Chapter 8
Animal Rotaviruses

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Abstract Rotaviruses (RVs) are ubiquitous and remain the major cause of acute viral gastroenteritis in young animals, bird species and children worldwide. The disease is acute, occurs predominantly in intensively reared animals and characterized by a short incubation period, anorexia and diarrhoea. Post-infection immunity and immune system and intestinal microbiome maturation make immunocompetent adults of different species resistant to clinical RV disease. RVs of groups A, B, C, E, H, I and J have been detected in sporadic, endemic or epidemic infections of various mammalian species, whereas RV strains of groups D, F and G are only found in poultry, such as chickens and turkeys. Recently identified novel RVs in sheltered dogs in Hungary and bats in Serbia are tentatively identified as group I and J, respectively. Historically, diagnosis of RV infections relied on conventional techniques such as isolation in cell culture, electron microscopy, electropherotyping and
various serological tests. Presently, RT-PCR assays and molecular typing using sequencing or genomic hybridization techniques are used predominantly for RV diagnosis and classification. Because RVs are endemic in most animal populations and exhibit extreme genetic diversity due to frequent mutations and re-assortment events, available RV vaccines are only marginally efficient, and eradication of the pathogen remains a challenge. Thus, a better understanding of the historic and current prevalence and genetic diversity of animal RVs in different geographic regions, disease pathogenesis, available control strategies and zoonotic potential is needed. This knowledge will lead to the development of more optimal strategies to manage RV diarrhoeal disease in animals, birds and humans.

**Keywords** Animal rotaviruses · Porcine rotaviruses · Bovine rotaviruses · Wildlife rotaviruses · Avian rotaviruses · Epidemiology · Genetic variability · RV pathogenesis · Vaccines · Diagnosis · Zoonotic potential

### 8.1 Prologue

Rotaviruses (RVs) are a major cause of acute enteric disease in the young of many mammalian and avian species and children worldwide (Estes and Greenberg 2013). The disease is characterized by a short incubation period, anorexia and diarrhoea. Usually, the adults of different species acquire post-infection immunity and have a mature immune system which makes them immunocompetent and resistant to clinical diseases. However, rotavirus group B (RVB) infections are shown to be more frequently associated with diarrhoea in adults.

The name ‘Rotavirus’ is derived from a Latin word *rota* (which means wheel), due to its characteristic appearance when observed by negative-stain electron microscopy (EM). Rotavirus infection was first recognized in 1963 in mice, and soon after that, the SA11 (simian agent 11) was isolated from a healthy vervet monkey. In 1969, bovine group A RV (RVA) was isolated in cell culture and confirmed as a cause of calf diarrhoea (Mebus et al. 1971). These murine, simian and bovine agents (RVAs) were later found to share a common group antigen (VP6) and to be morphologically indistinguishable. Human RV was discovered soon after, in 1973, by Bishop et al. (1973), where wheel-shaped particles were observed in electron micrographs of the intestinal mucosa and stool samples of children with acute gastroenteritis (Bishop et al. 1973). Following studies documented the widespread prevalence of RVA infections in young animals, including calves and pigs, and their association with diarrhoea in animals <1 month of age (Malik et al. 2013a, b, c; Woode and Bridger 1975; McNulty et al. 1978; Saif and Jiang 1994). Animal RVs are considered as potential reservoirs for genetic exchange with human rotaviruses. Continuous reassortments event and due to direct transmission, animal rotaviruses have been found to infect humans which leads to the generations of peculiar reassortant strains which includes genes of human origin also.
In 1977 a study from the USA reported avian RV in turkey poults in the USA, and since then different RVs of group A (RVA), D (RVD), F (RVF) and G (RVG) have been described globally (Dhama et al. 2015). Bovine RVs (BRV) were among the earliest RVs to be successfully adapted to serial propagation in cell culture (Mebus et al. 1971) which facilitated research efforts toward their characterization. In 1980 group C RVs were first isolated in piglets and thereafter they have been identified in other animals and humans (Pedley et al. 1986; Saif and Jiang 1994). An RV-like agent was first described in a diarrhoeic pig in the 1980s which was later confirmed as porcine RVB (Bridger et al. 1983; Theil et al. 1986). In addition to pigs, RVB strains have also been detected in cattle (Chang et al. 1997; Tsunemitsu et al. 1999; Ghosh et al. 2007a), lambs (Shen et al. 1993) and rats. Group E RV (RVE) was reported as an atypical porcine RV in UK swine, in a serological survey where a widespread distribution of antibodies against this virus in 10 weeks older pigs was observed (Bridger 1987). Group H RV (RVH) strains were reported from pigs in Japan, Brazil and the USA, where they might be circulating since at least 2002 (Marthaler et al. 2014).

Rotaviruses have a worldwide distribution and commonly affect calves (Mebus et al. 1969a, b), lambs (Snodgrass et al. 1984), piglets, goat kids, foals (Malik et al. 2014; Flewett et al. 1975) and chickens (McNulty, et al. 1980).

8.2 Virus Structure

Complete infectious RV consists of three layers of protein and is termed triple-layered particle (TLP). The innermost layer is formed by 120 molecules of viral protein 2 (VP2) arranged in parallel asymmetric dimers. Five copies of the dimers radiate from the fivefold axis of symmetry to form a decamer, and 12 such decamers form the core protein layer which is uniform except for small pores along the fivefold axis (McClain et al. 2010). The core encloses the viral genome that consists of 11 segments of dsRNA as well as replication enzyme complexes, consisting of VP1 (the RNA-dependent RNA polymerase) and VP3 (the methyltransferase and guanylyltransferase). VP1 protein is modelled as cage-like structure disrupted by four channels which allow for (1) the entry of free nucleoside triphosphates (NTPs), (2) the entry of template ssRNA, (3) the exit of the (+) ssRNA product, and (4) the exit of (−) ssRNA and dsRNA (Estrozi et al. 2013). Rotavirus core is described as the ‘molecular machine’ owing to its capacity to synthesize capped viral mRNA transcripts.

The viral core is surrounded by 260 trimers of VP6, which is a highly conserved, group-specific viral protein, forms the middle layer and constitutes double-layered particles (DLPs). DLPs are the transcriptionally competent forms of the virus formed during the replication process. The chief protein of rotavirus particle is VP6 (based on weight percent). It plays an essential role in the overall organization of the rotavirus architecture wherein it interacts with the VP7 and VP4 (outer layer proteins), and VP2 (innermost layer protein) (Charpilienne et al. 2002). The middle
layer is covered by outermost capsid protein layer forming a nearly spherical icosahedron which consists of 260 trimers (780 copies) of VP7, decorated by 60 spikes, with each being formed by VP4 trimers (180 copies) to form the TLPs. VP7 is known as calcium-binding protein and comprises two domains: domain I has a disulphide bridge and displays a Rossmann fold, while the domain II possesses three disulphide bridges and displays a jelly-roll b-sandwich fold. To each subunit interface of trimer, two Ca2+ ions are attached. A plate-like trimer is formed when three VP7 subunits interact with each other which sit on top of the VP6 trimers. The N-terminal arms of three VP7 subunits then grasp the underlying VP6 trimers and intrude into the VP4 foot cavity. These interactions among different trimers indicate that the VP4 spikes have to be first attached to the DLPs before the addition of VP7 during virus assembly, and only after the addition of VP7 a shift in the underlying VP6 trimers takes place. The VP4 spike has a distinct structure comprising of two distal globular domains, a central body and an internal globular domain popped inside the VP7 layer in the peri-pentalonal channel of the T = 13 icosahedral lattice.

X-ray structures of proteolytic fragments of VP4, VP8*, and VP5* reveal strong evidence that the distal globular domain of the VP4 spike is composed of VP8* with the remaining body of the spike consisting of VP5*. Infectivity of rotaviruses increases when there is a proteolytic cleavage of VP4 yielding two proteins, VP5* and VP8* (Dormitzer et al. 2004).

The architecture of RV has a unique feature of the presence of large channels that penetrate through the VP7 and VP6 layers. These channels form a passage to the aqueous materials and biochemical substrates into and out of the capsid. The 132 channels at the fivefold and quasi sixfold positions of the T = 13 lattice are grouped into three distinct types. At the fivefold vertices of the capsid, there are twelve type I channels. 60 type II channels are present at each of the pentavalent locations surrounding the type I channels, and near to which VP4 is attached to VP7 and VP6. Surrounding the icosahedral threefold axes the remaining hexavalent positions on the capsid are occupied by the 60 type III channels (Jayaram et al. 2004).

### 8.3 Genome Structure and Organization

The RVs genome consists of 11 segments of dsRNA ranging in size from 667 to 3302 nucleotides and molecular weight ranging from $10^5$ to $10^6$ Da, enclosed within the virus core capsid. An open reading frame (ORF) is present in each RNA segment that encodes viral proteins. The RV genome segments code for both structural proteins (found in the virus particle) and the nonstructural proteins (found in infected cells but absent in mature virion particles). RVs encode for six structural proteins (VP1–VP4, VP6 and VP7) and six nonstructural proteins (NSP1–NSP5/6) (Manson et al. 1983). Except segment 11 which encodes for two proteins as NSP5 and NSP6 (in some serogroups), rest of the genomic segments are monocistronic. All the proteins encoded by rotavirus genes are well established with reviewed properties.
Table 8.1 Rotavirus genes and encoded proteins

| RNA segment | Size (bp) | Protein | Length (AA) | Location | Function |
|-------------|-----------|---------|-------------|----------|----------|
| 1           | 3302      | VP1     | 1088        | At the vertices | RNA-dependent RNA Polymerase |
| 2           | 2690      | VP2     | 881         | Forms inner shell of the core | Stimulates viral RNA replicase |
| 3           | 2591      | VP3     | 835         | At the vertices of the core | Guanylyl transferase mRNA capping enzyme |
| 4           | 2362      | VP4     | 776         | Surface spike | Cell attachment, virulence |
| 5           | 1611      | NSP1    | 495         | Nonstructural | Not essential to virus Growth |
| 6           | 1356      | VP6     | 397         | Inner capsid | Structural and species specific antigen |
| 7           | 1104      | NSP3    | 312         | Nonstructural | Enhances viral mRNA Activity and shut-offs Cellular protein synthesis |
| 8           | 1059      | NSP2    | 317         | Nonstructural | NTPase involved in RNA Packaging |
| 9           | 1062      | VP7     | 326         | Surface | Structural and neutralization antigen |
| 10          | 751       | NSP4    | 175         | Nonstructural | Enterotoxin |
| 11          | 667       | NSP5 NSP6 | 198 | Nonstructural | ssRNA and dsRNA binding modulator of NSP2 |

Table is based on the simian rotavirus strain SA11 (Desselberger 2000; Patton and Spencer 2000). RNA protein-coding assignments differ in some strains.

Segment 1 encodes the VP1 protein and functions as an RNA-dependent RNA polymerase. VP1 protein is complexed with VP3 protein in the core of the virion. The latter protein is encoded by segment 3. The fourth segment encodes VP4 protein which is an outer capsid protein, plays a major role as neutralizing antigen. Leaving some of the serogroups apart, most of the serogroups of RVs follow the same rule. In RVD, segment 3 encodes the VP4 protein, while segment 4 encodes the VP3 protein; this order is inverted compared with the gene–protein assignment of RVAs (Trojan et al. 2010).

8.4 Classification

Rotaviruses are dsRNA viruses in the Reoviridae family, and each RV is named after the species in which it occurs (Estes and Greenberg 2013). Reoviridae family is subdivided into two sub-families, i.e. Sedoreovirinae (e.g. genera Orbivirus, Rotavirus) and the Spinareovirinae (e.g. genera Coltivirus, Orthoreovirus). Rotavirus genome consists of 11 segments of dsRNA encoding 6 structural viral proteins (VP1–VP4, VP6 and VP7) and 5 nonstructural proteins (NSP1–NSP5/6) (Estes
and Greenberg 2013). The intact virus is composed of 3-capsid layers: an inner core, an intermediate capsid and an outer capsid with short radiating spikes. Three types of rotavirus particles visualized under the EM are (1) the complete infectious or triple-layered particles (TLP), (2) the double-layered particles (DLP) and (3) the core or single-layered particles, which harbour double-stranded RNA (dsRNA) genome (Estes and Kapikian 2007).

RVs are classified into ten groups (A–J) based on antigenic relationships of their VP6 proteins, with provisional I and J species recently identified in sheltered dogs in Hungary and bats in Serbia, respectively (Matthijnssens et al. 2011; Otto et al. 2012; Mihalov-Kovács et al. 2015; Bányai et al. 2017). Commonly groups A, B and C (RVA, RVB and RVC) infect humans and animals. Historically, RVA strains were the most prevalent and represented the most significant causes of acute diarrhoea from the public as well as veterinary health perspectives. Based on the outer capsid proteins (VP7 and VP4), which induce neutralizing antibodies, G and P dual typing system has been used to denote strains with a particular genotype (Estes and Greenberg 2013). To date, at least 31 different G- and 44 P-genotypes have been described in both humans and animals for RVAs (Matthijnssens et al. 2009). RVs of different groups are further classified into ‘P’ and ‘G’ genotypes based on the sequence identities within VP4 (‘P’/Protease sensitive) and VP7 (‘G’/Glycoprotein) genes, respectively. In 2008, Rotavirus Classification Working Group (RCWG) extended the dual (G/P) typing system of RVA strains to a full-genome sequence classification system, with nucleotide percent identity cut-off values established for all 11 gene segments, with the notations Gx-P[x]-Ix-Rx-Cx-Mx-Nx-Tx-Ex-Hx used for the VP7-VP4-VP6-VP1-VP2-NSP1-NSP2-NSP3-NSP4-NSP5/6 encoding genes, respectively (Matthijnssens et al. 2009; Ciarlet et al. 2008). Subsequently, to maintain the proposed guidelines and the classification system RCWG was formed (Matthijnssens et al. 2009; Ciarlet et al. 2008) which ensure complete and accurate classification of novel RVA strains.

On the contrary, till now only RVA classification has been developed which is being maintained by the RCWG, whereas very little is known regarding epidemiology and disease affliction associated with infection by other RV serotypes in different avian and mammal species. Using similar criteria established for RVA strains, RVCs were classified into nine different VP7 (G) genotypes, and now an 11 genome segment classification system has been adopted for RVC classification. Even higher genetic diversity was reported for RVB strains with 20 G-genotypes identified. Marthaler et al. (2012) findings suggested that porcine RVB strains have been circulating in the USA for a prolonged time (at least since the 1980s) and may be more prevalent than initially thought (Marthaler et al. 2012). This underestimation of RVB prevalence and diversity may be associated with the lack of adequate diagnostic tools, shorter and lower magnitude of the virus shedding as well as uncertain clinical significance for different age groups.

The RVC, RVE and RVH have been detected in the sporadic form in a few mammalian species. However, RVD, RVF and RVG are found only in poultry, such as chickens and turkeys (Kusumakar et al. 2008; McNulty et al. 1978; Martella et al. 2010; Trojnar et al. 2013). RVI and RVJ identified recently in sheltered dogs and
bats in Hungary and Serbia, respectively, although confirmation by the International Committee on Taxonomy of Viruses is pending (Mihalov-Kovács et al. 2015; Bányai et al. 2017).

8.4.1 Pathogenesis

The pathogenesis of RV infection in animals is very similar to that of enteric coronaviruses. The main transmission route is faecal-oral. The outcome of infection in all species depends on the virulence of the RV strain, the quantity of virus ingested, the presence of maternally derived or actively acquired antibodies in the lumen of the gut at the time of exposure, age-related resistance to the disease and animal management practices. Infection occurs shortly after birth, but it usually is subclinical in the presence of colostral antibodies in the gut. However, recent studies in the USA have shown a higher prevalence of RVC compared to RVAs in neonatal diarrhoeic piglets <3 weeks of age, where it appeared to be the only causative agent of diarrhoea that developed in suckling piglets and piglets on milk replacer.

RVs infect mature enterocytes at the tips of the villi of the small intestine (Fig. 8.1). As a result of infection, these cells, which have an absorptive function, are desquamated more rapidly (Fig. 8.1) and replaced by undifferentiated epithelial crypt cells which have a secretory function (Dhama et al. 2015). Due to resultant malabsorption, undigested carbohydrates in the lumen of the colon are fermented by bacteria to short-chain fatty acids, leading to accumulation of a hypertonic solution and subsequent osmotic fluid loss.

As a result of damage to the epithelium, the cellular sodium transport system is also disturbed, resulting in a net flow of fluid from the extracellular space into the

**Fig. 8.1** Rotavirus pathogenesis. Rotavirus infection of villous enterocytes results in the cell death, villous atrophy and leads to malabsorption
lumen of the gut. The total faecal output is thus markedly increased with a concurrent loss of Na⁺ and Ca²⁻ ions. Affected animals develop dehydration, electrolyte imbalance and concomitant acidosis if appropriate therapy is not used. Inflammatory changes in the intestine may cause hypermotility and aggravate the diarrhoea (Woode 1976). An immune evasion mechanism by RV mediated by downregulation of interferons and other cytokines was suggested based on gene expression profiling using microarrays (Aich et al. 2007). While uncomplicated RV disease is often self-resolved within a few days, immune-suppressive RV mechanisms promote colonization of the bowel by other infectious agents such as Salmonella serovars, clostridia and other bacteria and increase the severity of the condition (Woode and Bridger 1975). Complicated RV diarrhoea increases the risk of death. The extra-intestinal spread of RV was confirmed by detection of RV dsRNA, RV antigen or infectious RV in serum and different organs (Kim et al. 2014; Park et al. 2011a). Although the clinical significance of the extra-intestinal RV infections is not established, RV replication in the liver, the biliary system and the pancreas leads to biliary atresia and pancreatitis in immunocompromised hosts. Vomiting in RV-infected hosts was explained by the fact that RV can infect the enterochromaffin cells in the gut, stimulating the production of serotonin which activates the afferent vagus nerve and stimulates the brain stem structures controlling vomiting.

### 8.4.2 Clinical Signs

RV diarrhoea is often sporadic or self-resolving in nature because most infections in suckling animals with maternal immunity remain subclinical. However, in situations with limited or no transfer of maternal immunity or after the loss of maternal immunity (weaning) and where other predisposing factors co-occur, the prevalence of disease may reach epidemic proportions. Additionally, maternal immunity does not seem to confer sufficient protection against diarrhoea associated with RVC.

The incubation period in most animals is 18–96 h. Affected animals are initially depressed and anorexic (Woode and Bridger 1975). This is followed by profuse diarrhoea, dehydration, loss of body weight and lethargy. Diarrhoea may persist up to 14 days in piglets and become severe if the animal recovers sufficiently to resume feeding (Woode and Bridger 1975). The colour of the faeces may vary from yellow or brownish-grey to light green and normally does not contain blood or mucus unless secondary bacterial infections occur (Snodgrass et al. 1984). It is usually an afebrile disease unless complicated by a secondary bacterial infection. Affected animals may die as a result of dehydration, electrolyte imbalance and secondary infections. Diarrhoea and stunted growth become noticeable 4 days post-infection with avian RVs (Dhama et al. 2015).
8.4.3 Pathology

Upon necropsy, intestinal walls are thin and filled with yellow fluid. The stomach is often full of undigested milk. Microscopic lesions are generally confined to the villi of the small intestine. The proximal part of the duodenum is generally not affected, and there is a patchy distribution of affected areas throughout the rest of the small intestine. Some variations in RV antigen distribution in different species are reported. Immunofluorescence studies showed that viral antigens are confined to the cells at the tips of villi in the middle and distal small intestine of calves and piglets (Theil et al. 1986) that are shed within 4 days post-infection. In lambs, the antigen is also present in the enterocytes of the large intestine, but it is less abundant than in the small intestine. Within infected cells, the virus is associated with the rough endoplasmic reticulum.

Villi appear blunt, short and fused, giving the mucosa an almost avillous appearance. Shortening of the villi is due to the loss of brush-border columnar epithelial cells that are replaced by cuboidal or squamous cells lacking a brush border from the crypts. Infiltration of mononuclear inflammatory cells may occur in the lamina propria (Mebus et al. 1971).

8.5 Diagnosis

Virus isolation was historically considered the ‘gold standard’ for detecting viral pathogens in diagnostic samples. However, more rapid and sensitive methods (including ELISA and RT-PCR) became available in the last decades. Cell culture is used to isolate viruses for diagnostic purposes as well as virus propagation for vaccine development or virus genetic characterization. Many cell lines (e.g. MDBK, MA104, TF and PK-15 cells) have been used to isolate RV from animal faecal samples. Viral isolation has three advantages including (a) confirmation of the presence of the infectious virus in a clinical sample, (b) availability of the isolated virus for further genetic, immunity and pathogenesis studies and development of diagnostic kits and vaccine and (c) the method does not require virus/strain reagents. However, many field strains of RV, especially RVB and RVC, do not replicate in most cell cultures. Other disadvantages include low sensitivity, variable permissiveness of cells, dependence on proper collection and storage of samples for virus viability and non-applicability for cytotoxic specimens.

Transmission electron microscopy (TEM) of negatively stained faecal or intestinal content samples is commonly used for visualization of RV particles in the intestinal contents or faeces and RV diagnosis (Saif et al. 1991). This technique has the added advantage of demonstrating other infectious agents in cases of mixed enteric infections. Two different staining techniques (positive and negative staining) can be performed to visualize the target. Additionally, there are direct TEM and immune electron microscopy (IEM) (Saif et al. 1991). Immuno-electron microscopy
has greater sensitivity than direct TEM since the specimen is incubated with an antibody specific for the target virus that agglutinates the virus before staining.

Direct or indirect fluorescent antibody tests can be used to demonstrate antigen in cell culture, faecal smears and histological sections of the intestine (Mebus et al. 1969a, b; Woode and Bridger 1975).

Shared, group-specific protein (VP6)/VP6 antibody are used in commercial enzyme-linked immunosorbent assay (ELISA) kits that can be used to screen large numbers of faecal specimens fast. These kits are available at least for human, murine, porcine, or bovine RV detection. ELISA assay may also be used for serological screening, although high antibody prevalence in most populations negates the diagnostic value of this approach. A rapid, highly specific, and sensitive antigen capture ELISA (AC-ELISA) has been developed for detection of porcine RVA, by using VP6 rabbit polyclonal antibodies (capture antibody) and murine monoclonal antibodies. Similar VP7-specific ELISA was developed for detection and G typing of bovine RVA from beef and dairy calves.

Other tests that were used historically for antigen detection include complement fixation, counterimmuno-electrophoreses, radio-immunoassay and agar-gel diffusion. Polyacrylamide gel electrophoresis (PAGE) of viral RNA extracted from faeces or virus propagated in cell culture was commonly used in epidemiological studies, particularly for differentiating between RV groups and as a rapid means of detecting atypical RVs in faecal specimens (Pedley et al. 1986; Bridger et al. 1983; Chauhan and Singh 1992). However, their use is less common nowadays.

Based on the various hypervariable regions of outer capsid genes of RV molecular detection tools—hybridization tests have been developed using labelled cDNA probes that could characterize animal RV strains (Parwani et al. 1996). RT-PCR using validated primers designed from RV genes is currently the most widely used assay for detection of RVs in animals (Lee et al. 2003). Additionally, semi-nested or multiplex RT-PCR has been developed and used (Midgley et al. 2012) for the same purpose. RT-PCR is highly sensitive and specific and is suitable for genotyping RV, and it has become a gold standard for RV diagnostics. Methods like sequencing and oligonucleotide microarray hybridization that are sensitive and capable of discriminating mixed RV infections are also available.

### 8.5.1 Differential Diagnosis

The etiological diagnosis of neonatal calf diarrhoea is difficult (Tzipori 1985). A variety of infectious agents, including RVs, coronaviruses, enterotoxigenic *E. coli*, and cryptosporidia, may cause diarrhoea in neonatal calves. Laboratory assistance is thus necessary to arrive at a diagnosis. Variation in the frequency of RV and coronavirus detection in beef and dairy calves has been demonstrated. The studies showed that coronavirus are more common in beef calves and RV in dairy animals. The differential diagnoses of enteritis in lambs include colibacillosis, salmonellosis, coccidiosis, cryptosporidiosis and adenovirus infections (Theil et al. 1996).
Diarrhoea as a result of RV infection in foals should be differentiated from that caused by other infections such as *E. coli*, Salmonella serovars, *Rhodococcus equi*, *Actinobacillus equuli* and Clostridium spp., as well as foal-heat diarrhoea, nutritional factors and internal parasites.

The clinical signs, lesions and pathogenesis of porcine RV diarrhoea closely resemble those of porcine transmissible gastroenteritis (TGE), porcine epidemic diarrhoea (PED) or porcine delta coronavirus infection caused by coronaviruses but remain less severe. A multiplex RT-PCR has been developed that is reportedly able to differentiate TGEV, PEDV and porcine RVA. Porcine RV diarrhoea should also be differentiated from that caused by *E. coli*, clostridia, coccidia, cryptosporidia, *Brachyspira hyodysenteriae*, internal parasites and nutritional imbalances.

### 8.6 Porcine Rotavirus

Of the 9 RV genogroups RVA, RVB and RVC are fairly prevalent and associated with large or isolated outbreaks of diarrhoea in piglets (Bridger et al. 1983; Bridger 1987) (Table 8.1). Reported first several decades ago, porcine RVEs are highly uncommon, and their pathogenesis is not studied (Bridger 1987). A newly defined genogroup RVH was confirmed in diarrhoeic pigs in Japan, Brazil and the USA recently. RVHs were shown to be widespread, and their prevalence was shown to increase with age, while RVH association with diarrhoea in nursing piglets needs further evaluation. Porcine RVAs have been widely recognized and well-studied regarding their pathogenicity, compound epidemiology and high genetic diversity.

Based on the VP7 gene segment analysis a significant genetic diversity has been described recently for RVB and RVC porcine strains. Additionally, RVC was shown to be the most prevalent virus associated with diarrhoea in very young piglets.

RVA infection in pigs has been demonstrated in different age groups throughout the world with or without diarrhoea (Kusumakar et al. 2010; Martella et al. 2010; Ciarlet et al. 2008; Papp et al. 2013). The spatio-temporal fluctuations and re-emergence of certain genotypes like G9 and G1 have been reported, but no evidence of seasonal variation on RVA prevalence has been documented which usually ranges from 3.3 to 67.3% (Collins et al. 2014; Martella et al. 2010; Kim et al. 2014; Midgley et al. 2012), with farm-level prevalence reaching 61–74%. A total of 12 G genotypes (G1 to G6, G8 to G12 and G26) and 16 P genotypes (P[1]–P[8], P[11], P[13], P[19], P[23], P[26], P[27], P[32] and P[34]) have been reported in pigs for RVA (Martella et al. 2010; Collins et al. 2014; Papp et al. 2013) (Table 8.1). The most common genotypes circulating in swine population worldwide have been G3, G4, G5, G9 and G11 coupled with P[5], P[6], P[7], P[13] and P[28] (Matthijnssens et al. 2009; Ciarlet et al. 2008).

Similar to RVA, porcine RVCs have also been reported from all over the world (Kattoor et al. 2017; Pedley et al. 1986, Saif and Jiang 1994). Diarrhoea outbreaks associated with RVCs have been documented in nursing, weaning and post-weaning pigs (Saif and Jiang 1994; Chang et al. 1999), either alone or in mixed infection with
other enteric pathogens. High antibody prevalence of 58–100% demonstrates a very high rate of RVC infection may have been present and has circulated for many decades in porcine herds in developed countries (Saif and Jiang 1994). Studies from the USA and Canada on swine samples have revealed a very high rate of prevalence in very young (78%, ≤3 days old) and young (65%, 4–20 day old) piglets. Prototype porcine RVC strains Cowden and HF were initially assigned to RVC genotypes G1 and G3, respectively. Based on different sequence-based reports, RVC strains have been classified into a total of nine G genotypes (G1–G9), seven P genotypes (P[1]–P[7]) and seven I genotypes (I1–I7) (Marthaler et al. 2014). Moreover, majority of porcine RVCs belong to G1, G3, G5–G9 genotypes and a newly described genotype G10 (Table 8.2), while bovine, human and canine RVCs are classified as G2, G4 and G11 genotypes, respectively (Collins et al. 2014). Recently, two provisional G genotypes (G12 and G13 based on the 86% nucleotide identity cut-off value) have been described (Table 8.2).

Due to a difficult adaptive capability of RVB in cell culture, molecular characterization of RVB strains has been hampered (Saif and Jiang 1994). Furthermore, inadequate and inconstant faecal shedding and instability in faeces were shown for RVBs (Chang et al. 1997). In one of the studies from 2000 to 2007 in Japan, VP7 gene of 38 swine RVB strains was analysed and using 67% and 76% nucleotide cut-off values (66% and 79% on the amino acid level, respectively) 5 genotypes proposed were further divided into 12 clusters. An extensive diversity of porcine RVBs based on the analysis of VP7 gene of 68 RVB strains (collected in 2009 from 14 US states and Japan) was suggested (Marthaler et al. 2012) (Table 8.1). Around 20 G genotypes based on an 80% nucleotide identity cut-off value were described and it also provided the first indication that porcine RVB genotypes may be host species- and region-specific and can be disseminated into 17 tentative G-genotypes. Species wise RVB genotypes distribution has shown that G1, G2 and G3/G5 are only found in rats, humans and bovine species, respectively, whereas common porcine genotypes include G4, G7, G9, G13, G15 and G19 reported from Japan. A very small number of swine RVB strains have been associated with genotypes

| Genogroup | Diarrhoea in adult swine | Diarrhoea in piglets | Faecal shedding | Prevalence | Genotypes circulating in pigs |
|-----------|-------------------------|---------------------|----------------|------------|-----------------------------|
| A         | No                      | Yes                 | Can last beyond 10 days | High       | G1–G6, G8–G12 and G26; P[1]–P[8], P[11], P[13], P[19], P[23], P[26], P[27], P[32] and P[34] |
| B         | Yes                     | Yes                 | Shorter         | High       | G4, G6–G21                  |
| C         | No                      | Yes                 | Can last beyond 10 days | High       | G1, G3, G5–G10, G12, G13; P[1]–P[7] |
| E         | No                      | Yes                 | N/A             | Very low   | N/A                         |
| H         | No                      | Yes                 | N/A             | High       | At least 2 I genotypes      |
G10 and G17 which were reported in the USA. In India, a new G21 genotype has been detected in pigs.

In the beginning, strains ADRV-N, J19 and B219 were identified as three human RVH strains, whereas strain SKA-1 was identified as putative porcine RVH strain during 1997–2002. In 2012, three Brazilian porcine RVH strains BR63, BR60 and BR59 were again reported. Marthaler and colleagues demonstrated a surprisingly high prevalence of 15% of swine RVH strains in comparatively old age piglets of 21–55 days (Marthaler et al. 2014). These reports pointed towards a continuous circulation of porcine RVH strains in the US herds since 2002 and also described their distinct evolution from those of human and porcine RVH strains of Brazil and Japan (Marthaler et al. 2014). The novel RVH strain MRC-DPRU1575 identified in South Africa clustered together with the SKA-1 and known porcine strains from USA and Brazil (based on the available gene segments).

Porcine RVE has been only identified in the UK and Australia roughly three decades ago and therefore further data is required to estimate its epidemiological significance (Bridger 1987).

8.6.1 Zoonotic Potential of Porcine RVs

While, historically, RVs were believed to be host-specific, currently porcine, bovine, ovine, pteropine, rodent, avian and insectivore species are suggested to be sources of zoonotic RV infections (Midgley et al. 2012). Reports of some porcine origin G genotypes, G9 and G12, have emerged from human cases which arise due to gene reassortments (Tsunemitsu et al. 2005; Ghosh et al. 2007b, Matthijnssens et al. 2009). Around 10 G genotypes (G1-5, G9-G12 and G26) and 7 P genotypes (P[4], P[6], P[8], P[13], P[14], P[19] and P[25]) of swine-origin have been identified in humans till date out of which few genotypes like G10, G11, G12, G26, P[13], P[14], P[19] and P[25] are found in Asian or African countries only, while the rest are emerging globally. Histo-blood group antigens (HBGA, ABOH, Lewis) and sialic acids receptors are known to interact with different RVA strains via VP4 gene which may provide further insights into the local distribution and increased zoonotic potential of some RVAs of porcine origin, as similar polymorphic HBGAs are also witnessed in pigs (A and H antigens). These observations may provide insights into why P[6] genotype of certain RVA strains (that recognize H antigen) is more frequently transmitted between pigs and humans in different countries, whereas a potent porcine origin genotype P[19] found in humans continues to be restricted in Indian, Asian and African countries which coincides with distinct polymorphisms in Lewis antigens associated with Caucasian and other populations.

Similar to porcine RVA strains, there is growing evidence of porcine RVC zoonotic potential. There have been few reports of human and bovine RVC where porcine origin genes have been reported. Bovine RVC strain WD534tc has been identified to be of possible porcine origin (Chang et al. 1999), whole genome sequencing and analysis of certain porcine RVC strains from Japan have advocated
towards a close phylogenetic relationship between human and porcine RVC strains. Nevertheless, the hypothesis regarding the possible zoonotic transmission of animal RVCs has also been described in view of increased seroprevalence of RVC in humans and high prevalence of RVC in few particular geographical regions where they may attribute towards <5% of gastroenteritis-associated hospitalizations in childhood. Recently, human-like RVC VP6 and VP3 genes were identified in porcine RVC strains identified in India and Japan, respectively. Though, it is important to note that the limited genetic variability of RVCs in humans contrasts with the high genetic diversity currently seen in pigs.

More recently, RVB strains were identified from sporadic cases of infantile diarrhoea in Bangladesh as opposed to adult diarrhoea cases associated with RVB in China and India. Though, the recently reported Chinese RVB strains differed genetically which suggest that human RVB is different. Medici and colleagues provided limited evidence of the zoonotic potential of some RVB strains wherein they demonstrated a high nucleotide identity between human and porcine NSP2 gene sequences.

Apart from the epidemiological data of porcine RVA, information has been scarce concerning porcine RVB/RVC/RVH which is warranted towards the need to control their regional and global zoonotic spread.

### 8.6.2 Vaccines and Control Strategies

In livestock, based on the induction of active and passive immunity of herds vaccination strategies are planned. Maternal RV vaccines in the field are influenced by strain, vaccine dose, adjuvant, route of administration, inactivating agent and porcine RV exposure levels. Nevertheless, oral vaccines of attenuated RV vaccines given to piglets and calves were often inefficient (Saif and Fernandez1996). Due to the ubiquitous and endemic nature of RV infections, there has been a need to boost the lactogenic immunity to provide passive antibodies to the newborn with milk and colostrum.

Due to the replication-independent mechanism of genetically engineered VLP vaccines which allows circumvention of maternal antibodies, they are being used as promising tools to boost antibodies in mammary secretions. However, because of the low protective efficacy of such vaccines, priming with live attenuated RV vaccines was deemed necessary. Yet, field application of G5P[7] (porcine RVA OSU) based vaccines or ProSystem porcine RV vaccine (which contained modified live porcine RVA strains of G4P[6] and G5P[7] genotype combinations) have resulted in circulation of porcine RVA with these genotypes and their latest substitution by G9 and G11 genotypes or reassortant G4 and G5 variants. On the other hand, they could generate herd immunity progressively reducing the prevalence of the G4/G5 porcine RVA genotypes and allowing the spread of novel emerging swine RVAs.
8.7 Bovine Rotavirus

Among different infectious diseases in neonatal calves, diarrhoea is a major concern. The aetiology of diarrhoea in bovines is complex, which often involves many infectious agents and a range of other factors like nutritional, immunological and environmental. Many etiological agents, including *E. coli*, *Clostridium*, *Salmonella*, *Cryptosporidium* and *Coccidia* have been suggested to be associated with calf diarrhoea. Among viral agents, RVs, coronavirus (CoVs), norovirus (NoVs), bovine viral diarrhoea (BVDV) have been described to be the most significant contributors to the diarrhoeal disease complex in young calves. Young calves of 2–10 weeks are susceptible to RV disease, and with age progression, adults develop immunity against the virus. The severity of disease and clinical signs are almost similar in all species with symptoms ranging from asymptomatic to severe enteritis. The earliest known documentation of rotavirus and its symptoms in bovine were reported in 1969 in the USA (Mebus et al. 1969a, b) and consequently they were the earliest known RVs to be adapted in the cell culture system (Mebus et al. 1971). Since then many reports emerged describing RV as the causative agent of calf diarrhoea which suggests its global distribution (Woode 1976; Woode and Bridger 1975; Castrucci et al. 1988; Kapikian 1994; Chauhan and Singh 1996; Vende et al. 1999; Bendali et al. 1999; Pisanelli et al. 2005; Alfiieri et al. 2006; Ghosh et al. 2007a; Collins et al. 2014; Malik et al. 2016).

8.7.1 Clinical Manifestations

Usually, those calves which have been exposed to the virus via water, milk and feed display the symptoms of diarrhoea. Virus shedding from infected calves causes environmental contamination which in turn becomes pervasive. Grouping of calves in a smaller area also facilitates the transmission over direct contact. It has been observed that the pregnant cattle used to shed the virus during pregnancy which may act as a source of infection for the neonates. Within the second day of infection infected calves start to shed the virus which usually continues for a week and calves under the age of 3 weeks are more susceptible towards the infection (Gomez and Weese 2017). Usually, the infection ceases after 3 months of age in cattle calves, whereas, however, asymptomatic RV infections have been documented up to 6 months of age in buffalo calves and are common in adult cattle.

Additionally, RVB was shown to be associated with diarrhoeal disease in adult cattle as seen with other species (Chang et al. 1997). The incubation period of RV mediated diarrhoea in calves ranges from 12–24 h which may sometimes goes up to 18–96 h. The disease is usually characterized by complications due to secondary pathogens infection in which mortality rate goes up to 80% but usually described to be around 10–20%. Bovine RVs are universal and cause severe diarrhoea by compromising the absorptive capability of an intestinal surface to cause diarrhoea
The diseased calves display varied clinical conditions characterized by diarrhoea, dehydration, increased salivation, loss of appetite and inability to move. Unless secondary bacterial pathogens are present, the faeces are free from mucus or blood. Due to the reoccurrence of diarrhoea exhibited by less colostrum and fluid intake often leads to the death of the calf. The nature of diarrhoea in calves is often malabsorptive, but few studies have also described that a toxin-mediated secretory factor can also be present (Foster and Smith 2009).

8.7.2 Epidemiology of Bovine Rotaviruses

RVs are classified into 10 groups (A–J) based on antigenic relationships of their VP6 proteins. To date, RVA, RVB and RVC genogroups have been described to cause diarrhoea in bovines with varied clinical manifestations.

8.7.2.1 Bovine Rotavirus A (BoRVA)

Out of the different genogroups of RVs described in bovines, RVA accounts for the majority of infections in cattle and buffaloes. Since its first discovery in 1969, where earliest study recorded a high BoRVA prevalence from the USA (98%) and Italy (90%) (Castrucci et al. 1988; Schlafer and Scott 1979). BoRVA infection has been reported globally, which describes its ubiquitous nature. Apart from the North American continent where it was first recorded, incidence and prevalence of BoRVA infection has been widely described from different European countries like England 67% (Woode 1976), Ireland 91% (Reidy et al. 2006), Netherlands 46% (De Leeuw et al. 1980), Italy 90% (Castrucci et al. 1988), Sweden 43.8% (Svensson 1998), France 45.1% (Vende et al. 1999), Switzerland 46% (Luginbühl et al. 2005), Bulgaria 42% (Kharalambiev et al. 1983). In Asia, BoRVA has been reported in India with varied prevalence ranging from 4.3 to 46% (Chauhan and Singh 1996; Malik et al. 2012; Basera et al. 2010; Niture et al. 2009; Saravanan et al. 2006). The low prevalence reports these studies could be attributed to the detection method used (RNA-PAGE) which is considered as less sensitive compared to RT-PCR assay. BoRVA prevalence in other Asian countries includes Japan 16.7% (Fukai et al. 1998), Turkey 41.2% (Gumusova et al. 2007), Bangladesh 7% (Selim et al. 1991), Sri Lanka 68.5% (Sunil-Chandra and Mahalingam 1994). Reports from Latin American countries include Argentina 62.5% (Garaicoechea et al. 2006), Brazil 17% (Barbosa et al. 1998) and Venezuela 11.7% (Ciarlet et al. 1997). Among the Oceanian continents, BoRVA prevalence was 49% in Australia (Tzipori 1985) and New Zealand 13% (Schroeder et al. 1983).
8.7.2.2 Bovine Rotavirus B (RVB)

Apart from RVA, there have been few reports of RVB circulating in the bovine population. However, RVB has been primarily linked to adult diarrhoeal cases. In bovine species, only a few countries have reported the presence of RVB in cattle. Earliest known documentation of non-group A rotavirus has been described in cattle in 1984 and 1987 (Bridger 1987; Snodgrass et al. 1984). In the year 1991, RVB was reported in herds of cows with winter dysentery along with co-infection of CoV, which were detected by IEM (Saif et al. 1991). However, the same group identified RVB of short genome profile in the year 1996 following their identification through IEM (Parwani et al. 1996). Following these few earlier reports of atypical RVs (non-RVA), reports of RVB detection by RT-PCR in bovines emerged from the USA in the year 1994, 1995 and 1997 (Chinsangaram et al. 1995, 1994; Chang et al. 1997). RVB was first detected from Japan in the year 1999 in adult cows followed by its detection in 2001 and 2005 from dairy herds (Tsunemitsu et al. 1999, 2005; Hayashi et al. 2001). In India, RVB detection in bovines was first documented in 2001 through the atypical pattern on RNA-PAGE and also due to the non-reactivity of the virus with antibodies of RVA (Khurana and Pandey 2001), whereas in 2004 sequence report based on VP7 and NSP5 gene was described followed by its occurrence in the Eastern part of India which were named as ‘Kolkata Strains’ (Ghosh et al. 2007b). This study also highlighted the interstate transmission of RVB strains from adjoining states of West Bengal, India. Serological detection of RVB antibodies has also been reported from Japan and UK from bovine species (Brown et al. 1987; Tsunemitsu et al. 2005).

8.7.2.3 Bovine Rotavirus C (RVC)

Reports on RVC in cattle have been much less common as compared to RVA and RVB. Primarily, RVC has been associated with diarrhoea in porcine and human species. Earlier studies have reported RVC antibodies in cattle (Bridger et al. 1983; Saif and Jiang 1994; Tsunemitsu et al. 1991). The very first characterization was reported from Japan in 1991 when the bovine strain RVC Shintoku was propagated in MA104 cells which were also confirmed by its peculiar electropherotype pattern of 4-3-2-2 on RNA-PAGE (Tsunemitsu et al. 1991). After that, Mawatari et al. (2004) reported BoRVC in six farms in Japan from 2003 to 2010. This study also described the comparative sequence analysis of VP6 and VP7 gene from six bovine RVC strains detected in studied farms in Yamagata. Dual infection of gnotobiotic calves with RVA and RVC was also reported from the USA (Chang et al. 1999). RVC in cattle has been associated with adult diarrhoea which in turn found to influence the milk yielding capacity, thereby decreasing the milk production (Mawatari et al. 2004). Due to a limited number of reports on bovine RVC from restricted geographical areas, the worldwide distribution of RVC in cattle remains
uncertain. Apart from Japan and the USA, a report from South Korea in 2011 described the prevalence of RVC in diarrhoeic calves (Park et al. 2011a).

8.7.3 Genotype Diversity Among Bovine RVs

Similar to other RVs, interspecies transmission and reassortment events are common and generate diverse genotype combinations of bovine RVs. Bovine RVA s mostly belong to genotype G3, G6, G8 and G10, and P[1], P[5], P[6] or P[11] for VP7 and VP4 genes, respectively (Malik et al. 2013a, b, c). The typical genetic backbone of bovine RVAs consists of I2-R2-C2-M2-A3/A13-N2-T6-E2-H3 types (Fig. 8.2) (Martella et al. 2010). Many unusual genotypes for G types (G1–G6, G8, G10–G12, G15, G21, G24) and P types P[1], P[3], P[5], P[6], P[7], P[10], P[11], P[14], P[17], P[21], P[29], P[33] have also been reported from various countries (Abe et al. 2011; Ghosh and Kobayashi 2011; Malik et al. 2016; Masuda et al. 2014; Midgley et al. 2012; Papp et al. 2013; Park et al. 2011b; Reidy et al. 2006). Many common human genotypes like G1 and G9 have also been described in cattle (Blackhall et al. 1992; Kumar et al. 2018). Apart from human-like genotypes, porcine-like genotypes have also been reported from bovines (Ha et al. 2009; Park et al. 2011b).

8.7.4 Diagnosis

Quick detection of the etiological agent is most important to stop the further spread of the disease. RV diagnosis is made by identification and isolation of the virion in faeces of the diseased animal. Similar to other RVs, historically, isolation of bovine RVA has been achieved in monkey kidney cell line MA104. Immunoperoxidase test (IPT), immunofluorescence test (IFT) and the RNA-PAGE gel have been employed to detect the presence of RVs in the faeces of bovine. Few rapid tests like latex agglutination test (LAT), dot-blot assays have also been developed for the early detection of the virus in field conditions (Chauhan and Singh 1992; Hammami et al. 1990; Pirkooh and Shahrabadi 2015). Enzyme-linked immunosorbent assays (ELISA) have been developed by many research groups which are highly sensitive and specific for the identification of RVs. Antigen capture assays have also been developed by improving the ELISA using type-specific antibodies. Further, the use of multiple antigenic peptides (MAPs) for raising Abs against RV antigen has also been found successful in the development of antigen capture ELISA (Kumar et al. 2016). These antigenic peptides are based on the outer capsid protein VP6 of RVs, which is conserved in different species and are produced in abundance during acute infection. Recently, more sensitive tests like PCR and RT-PCR have been the choice of researchers for the detection of RVs in bovine faeces. RT-PCR assays exploiting the use of the VP7 and VP4 gene-based primers are widely used for the diagnosis of RVs (Malik et al. 2013a, b, c). The manipulation of PCR techniques as semi-nested
Fig. 8.2 Comparison of genomic constellations of bovine RVA strains and RVA strains having a bovine-like backbone. Individual gene segments of all strains are colour coded based on the maximum homology with the RVA strains available in the public domain.
and multiplex RT-PCR have been developed which helped in the G and P typing of various bovine isolates circulating in the field (Luan et al. 2006). Use of microarrays for characterizing the genotype to know the G and P-type has also been described (Aich et al. 2007).

8.7.5 Prevention and Disease Control

Better management and proper hygiene practices are beneficial to reduce the severity of disease in bovine herds. Support of antibiotics to minimize the secondary bacterial infection followed by the administration of electrolyte and fluid intake may help to save the life of calves. Local and mucosal immunity has to be boosted in cows, which is critical in protecting the calves. Colostrum-derived antibodies are crucial in neutralizing the virus in the neonates (Agrawal et al. 2002). Actively acquired mucosal immunity is considered better in comparison to the immunity provided by colostrum-based antibodies. Immunization of pregnant dams before parturition is recommended to supplement the protection levels in neonates (Barrandeguy et al. 1998). Vaccination of pregnant cows through intra-mammary and intramuscular routes could contribute to considerable increase in the titers of colostrum and serum antibodies (Saif and Fernandez 1996). Administration of artificial colostrum, whey protein and vegetable oils are also given as an alternative measure to strengthen the immunity of calves (Murakami et al. 1986). Chicken egg yolk immunoglobulins have also been found beneficial in defending neonatal calves from RV mediated diarrhoea.

8.8 Avian Rotaviruses

Most significant viruses involved in enteric diseases in avian spp. include rotavirus, astrovirus, calicivirus, adenovirus and coronavirus (Farkas and Jiang 2009). Apart from mammalian spp., rotaviruses (RVs) are an important cause of gastroenteritis in a wide variety of avian species (Guy 1998). The first record of avian RV dates back to 1977, when it was identified as a potential cause of enteritis in turkey poult (Bergeland et al. 1977) and was later identified in chickens (McNulty et al. 1978). Since then, avian RVs have been described in several avian hosts including pheasants, ducks, pigeons, wild birds, etc. (McNulty et al. 1978; Takehara et al. 1991; Legrottaglie et al. 1997). To date, RVs have been reported in many countries including USA, UK, Europe, Russia, Argentina, Brazil, China, Bangladesh and India. In field conditions, avian RVs may induce subclinical manifestations, or they may be associated with diarrhoea, dehydration, anorexia, low weight gain and increased mortality where dehydration is the major contributor to mortality (Tamehiro et al. 2003). Recently, avian RVs have been reported as one of the causes of running and stunting syndrome (RSS), a major syndrome having a destructive
impact on the poultry industry. Rotavirus infection in turkeys was found to be associated with poult enteritis syndrome (PES), along with other enteric pathogens. Although RVs cause enteric disease, they have also been reported from healthy asymptomatic flocks of chickens (Bezerra et al. 2014). Avian RVs evolved early from their mammalian counterparts (Mori et al. 2002; Trojnar et al. 2010). Thus far, avian RVs are under-investigated as compared to mammalian RVs. Limited literature is available on these dsRNA viruses of avians. However, epidemiological studies have shown their presence worldwide. Phylogenetic studies of the available sequences of avian RVs show geographical segregation of different species (Kattoor et al. 2013). An in-silico analysis on avian RVs based on VP6 gene confirmed biasness in the codon usage for the host as well as for geographical locations (Kattoor et al. 2015).

8.8.1 Classification

Based on antigenic relationships of VP6 proteins used to classify RVs, four species (RVA, RVD, RVF and RVG) have been described in poultry (Otto et al. 2006; Johne et al. 2011). Of these, RVD, RVF and RVG are solely found in poultry (Otto et al. 2012). Among avian RVs, most detected groups are RVA and RVD, while RVF and RVG are less frequent. Genetic reassortment occurs within each species of RVs but never between the members of different serogroups. Each serogroup in RVs is considered as a unique species (Estes and Greenberg 2013). Two clades can be constituted based on the phylogenetic analysis of RVs, rotavirus A/C/D/F (Clade1) and rotavirus B/G/H (Clade2) (Kindler et al. 2013) owing to the diverse nature of RVs.

8.8.1.1 Avian Rotavirus A (RVA)

Rotavirus A infections are most common and most abundant among all the avian RVs. These are well characterized as compared to RVD, RVF and RVG infections. Analysis of the VP7 gene of avian RVA facilitated the classification of available strains into five different G genotypes, G7, G17, G18, G19 and G22 (Ursu et al. 2009). As shown by the studies conducted in rats, avian RVs have the capacity to disseminate in various organs, such as the liver, spleen and pancreas; however, the mechanism by which RVA escapes the gastrointestinal tract remains unknown (Crawford et al. 2006). This has been confirmed by a study conducted in 2016, where avian RVAs were detected from pancreas and spleen of broilers with RSS (Nuñez et al. 2016). Although, the reactivity of monoclonal antibodies with VP6 protein indicates a common classification for avian and mammalian RVs (Minamoto et al. 1993), the electrophoretic (PAGE) mobility pattern of genome segments tells a different story. Electropherotype of avian RVA (5:1:3:2) is different from mammalian RVA (4:2:3:2) wherein the major differences have been observed in the fifth
genome segment. In mammalian RVAs fifth segment migrates close to fourth, but in avian RVAs, it migrates close to the sixth segment (Wani et al. 2003). The first avian RV to be sequenced belonged to group A which was isolated from a pigeon (strain PO-13) with a length of 18,845 nucleotides (Ito et al. 2001). So far, only a handful of genome sequences of avian RVAs (as compared to mammalian RVAs) are available which impair the in-depth molecular characterization of avian RVA (Ito et al. 2001; Trojnar et al. 2013). The antigenic structure of NSP4 and VP6 genes of PO-13 (pigeon) strain of avian RVA has been determined using monoclonal antibodies (Minamoto et al. 1993; Borgan et al. 2003). Avian RVAs have been experimentally transmitted to mice, but the natural transmission seems rare with one report of transmission of avian RVA to calf under field conditions (Brüssow et al. 1992). A report (based on the electrophoretic migration pattern of RNA segments) is available describing the presence of mammalian like RVA in chickens suffering from diarrhoea (Wani et al. 2003). Available data suggest that ancestral strain of avian RVA and RVD has undergone reassortment based on NSP1 encoding gene segment as RVD was found to possess RVA like conserved termini (Trojnar et al. 2010; Matthijnssens et al. 2011; Kindler et al. 2013). Thus, a reassortment event can be predicted. Although interspecies transmission and reassortment have been elucidated for avian RVs (Schumann et al. 2009), detailed studies are required to comment on the cross-species transmission of avian RVA as well as to understand the origin of unusual mammalian strains of RVs.

8.8.1.2 Avian Rotavirus D (RVD)

Initially, RVD was described as virus 132 or D/132 in chickens and rotavirus-like viruses (RVLV) in poultry (McNulty et al. 1981; Pedley et al. 1986; Reynolds et al. 1987), based on the electrophoretic mobility pattern (4:2:2:2). Like other RVs, RVD causes diarrhoea, growth retardation, anorexia, etc. However, it also has a role in causing stunted growth, which was described early in 1994 and was further supported by Otto and co-workers in 2006 where they reported the importance of RVD in the pathogenesis of RSS in chicken flocks with severe villous atrophy (Otto et al. 2006; Roth 2016). The occurrence of RVD has also been reported in apparently healthy asymptomatic chickens (Bezerra et al. 2014). Epidemiological studies suggest the presence of RVD in European countries (Germany, Sweden, Scotland, etc.), Egypt, Asia (India, Bangladesh), Brazil and Nigeria (Ahmed and Ahmed 2006; Otto et al. 2012; Hemida 2013; Pauly et al. 2017). Over the last few years, an increase in the frequency of RVD infections has been observed in some geographical locations based on the molecular-based assays (Bezerra et al. 2014; Deol et al. 2017). Moreover, the detection rates of RVD are higher than RVA at some geographical locations (Otto et al. 2012). In turkeys and chickens, RVD has been designated as the most common and the most frequently occurring RV infection, respectively (Otto et al. 2012). Although structurally RVD is somewhat similar to other RVs, but a slight variation is found in gene-protein coding assignments. For example, in RVD, VP4 and VP3 proteins are encoded by segment 3 and 4, respectively, but for RVA
vice versa is true. The molecular studies on RVD are scarce, and only a single whole genome sequence is available for this species (Trojnjar et al. 2010). Hence, unlike RVA, no genotype classification system is available for RVD. Maximum no. of the sequence is available for the VP6 gene, based on which geographical segregation of RVD isolates is presumed (Kattoor et al. 2013). However, to confirm such studies, sequencing information on the other genes of RVD is required as well.

8.8.1.3 Avian Rotavirus F (RVF) and Rotavirus G (RVG)

Avian RVF was first described in turkey faeces and RVG in gut contents of chickens from Northern Ireland, based on the electrophoretic (PAGE-electrophoresis) migration pattern of their genome segments (Theil et al. 1986). Electrophoretic mobility patterns of 4:1:2:2:2 and 4:2:2:3 were described for RVF and RVG, respectively. Later, both of these serogroups were identified from turkeys (Kang et al. 1988). Although the association of these serogroups with clinical disease is still unclear, they have been described as one of the causative agents of RSS in broiler chicks (Otto et al. 2006). Epidemiological studies of RVF and RVG in chickens and turkeys have been carried out, where low incidence and frequency was noted, as compared to other avian RVs (RVA and RVD) (Otto et al. 2012). Currently, these groups may be termed as rare RVs in poultry; the reason behind this rationale might be the lack of more robust diagnostic tools. Not very long ago (in 2012), the complete genome sequences of RVF (03V0568-18,341bp) and RVG (03V0567-18,186bp) from diarrhoeic chickens were deciphered, having ORFs for viral proteins VP1-VP6 and NSP1-NSP5 within the 11 segmented genomes. This opened the opportunity to study RVF and RVG at the molecular level. Based on the phylogenetic analysis, RVF belonged with A/C/D clade, and RVG belonged to B/G/H clade (Ogden et al. 2012). These clades are defined based on all the structural proteins (VP1-VP6) and two nonstructural proteins (NSP2 and NSP5) (Kindler et al. 2013).

8.8.2 Pathogenesis

Viruses, bacteria and parasites are other common pathogens detected alongside avian RVs. Avian RVs have been known to be linked with intestinal illness in commercial poultry, but their particular role in the pathogenesis of diseases has not yet known completely (Falcone et al. 2015). RVs mainly infect mature villous epithelium of small intestine, resulting in impaired absorption. Apart from the intestine, avian RVs also multiply in caecum and colon (McNulty et al. 1983). Infection of avian RVs cannot be prevented even in the presence of maternal antibodies, although the latter may delay the establishment of infection in chickens (Yason and Schat 1986). In experimental infection, RVs were found to cause watery diarrhoea in turkey poult, whereas in chickens no clinical diarrhoea was observed. Like RV infection of gnotobiotic pigs, calves, etc., pathological studies on turkey
RVs (in SPF turkey poult) also confirmed the increase in cellular activity in the infected cells (lamina propria) with the predominance of mononuclear cells. In turkeys and chickens, the differences in clinical manifestation of RVs might be due to physiology, immune status, etc., but replication and antibody development strategies in both the species of poultry were described to be similar (McNulty et al. 1983).

8.8.3 Diagnosis

Avian RVs can remain asymptomatic or can cause diarrhoea, dehydration, anorexia, reduction in growth rate, etc. These clinical manifestations are not sufficient to differentiate RV infections from other enteric pathogens. For confirmatory diagnosis, virus detection or viral antigen/antibody detection is required. Apart from these techniques, PAGE (polyacrylamide gel electrophoresis) being rapid and easy was also used satisfactorily in the past, to detect avian RVs and also to classify them based on typical electrophoretic migration patterns. However, distinct patterns may arise because of events like recombination, mutations, etc. Therefore, PAGE cannot be used as a definitive tool for classification of different strains. Apart from EM, virus isolation and PAGE, serological assays including ELISA, latex agglutination test, etc. have been used for detection of avian RVs (Dhama et al. 2015). At present, the most sensitive diagnostic tool for detection of avian RVs is reverse transcriptase PCR (RT-PCR), but only a few protocols are available, mostly for RVA and some for RVD (Table 8.3) (Bezerra et al. 2012). A multiplex RT-PCR has been developed that can differentiate avian RVs from other viruses causing enteric infections (Jindal et al. 2012). From time to time, different detection systems with different sensitivity and specificity were used to know the status of avian RVs which lead to variable estimation of their prevalence, so better optimized molecular assays for all the group of avian RVs should be made available shortly.

8.9 Ovine Rotaviruses

Sheep is one of the essential resources in agriculture worldwide; however, reports about ovine RV strains still scarce. First evidence regarding RV infection in diarrhoeic lambs came from the United Kingdom and Japan (Theil et al. 1995). Since then, several other countries have attempted to characterize RV strains and ascertain prevalence in sheep. So far, RVA and RVB have been the only two groups of RVs that were detected in lambs. In the 1980s and 1990s, RVB was detected in some outbreaks of neonatal diarrhoea among lambs in the USA and the United Kingdom (Snodgrass et al. 1984; Theil et al. 1995). Morbidity in the above
| Name       | Gene targeted | Sequences (5’ to 3’) | Amplicon size (bp) | Assay          | Reference             |
|------------|---------------|----------------------|--------------------|----------------|-----------------------|
| **RVD**    |               |                      |                    |                |                       |
| RD6F       | VP6           | GGAGGGCGCTGTCTTCAATTTGGC TGGCCAATAGTGTGTGGCAGCT  | 742                | RT-PCR         | Bezerra et al. (2012) |
| RD6R       |               |                      |                    |                |                       |
| RD9F       | VP7           | ACCATATAGGAGTGACGCACCT AGGCCCCACTTCTCTCCAAT     | 879                | RT-PCR         | Bezerra et al. (2014) |
| RD9R       |               |                      |                    |                |                       |
| ARVD6-1F   | VP6           | GCGACAACCTGAG ACAACTG GGAAGCAGTGTGCATCAAC TTGCTATAGTATGGTCTCGTGG TGTATA | 186                | Real time RT-PCR | Otto et al. (2012)   |
| ARVD6-1R   |               |                      |                    |                |                       |
| ARVD6probe1|               |                      |                    |                |                       |
| ARVDVP6-D-F| VP6           | GCTATACATTTCGCTTCATTTG TGGCCAATAGTGTGTGGCAGCT  | 185                | RT-PCR         | Kattoor et al. (2013) |
| ARVDVP6-D-R|               |                      |                    |                |                       |
| **Avian RVA** |            |                      |                    |                |                       |
| RT-1       | VP6           | GGCTTTTAACAGAAGTCCTTC GGTTCAGATCCTCCCTCACT     | 1350               | RT-PCR         | Ito et al. (2001)    |
| RT-4       |               |                      |                    |                |                       |
| NSP4 F30   | NSP4          | GGGCGGTGCCGAAAGATGGAGAAC GGGGTTGGGTTACCAAGGG ATTAAG | 630                | Multiplex RT-PCR | Jindal et al. (2012) |
| NSP4 R660  |               |                      |                    |                |                       |
| ARVA6-1F   | VP6           | CACCAGACTTTATGCAGAGA CTCGAAATGGAGTCGACTGTTAGTT | 493                | RT-PCR         | Otto et al. (2012)   |
| ARVA6-1R   |               |                      |                    |                |                       |
| ARVA6probe3|               |                      |                    |                |                       |
| ARVA6-9F   | VP6           | GAGCAACATTTAGATTACTTCATTTGAAAGTTCCTARTGAGATTAGA AGGAGCTATCCATACGTGGGATTC | 114                | Real time RT-PCR  | Otto et al. (2012)   |
| ARVA6-9R   |               |                      |                    |                |                       |
| ARVA6probe3|               |                      |                    |                |                       |
outbreaks varied between 50% and 100%, and the mortality rate ranged from 10% to 50%. All the samples taken from the infected lambs were positive to RVB.

The following four RVA strains in sheep were characterized in the United Kingdom: G3P[1], G6P[11], G9P[8], G10P[14] (Fitzgerald et al. 1995). In China, exclusively one genotype was found in the examined RVA strains over the years, the G10P[15] (Shen et al. 1993; Chen et al. 2009; Zhang et al. 2011). Out of these strains, two were sequenced entirely (Lamb-NT, CC0812). In Spain, two strains were identified, G8P[14] and G8P[1] which is considered to be the causal agent of an ovine diarrhoeic syndrome outbreak, where the mortality rate was 17% (Ciarlet et al. 2008; Galindo-Cardiel et al. 2011). In India, one exhaustive study (500 samples) revealed numerous circulating RVA G and P genotypes (total 52 strains). Among the two observed G genotypes, G6 was predominant (48%) followed by G10 (36%). The only VP4 gene found was the genotype P[11], and few samples carried mixed genotype G6+G10 (Gazal et al. 2012). In Greece, out of three RVA positive samples, one was G10P[8], and the two others were untyped (Chatzopoulos et al. 2016). The extant characterized ovine RVs show a high genetic heterogeneity, as most strains have their different G and P genotype combinations.

Apart from the genotypes of ovine RVA and RVB strains have been analysed already, several other studies have been focused on attaining information about the prevalence of rotavirus infection in sheep. The RVA detection rates reportedly are highly variable in samples from diarrhoeic sheep. The first large dataset was obtained in North West Spain, where neonatal diarrhoea has been considered as the major health problem affecting lambs. However, this study detected a low prevalence of RVs, 2.1% in diarrhoeic lambs and 6.5% in the case of the outbreaks (Muñoz et al. 1996). Further comprehensive research showed a higher RVA prevalence (60%) in diarrhoeic lambs in Trinidad. A study on the role of RVs in diarrhoea and estimating the successfulness of the used diagnostic tests were conducted in Egypt, where the adjusted prevalence of RVs was 16.1% among the infected lambs (Khafagi et al. 2010). Currently, multiple extensive analyses have been made in India and depending on the diagnostic assay utilized, RVA prevalence varies from 0.3% to 13.2% (Gazal et al. 2012; Singh et al. 2017). In Greece, 2.5% RV prevalence was recorded in two different monitored flocks (Chatzopoulos et al. 2016). Kingdom of Saudi Arabia has few publications concerning the cause of diarrhoea in farm animals. So far, one overall study has revealed a relatively high prevalence of RVs (31.7%) (Shabana et al. 2017).

8.10 Caprine Rotaviruses

Similar to the ovine RVs, detailed information on the epidemiology of caprine RVs is unavailable. RVA and RVB infections were first described in diarrhoeic goats in the 1980s. One of the earliest reports aimed to make preceding characterization efforts of RV strains detected from South Africa. Around this time, another extensive report about RVA infection in livestock came from Trinidad; the results were two
positive RVA samples from four diarrhoeic goat kids (Kaminjolo and Adesiyun 1994). In Spain, several major studies were conducted, where seven goat kids were affected by severe diarrhoea in a dairy herd, and five of them proved to be infected with RVB (Muñoz et al. 1995). Another investigation identified RVA in three goat kids (8.1%), RVB in five goat kids (13.5%) and for the first time RVC in four non-diarrhoeic goat kids (Muñoz et al. 1996). A 2-year study conducted in France examined eight faecal specimens from goat kids, and seven of them were detected positive for RVB (Gueguen et al. 1996). Faecal specimens (8.68%) were found to be RV positive by electrophoresis in a survey handling with high sample numbers ($n = 484$) in Bangladesh, but no further examination was made for specifying them (Dey et al. 2007). In Egypt, overall, 13.2% of goat kids were positive for RV based on parallel diagnostic tests (Khafagi et al. 2010). In Sudan, a wide range of survey regarding rotavirus infection was taken including several livestock species. 21.7% of the sampled goat kids were positive for RVA (Ali et al. 2011). During a large outbreak of enteritis in Turkey, high morbidity (45%) and mortality (28.2%) rates were detected. Commercial ELISA identified RVA in four stools of goat kids (Alkan et al. 2012). Two recent extensive studies were executed in Asia; both had determined the prevalence of rotavirus infection among sheep and goats. The prevalence of caprine RVA was 8% and $\sim$27% in India and Medina, respectively (Singh et al. 2017; Shabana et al. 2017).

G6P[1] genotype combination was detected in two RVA strains in Italy, and G3P[3] was found in a Korean goat (Pratelli et al. 1999; Lee et al. 2003). During an enteritis outbreak in Turkey, one strain proved to carry genotype G8P[1] (Alkan et al. 2012). The first full genomic analysis of caprine RVs were made in Bangladesh, and it revealed genotype G6P[1] RVA strain (Ghosh et al. 2010). In Argentina, several samples were found to be positive for RVA (4/20) and one of them was genotyped as G8P[1] (Louge Uriarte et al. 2014). A study investigating the possible transmission of RVAs among human and domestic animals describes the G6P[1] genotype combination. The whole genome was sequenced for this strain as well (Bwogi et al. 2017). According to GenBank records additional unpublished genotyped RVA strains are available, such as G6P[14] from South Africa, G6P[1] from Turkey, G10P[15] from China and G8 from India. Further record data comes from strains found in Morocco, where two strains are genotyped as G10 or G6 in combination with P[14].

In the case of the RVB strains, one complete and one partial genomic sequences are available in the literature. One of them was obtained from pooled samples that were collected from two diarrhoeic goat kids in Minnesota; the other strain came from a single Californian goat. The whole genome sequence showed the following conserved genome constellation: G3-P[3]-I3-R3-C3-M3-A3-N3-T3-E3-H3 (Chen et al. 2018). The incomplete one presents the same constellation except for the VP1 gene and VP3 gene, which could not be retrieved as the viral read count was low (Shepherd et al. 2018).
8.11 New-World Camelids Rotavirus

The llama and the alpaca are the domesticated species of South American camelids. The others, the guanaco and the vicuna, are the wild-living species. The llamas and guanacos appear to be highly susceptible to RV infection based on the early reports. A serological survey in Argentina showed 87.7% prevalence of RV antibody in the collected llama sera from different provinces. Compared to the RVs, the other investigated viral antibody rates were low (Puntel et al. 1999). In Patagonia, guanacos affected by a severe outbreak of diarrhoea (100% morbidity and 83% mortality) were screened for RV antigen and antibody. Ninety-five percent of the collected serum samples were positive for RV antibodies. Also, two RV strains were isolated from the young guanacos with acute diarrhoea during the sampling time and were determined as RVA (Parreño et al. 2001). The prevalence of RV antibodies was 100% in another study involving 11 wild-born guanacos from Patagonia (Marcoppido et al. 2011). The first studies investigating the cause of diarrhoea in wild vicunas were released relatively late compared to the ones mentioned above. RV antibodies have been seen in free-living vicunas, llamas and domestic cattle. The entire serum sample found to be positive, but RV shedding was not observed. In Peru, alpacas suffering from a diarrhoea outbreak were tested for several infectious pathogens and 32% of the animals were shown to be infected with RV (Rojas et al. 2016a).

G8P[1] and G8P[14] genotype combinations were reported in young guanacos for the first time in Patagonia (Parreño et al. 2004). Seven more RVA strains found in guanacos were found to be genotype G8P[1] in Argentina (Marcoppido et al. 2011). Several RVA strains found in alpacas were described in Peru, such as G8P[1], G8P [14], G3P[14], G3P[11], G3Px-, G3P[40] and G35P[50] (Badaracco et al. 2014; Garmendia et al. 2015; Rojas et al. 2016b). RVA in wild vicuna was typed as G8P [14] (Badaracco et al. 2013). The complete genome of RVA strains found in most of the alpacas and the vicuna has been reported.

8.12 Old-World Camelids Rotavirus

Camels are essential livestock species either in economy or culture in the African, Arabian and Asian (semi-) deserts (Burger 2016). Despite the increased number of statements about the high incidence of diarrhoea that induced mortality among <6-month-old calves, relatively few studies were concerned with the determination of the causative agents.

Each of the published reports originates either from Africa (Sudan, Egypt) or Arabian Peninsula (Saudi Arabia, Kuwait). The first detailed evidence associated with camel diarrhoea was published in Sudan. During a 2-year (2000–2002) surveillance study which covered a wide range of Sudan, faecal and serum samples were collected from diarrhoeic, healthy and recovered calves. The average
prevalence of RVA in faecal samples analysed by several diagnostic tests was ~20% (Ali et al. 2005a, b). The detection rate of RVA was higher in serum samples (48.1%) (Ali et al. 2005a, b). In another study in Sudan, RVA was detected in 6% (3/50) of the samples collected from diarrhoeic camel calves (Ali et al. 2011). One report came from Egypt, where 8 out of 85 faecal samples were positive for RVA by ELISA (Eman et al. 2009). A study from Kuwait during 2008–2010 in five camel farms and a subsequent sample set collected in 2010 were monitored for RVs by antigen detection kits and RT-PCR based on the VP6 gene, respectively. The RV detection rates were 0.2% (1/408) and 7.3% (8/109) (Papp et al. 2012). Six different parts of Saudi Arabia were surveyed in order to ascertain the viral and bacterial agents causing diarrhoea in camel calves. Depending on the diagnostic test utilized, the prevalence of RVA varied from 13.3% to 18.7% (Al-Ruwaili et al. 2012). One other region of Saudi Arabia showed 6% RV prevalence among diarrhoeic calves (El Wathig and Faye 2016). In the Eastern part of Saudi Arabia, RVA was recorded in 10% and 12% of samples detected by IC and ELISA, respectively (El-Sabagh et al. 2017).

So far, characterization of RVA genotypes in camels has been minimal. Sequencing of the VP7 gene revealed genotype G10 in two isolates from Egypt and one strain from Kuwait (Eman et al. 2009; Papp et al. 2012). Partial VP4 sequence of the latter strain was later identified as P[15]. To date, the whole genome sequence of only one African camel RVA strain was described (G8P[11]) (Jere et al. 2014).

### 8.13 Rotaviruses in Wildlife Hosts

Species, especially domesticated animals, holding a sort of benefit for the nations have been the main focus of RV infection surveys. Although some reports about RV strains in wild hoofed mammals are available. Some of the accessible information arises from unique cases that have occurred in zoos, zoo nurseries or commercial farms of wild animals. Others reported by studies investigating reassortment events among RV strains of different host species. The first evidence in wild ungulates came from a zoo nursery in the USA, where infants (an impala, an addax and a Thomson’s gazelle) were infected by a bovine RV (Eugster et al. 1978). In another zoo in Toronto, an exhaustive study was conducted to test sera of several species for RV antibodies (Petric et al. 1981). A review about diseases of farmed wild animals mentioned RV infection either in red deer (Cervus elaphus) or wapiti (Cervus elaphus subssp.) (Haigh et al. 2002). The whole genome sequence of two RVA strains detected in Slovenian roe deer (Capreolus capreolus) were determined (G6-P[15]-I2-R2-C2-M2-A3-N2-T6-E2-H3; G8-P[14]-I2-R2-C2-M2-A3-N2-T6-E2-H3) (Jamnikar-Ciglenecki et al. 2016, 2017). In Korea, out of 60 samples collected from water deer (Hydropotes inermis) one was positive for RVs by RT-PCR (Kim et al. 2014). RV strain was reported in a giraffe suffering from acute diarrhoea and was genotyped as G10P[11] and was shown to be closely related to bovine RVA strains (Mulherin et al. 2008). Several years later the whole genome was sequenced.
of this giraffe RVA strain (G10-P[11]-I2-R2-C2-M2-A3- N2-T6-E2-H3) (O’Shea et al. 2014). The complete genome of RV strain found in a South African sable antelope was also sequenced (Matthijnssens et al. 2009). In India, several studies have investigated diarrhoeic buffalo calves. In Western India, 12.5% of the stool samples were positive for RV, and all of them characterized as RVA (Niture et al. 2011). A surveillance study in Mumbai demonstrated the prevalence of RVA similar to the abovementioned (11.8%) (Mondal et al. 2013). In studies conducted in North India, RVA was detected in 4.6% or 10.7% of the faecal samples (Manuja et al. 2008). Some of the observed RVA strains in buffaloes were further analysed and revealed the following genotype combinations: G10P[11], G6P[11], G10P[3].

8.14 Conclusion and Future Perspectives

The high diversity and fast evolution rate of RVs indicate a need for continuous research on molecular characterization, geographical distribution and temporal fluctuations of endemic and emerging RVs. There have been few reports of some unusual G and P RVA genotypes with new RV groups being discovered in different geographic locations and the increasing evidence of high RV prevalence points towards the need to update the molecular diagnostic and characterization toolkits to include the novel RV variants which will ensure accurate epidemiological monitoring (Prasad et al. 2005). Discovery of diverse RVs in various wildlife species indicates that they can serve as natural reservoirs further contributing to the genetic diversity of RVs. While zoonotic and inter-species transmission potential has been demonstrated for bovine and porcine RVs, it was not evaluated for other wildlife and livestock species. A better understanding of RV molecular pathogenesis and immunity is needed to optimize the existing vaccines and improve control of RV infections and spread. Recent research on human and porcine RVAs raised the awareness that attenuated replicating RVA vaccines may be contributing directly to the genetic diversity of RVAs (via reassortment between vaccine and wild type strains) and the emergence of novel genetic variants/RV genogroups that can evade herd immunity against the vaccine strains. Thus, alternative approaches including wide-scale use of probiotics or antivirals, to lessen the RV shedding and decrease the environmental contamination, and to ease porcine RV-mediated intestinal damage are needed. Certain genogroups/genotypes have increased ability to re-assort and cross the interspecies barrier more frequently than other therefore additional studies to decipher their role in infection is needed. In addition to the knowledge of interactions between different porcine RV genotypes with the histo-blood group, antigens are also warranted.
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