RT-PCR assay. *Chinese Journal of Zoonoses*, 22, 671–673

Luginbuhl, A., Reitt, K., Metzler, A., Kollbrunner, M., Corboz, L. and Deplazes, P., 2005. Field study about prevalence and diagnostics of diarrhea causing agents in the new-born calf in a Swiss veterinary practice area. *Schweiz Arch Tierheilkd*, 147, 245–252

Malik, S.V.S., Kumar, A. and Bhilegaonkar, K.N., 1995. Rotavirus an emerging enteropathogen of man and animals: an overview. *Journal of Communicable Diseases*, 27, 199–207

Malik, S.V.S., Barbuddhe, S.B., Rawool, D.B., Vaidya, V.M. and Sahare, A.M., 2005. Data sheet on Rotaviruses (Global status of Rotavirus infections in man and animals), In: Animal Health and Production Compendium, CAB International, Wallingford, UK.

Martella, V., Pratelli, A., Greco, G., Gentile, M., Fiorente, P., Tempesta, M. and Buonavoglia, C., 2001a. Nucleotide sequence variation of the VP7 gene of two G3-type rotaviruses isolated from dogs. *Virus Research*, 74, 17–25

Martella, V., Pratelli, A., Elia, G., Decaro, N., 2001b. Tempesta M., Buonavoglia C., Isolation and genetic characterization of two G3P5A [3] canine rotavirus strains in Italy. *Journal of Virological Methods*, 96, 43–49

Martella, V., Banyai, K., Lorusso, E., Bellacicco, A.L., Decaro, N., Camero, M., Bozzo, G., Moschidou, P., Arista, S., Pezzotti, G., Lavazza, A. and Buonavoglia, C., 2007a. Prevalence of group C rotaviruses in weaning and post-weaning pigs with enteritis. *Veterinary Microbiology*, 123, 26–33

Martella, V., Ciarlet, M., Banyai, K., Lorusso, E., Arista, S., Lavazza, A., Pezzotti, G., Decaro, N., Cavalli, A. and Lucente, M.S., 2007b. Identification of group A porcine rotavirus strains bearing a novel VP4 (P) Genotype in Italian swine herds. *Journal of Clinical Microbiology*, 45, 577–580

Mascarenhas, J.D., Leite, J.P., Lima, J.C., Heinemann, M.B., Oliveira, D.S., Araujo, I.T., Soares, L.S., Gusmao, R.H., Gabbay, Y.B. and Linhares, A.C., 2007. Detection of a neonatal human rotavirus strain with VP4 and NSP4 genes of porcine origin. *Journal of Medical Microbiology*, 56, 524–532

McNulty, M.S., 2003. Rotavirus infections, in: Saif Y.M., Barnes H.J., Glisson J.R., Fadly A.M., McDougald L.R., Swayne D.E., (eds), Diseases of poultry, Iowa state press, Ames, USA, 308–317.

McNulty, M. S., Allan, G. M., Thompson, D. J., O'Boyle, J. D., 1978. Antibody to rotavirus in dogs and cats. *Veterinary Record*, 102, 534–535

Mebus, C.A., Underdahl, N.R., Rhodes, M.B. and Twiehaus, M.J., 1969. Calf diarrhea (scours) reproduced with a virus from a field outbreak. *University of Nebraska Agriculture Research Bulletin*, 233, 1–16

Mebus, C.A., Kono, M., Underdahl, N.R. and Twiehaus, M.J., 1971a. Cell culture propagation of neonatal calf diarrhea (Scour) virus. *Canadian Veterinary Journal*, 12, 69–72

Mebus, C.A., Stair, E.L., Underdahl, N.R. and Twiehaus, M.J., 1971b. Pathology of neonatal calf diarrhea induced by a reo-like virus. *Veterinary Pathology*, 8, 490–505

Mebus, C.A., Wyatt, R.G. and Kapikian, A.Z., 1977. Intestinal lesions induced in gnotobiotic calves by the virus of human infantile gastroenteritis. *Veterinary Pathology*, 14, 273–282

Mendes, V.M., De Beer, M.C., Goosen, G.H. and Steele, A.D., 1994. Isolation and preliminary characterization of a caprine rotavirus. *Onderstepoort Journal of Veterinary Research*, 61, 291–294

Mochizuki, M., Nakagomi, T. and Nakagomi, O., 1997. Isolation from diarrheal and asymptomatic kittens of three rotavirus strains that belong to the AU-1 genogroup of human rotaviruses. *Journal of Clinical Microbiology*, 35, 1272–1275

Mori, Y., Sugiyama, M., Takayama, M., Atoji, Y., Masegi, T., Minamoto, N., 2001. Avian-to-mammal transmission of an avian rotavirus: analysis of its pathogenicity in a heterologous mouse model. *Virology*, 288, 63–70

Muller, H. and Johne, R., 2007. Rotaviruses: diversity and zoonotic potential-a brief review. *Berlin Munch Tierarztl Wochenschr*, 120, 108–112

Muniappa, L., Georgiev, G.K. and Kharalambiev, K., 1987. Rotavirus enteritis in buffaloes. *Veterinary Medicine Nauki*, 24, 10–14

Munoz, M., Lanza, I., Alvarez, M. and Carmenes, P., 1995a. Prevalence of neutralizing antibodies to 9 rotavirus strains representing 7 G-serotypes in sheep sera. *Veterinary Microbiology*, 45, 351–361

Munoz, M., Alvarez, M., Lanza, I. and Carmenes, P., 1995b. An outbreak of diarrhoea associated with atypical rotaviruses in goat kids. *Research in Veterinary Science*, 59, 180–182

Murakami, T., Hirano, N., Inque, A., Chitose, K., Tsushiya, K., Ono, K., Naito, Y., Yangihara, T., 1986. Protective effects of orally administered immunoglobulins against experimental calf diarrhea. *Japanese Journal of Veterinary Science*, 48, 237–245

Murphy, F.A., Gibbs, E.P.J., Horzinek, M.C. and Studdert, M.J., 1999. Reoviridae. In: F.A. Murphy, E.P.J. Gibbs, M.C. Horzinek and M.J. Studdert (eds), Veterinary Virology, Academic Press, USA, 391–404

Myers, T.J. and Schat, K.A., 1990. Natural killer cell activity of chicken intraepithelial leukocytes against rotavirus-infected target cells. *Veterinary Immunology and Immunopathology*, 26, 157–170

Nakagomi, O. and Nakagomi, T., 1991. Genetic diversity and similarity among mammalian rotaviruses in relation to interspecies transmission of rotavirus. *Archives of Virology*, 120, 43–55

Nakagomi, T., Matsuda, Y., Ohshima, A., Mochizuki, M. and Nakagomi, O., 1989. Characterization of a canine rotavirus strain by neutralization and molecular hybridization assays. *Archives of Virology*, 106, 145–150

Nakagomi, O., Ohshima, A., Aboudy, Y., Shif, I., Mochizuki, M., Nakagomi, T. and Gotlieb-Stematsky, T., 1990. Molecular identification by RNA-RNA hybridization of a human rotavirus that is closely related to rotaviruses of feline and canine origin. *Journal of Clinical Microbiology*, 28, 1198–1203

Netherwood, T., Wood, J.L., Townsend, H.G., Mumford, J.A. and Chanter, N., 1996. Foal diarrhoea between 1991 and 1994 in the United Kingdom associated with *Clostridium perfringens*, rotavirus, *Strongyloides westeri* and *Cryptosporidium spp. Epidemiology of Infections*, 117, 375–383

Otto, P., Liebler-Tenorio, E.M., Elschner, M., Reetz, J., Lohren, U. and Diller, R., 2006. Detection of rotaviruses and intestinal lesions in broiler chicks from flocks with runting and stunting syndrome (RSS). *Avian Diseases*, 50, 411–418

Palombo, E.A., 2002. Genetic analysis of Group A rotaviruses: evidence for interspecies transmission of rotavirus genes. *Virus Genes*, 24, 11–20

Park, S.H., Saif, L.J., Jeong, C., Lim, G.K., Park, S.I., Kim, H.H., Park, S.J., Kim, Y.J., Jeong, J.H., Kang, M.I. and Cho, K.O., 2006. Molecular characterization of novel G5 bovine rotavirus strains. *Journal of Clinical Microbiology*, 44, 4101–4112

Parra, G.I., Vidales, G., Gomez, J.A., Fernandez, F.M., Parreno, V. and Bok, K., 2008. Phylogenetic analysis of porcine rotavirus in Argentina: Increasing diversity of G4 strains and evidence of interspecies transmission. *Veterinary Microbiology*, 126, 243–250

Paul, P.S. and Lyoo, Y.S., 1993. Immunogens of rotaviruses. *Veterinary Microbiology*, 37, 299–317

Pisanelli, G., Martella, V., Pagnini, U., DeMartino, L., Lorusso, E., Iovane, G. and Buonavoglia, C., 2005. Distribution of G (VP7) and P (VP4) genotypes in buffalo group A rotaviruses isolated in Southern Italy. *Veterinary Microbiology*, 110, 1–6

Ramani, S. and Kang, P., 2007. Burden of disease and molecular epidemiology of group A rotavirus infections in India. *Indian Journal of Medical Research*, 125, 619–632

Ramig, R.F., 2004. Pathogenesis of intestinal and systemic rotavirus infection. *Journal of Virology*, 78, 10213–10220

Rao, C.D., Gowda, K. and Reddy, B.S., 2000. Sequence analysis of VP4 and VP7 genes of nontypeable strains identifies a new pair of outer capsid proteins representing novel P and G genotypes in bovine rotaviruses. *Virology*, 276, 104–113

Rathi, R., Kadian, S.K., Khurana, B., Grover, Y.P. and Gulati, B.R., 2007. Evaluation of immune response to bovine rotavirus following oral and intraperitoneal inoculation in mice. *Indian Journal of Experimental Biology*, 45, 212–216

Reading, P.C., Holmskov, U. and Anders, E.M., 1998. Antiviral activity of bovine collectins against rotaviruses. *Journal of General Virology*, 79, 2255–2263

Reidy, N., Lennon, G., Fanning, S., Power, E. and O' Shea, H., 2006. Molecular characterization and analysis of bovine rotavirus strains circulating in Ireland 2002–2004. *Veterinary Microbiology*, 117, 242–247

Rohwedder, A., Schutz, K.I., Minamoto, N. and Brussow, H., 1995. Sequence analysis of pigeon, turkey, and chicken rotavirus VP8* identifies rotavirus 993/83, isolated from calf feces, as a pigeon rotavirus. *Virology*, 210, 231–235

Saif, L.J. and Fernandez, F.M., 1996. Group A rotavirus veterinary vaccines. *Journal of Infectious Diseases*, 174, 98–106

Sato, K., Inaka, Y., Shinozaki, T. and Matumoto, M., 1981. Neutralizing antibody to bovine rotavirus in various animal species. *Veterinary Microbiology*, 6, 259–261

Schlafer, D.H. and Scott, F.W., 1979. Prevalence of neutralizing antibody to the calf rotavirus in NewYork cattle. *Cornell Veterinarian*, 69, 262–271

Schroeder, B.A., Street, J.E., Kalmakoff, J. and Bellamy, A.R., 1982. Sequence relationships between the genome segments of human and animal rotavirus strains. *Journal of Virology*, 43, 379–385

Schwers, A., Hoyois, P., Chappuis, G., Dagenais, L. and Pastoret, P.P., 1982. Propagation of bovine rotavirus by cats and dogs. *Annals Research in Veterinary Science*, 13, 303–308

Selim, S.A., Aziz, K.M., Sarker, A.J. and Rahman, H., 1991. Rotavirus infection in calves in Bangladesh. *Veterinary Research Communications*, 15, 327–333

Shawky, S.A., Saif, Y.M. and Swayne, D.E., 1993. Role of circulating maternal antirotavirus IgG in protection of intestinal mucosal surface in turkey poult. *Avian Diseases*, 37, 1041–1050

Shen, S., Burke, B. and Desselberger, U., 1994. Rearrangement of VP6 gene of a group A rotavirus in combination with a point mutation affecting trimer stability. *Journal of Virology*, 68, 1682–1688

Snodgrass, D.R., Herring, J.A., Campbell, I., Inglis, J.M., Hargreaves, F.D., 1984. Comparison of atypical rotavirus from calves, piglets, lambs and man. *Journal of General Virology*, 65, 909–914

Snodgrass, D.R., Fitzgerald, T., Campbell, I., Scott, F.M., Browning, G.F., Miller, D.L., Herring, A.J. and Greenberg, H.B., 1990. Rotavirus serotypes 6 and 10 predominate in cattle. *Journal of Clinical Microbiology*, 28, 504–507

Song, D.S., Kang, B.K., Oh, J.S., Ha, G.W., Yang, J.S., Moon, H.J., Jang, Y.S. and Park, B.K., 2006. Multiplex reverse transcription-PCR for rapid differential detection of porcine epidemic diarrhea virus, transmissible gastroenteritis virus, and porcine group A rotavirus. *Journal of Veterinary Diagnostic Investigation*, 18, 278–281

Steele, A.D., Geyer, A. and Gerdes, G.H., 2004. Rotavirus infections. In: Coetzer, J.A.W. and Tustin, R.C. (eds), Infectious diseases of Livestock, Oxford University Press, Southern Africa, 1256–1264.

Steyer, A., Poljsak-Prijatelj, M., Barlic-Maganja, D., Jamnikar, U., Mijovski, J.Z., Marin, J., 2007. Molecular characterization of a new porcine rotavirus P genotype found in an asymptomatic pig in Slovenia. *Virology*, 359, 275–282

Sugiyama, M., Goto, K., Uemukai, H., Mori, Y., Ito, N., Minamoto, N., 2004. Attachment and infection to MA104 cells of avian rotaviruses require the presence of sialic acid on the cell surface. *Journal of Veterinary Medical Science*, 66, 461–463

Sunil-Chandra, N.P. and Mahalingam, S., 1994. Rotavirus-associated diarrhea in buffalo calves in Sri Lanka. *Research in Veterinary Science*, 56, 393–396

Svensson, L., 2000. Diagnosis of foodborne viral infection in patients. *International Journal of Food Microbiology*, 59, 117–126

Swain, P. and Dhama, K., 1999. Calf diarrhea. *Indian Farming*, 48, 25–27

Tan, J.A. and Schnagl, R., 1981. Inactivation of a rotavirus by disinfectants. *Medical Journal of Australia*, 1, 19–32

Teodoroff, T.A., Tsunemitsu, H., Okamoto, K., Katsuda, K., Kohmoto, M., Kawashima, K., Nakagomi, T. and Nakagomi, O., 2005. Predominance of porcine rotavirus G9 in Japanese piglets with diarrhea: close relationship of their VP7 genes with those of recent human G9 strains. *Journal of Clinical Microbiology*, 43, 1377–1378

Terrett, L.A., Saif, L.J., Theil, K.W. and Kohler, E.M., 1987. Physicochemical characterization of porcine pararotavirus and detection of virus and viral antibodies using cell culture immunofluorescence. *Journal of Clinical Microbiology*, 25, 268–272

Theil, K.W., Lance, S.E. and McCloskey, C.M., 1996. Rotaviruses associated with neonatal lamb diarrhea in two Wyoming shed-lambing operations. *Journal of Veterinary Diagnostic Investigation*, 8, 245–248

Tsunemitsu, H., Imagawa, H., Togo, M., Shouji, T., Kawashima, K., Horino, R., Imai, K., Nishimori, T., Takagi, M. and Higuchi, T., 2001. Predominance of G3B and G14 equine group A rotaviruses of a single VP4 serotype in Japan. *Archives of Virology*, 146, 1949–1962

Tzipori, S., Sherwood, D., Angus, K.W., Campbell, I. and Gordon, M., 1981. Diarrhea in lambs: experimental infections with enterotoxigenic Escherichia coli, rotavirus, and Cryptosporidium sp. *Infection and Immunity*, 33, 401–406

Tzipori, S., 1985. The relative importance of enteric pathogens affecting neonates of domestic animals. *Advances in Veterinary Science and Comparative Medicine*, 29, 103–193

Van Pinxteren, L.A., Bruce, M.G., Campbell, I., Wood, A., Clarke, C.J., Bellman, A., Morein, B. and Snodgrass, D.R., 1999. Effect of oral rotavirus/Iscom vaccines on immune responses in gnotobiotic lambs. *Veterinary Immunology and Immunopathology*, 71, 53–67

Varghese, V., Ghosh, S., Das, S., Bhattacharya, S.K., Krishnan, T., Karmakar, P., Kobayashi, N. and Naik, T.N., 2006. Characterization of VP1, VP2 and VP3 gene segments of a human rotavirus closely related to porcine strains. *Virus Genes*, 32, 241–247

Varshney, B., Jagannath, M.R., Vethanayagam, R.R., Kodhandharaman, S., Jagannath, H.V., Gowda, K., Singh, D.K. and Rao, C.D., 2002. Prevalence of, and antigenic variation in, serotype G10 rotaviruses and detection of serotype G3 strains in diarrheic calves: implications for the origin of G10P11 or P11 type reassortant asymptomatic strains in newborn children in India. *Archives of Virology*, 147, 143–165

Vende, P., Karoum, R., Manet, G., Rizet, C., Schelcher, F., Cohen, J. and Navetat, H., 1999. Molecular epidemiology or bovine rotaviruses from the Charolais area. *Veterinary Research*, 30, 451–456

Villarreal, L.Y.B., Uliana, G., Valenzuela, C., Chacon, J.L.V., Saidenberg, A.B.S., Sanches, A.A., Brandao, P.E., Jerez, J.A. and Ferreira, A.J.P., 2006. Rotavirus detection and isolation from chickens with or without symptoms. *Revue Brasilia Ciencia Avicola*, 8, 187–191

Wani, S.A., Bhat, M.A., Ishaq, S.M., Ashrafi, M.A., Buchh, A.S. and Haq, M., 2003. Detection of a mammalian-like group A rotavirus in diarrhoeic chicken. *Veterinary Microbiology*, 94, 13–18

Wani, S.A., Bhat, M.A., Nawchoo, R., Munshi, Z.H. and Bach, A.S., 2004. Evidence of rotavirus associated with neonatal lamb diarrhoea in India. *Tropical Animal Health and Production*, 36, 27–32

Watanabe, T., Ohta, C., Shirahata, T., Goto, H., Tsunoda, N., Tagami, M. and Akita, H., 1993. Preventive administration of bovine colostral immunoglobulins for foal diarrhea with rotavirus. *Journal of Veterinary Medical Science*, 55, 1039–1040

Wigdorovitz, A., Mozgovoj, M., Santos, M.J.D., Parreno, V., Gomez, C., Perez-Filgueira, D.M., Trono, K.G., Rios, R.D., Franzone, P.M., Fernandez, F., Carillo, C., Babiuk, L.A., Escribano, J.M. and Borac, M.V., 2004. Protective lactogenic immunity conferred by an edible peptide vaccine to bovine rotavirus produced in transgenic plants. *Journal of General Virology*, 85, 1825–1832

Woode, G.N., 1976. Viral diarrhea in calves. *Veterinary Annual*, 16, 30–34

Woode, G.N. and Bridger, J.C., 1975. Viral enteritis of calves. *Veterinary Record*, 96, 85–88

Woode, G.N. and Crouch, C.F., 1978. Naturally occurring and experimentally induced rotavirus infection of domestic and laboratory animals. *Journal of American Veterinary Medical Association*, 173, 522–526

Woode, G.N., Bew, M.E. and Dennis, M.J., 1978. Studies on cross protection induced in calves by rotaviruses of calves, children and foals. *Veterinary Record*, 103, 32–34

Yason, C.V. and Schat, K.A., 1985. Isolation and characterization of avian rotaviruses. *Avian Diseases*, 29, 499–508

Yason, C.V. and Schat, K.A., 1987. Pathogenesis of rotavirus infection in various age groups of chickens and turkeys: clinical signs and virology. *American Journal of Veterinary Research*, 48, 977–983

Yolken, R.H., Losonsky, G.A., Vonderfecht, S., Leister, F. and Wee, S.B., 1985. Antibody to human rotavirus in cow's milk. New England Journal of Medicine, 312, 605–610