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, electrophorotyping, 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-
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.
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, immunoperoxidase 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 Ca²⁺ 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 (Th) 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 infecting 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). Further, 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); Sri Lanka [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 1992c; 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.
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 occasionally 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.
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. Diagnosis 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 ovinos, 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 ovinos (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 camels, 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 diversity 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. 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.
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