Health repercussions of Avian Rotaviruses on Poultry and Fancy Pigeons

*V. Kunić, Ž. Gottstein, M. Prišlin, V. Savić and D. Brnić**

Abstract

Multicausal enteric diseases pose significant challenges to the global poultry industry, leading to substantial economic losses. This review focuses on the role of Avian Rotaviruses (AvRVs) in poultry enteritis and Runting Stunting Syndrome and highlights the importance of interspecies transmission. Avian rotaviruses, particularly species *Rotavirus A* and *Rotavirus D*, have been implicated in poultry enteritis, contributing to the complexity of clinical signs associated with coinfections involving various pathogens. The rotavirus virion, with its characteristic wheel-shaped appearance, targets mature enterocytes in the small intestine, leading to malabsorption, shortening of intestinal villi, and watery diarrhoea. Avian RVs exhibit a complex epidemiology with horizontal transmission through the faecal-oral route or via direct contact. High flock density and prolonged environmental survival of AvRVs contribute to their persistence in poultry environments. Likewise, AvRV outbreaks in pigeon pageants have been associated with severe clinical manifestations, including hepatic necrosis and digestive system abnormalities. The prevalence of AvRV in pigeons during such events can be substantial, reaching up to 90%. Notably, interspecies transmission between avian and mammalian hosts has been observed, although zoonotic transmission of AvRVs has not been reported. Laboratory diagnostic methods play pivotal roles in identifying AvRV infections, considering the absence of pathognomonic clinical signs. Vaccine development is facing challenges due to high antigenic variation, but promising alternatives, such as oral administration of egg-derived IgY antibodies, show potential for prophylaxis and therapy. Biosecurity measures and treatment options, including oral electrolyte solutions and antibiotics for secondary bacterial infections, are crucial in controlling AvRV mortality. Despite the challenges, advancements in molecular diagnostics and innovative prophylaxis strategies offer promising avenues for mitigating the impacts of AvRV on poultry health.

Key words: *Rotavirus A; Rotavirus D; poultry; fancy pigeon; interspecies transmission; Runting Stunting Syndrome*

Valentina KUNIĆ, DVM, Assistant, Croatian Veterinary Institute, Zagreb, Croatia; Željko GOTTSTEIN, DVM, PhD, Associate Professor, Faculty of Veterinary Medicine, University of Zagreb, Croatia; Marina PRIŠLIN, DVM, Assistant, Croatian Veterinary Institute, Zagreb, Croatia; Vladimir SAVIĆ, DVM, PhD, Senior Scientist, Assistant Professor, Poultry Centre, Croatian Veterinary Institute, Zagreb, Croatia; Dragan BRNIĆ* (Corresponding author, e-mail: brnic@veinst.hr), DVM, PhD, Senior Research Associate, Croatian Veterinary Institute, Zagreb, Croatia

Introduction

Multicausal enteric diseases are among the most prominent health issues affecting the poultry industry worldwide, presenting a production loss with significant economic impact (Otto et al., 2012). Especially in turkeys and chickens, several pathogens have been related to gastrointestinal (GI) infections resulting in malabsorption syndrome, also referred to as Runting Stunting Syndrome (RSS) (Mettifogo et al., 2014). For instance, adenoviruses, astroviruses, turkey coronaviruses, enterovirus-like viruses, reoviruses, rotaviruses (RVs), and turkey toroviruses have been associated (Reynolds et al., 1987; Fitzgerald, 2008; Jones, 2008; Reynolds and Schultz-Cherry, 2008; Saif, 2008). In addition to avian species, RVs are also a leading cause of enteritis in mammals, imposing economic losses on the global livestock industry (Estes and Greenberg, 2013). Most importantly, *Rotavirus A* (RVA) induced acute gastroenteritis (AGE) causes approximately 128,500 deaths in children under five years of age every year (Troeger et al., 2018). Following the discovery of RVs in mammalian hosts (Bishop et al., 1973), RVs were discovered in avian hosts, examining the intestinal contents of turkey poults using electron microscopy (EM) and finding particles morphologically identical to rotavirus (Bergeland et al., 1977). Since then, RV infections in poultry flocks have been detected numerous times (Otto et al., 2012). Besides RVA, other rotaviruses in avian hosts (AvRVs) include *Rotavirus D* (RVD), *Rotavirus F* (RVF), and *Rotavirus* G (RVG), which may also contribute to RSS. However, their significance is inconclusive (Gallego et al., 2022). In non-experimental conditions, AvRVs are often detected as one of the pathogens in coinfection, usually with astroviruses, enteroviruses, reoviruses, paramyxoviruses, adenoviruses, *Salmonella* spp., *Escherichia coli*, *Cryptosporidium* and *Eimeria* spp. Coinfections commonly worsen the severity of clinical signs and disease outcomes. Consequently, for birds that have overcome viral infection or coinfection, secondary bacterial infections, mostly *E. coli* and *Salmonella* spp., still threaten the depleted flock. The multifactorial nature of RSS makes it highly unlikely that the exact cause can be determined from a field situation alone (Dhama et al., 2015). Therefore, this review focuses on the role of RVs in RSS and their impact on domestic poultry.

Rotavirus structure and classification

The rotavirus virion is approximately 75 nm in diameter and is known for its characteristic wheel-shaped appearance under the EM (Estes and Greenberg, 2013). The RV viral genome consists of 11 segments of double-stranded RNA, encoding for six viral structural proteins (VP1–VP4, VP6 and VP7) and six non-structural proteins (NSP1–NSP6). Interestingly, some chicken RVAs lack the Open Reading Frame (ORF) for NSP6 expression, in contrast to mammalian RVAs, supporting the notion that NSP6 may be non-essential for the AvRV (Schumann et al., 2009). Gene segments VP4 and VP7 code for outer capsid protease sensitive (P) and glycosylated (G) viral proteins, with P and G genotypes providing the basis for dual RV classification (Estes and Kapikian, 2007). However, a newer classification system is based on all 11 RV genome segments, comprehensively characterizing RV strains while considering possible reassortment events (Matthijnssens et al., 2008). The genus *Rotavirus*, within the *Reoviridae* family, includes

nine species: *Rotavirus A–J* (ICTV, 2023). Birds can be infected by RV species RVA, RVD, RVF, and RVG (Todd and McNulty, 1986). So far, *Rotavirus B* (RVB) and *Rotavirus C* (RVC) have been found only in mammals, while RVD, RVF, and RVG have been detected exclusively in birds (McNulty, 2003; Pinheiro et al., 2023). The most prominent species of AvRVs in chickens and turkeys with diarrhoea, growth retardation, and RSS are RVA and RVD, with 16.1 and 39.2% prevalence, respectively (Otto et al., 2012). According to an NCBI Virus Variation Resource and Rotavirus Classification Working Group (RCWG), eight G (G6, G7, G17, G18, G19, G22, G23, G40) and ten P (P[1], P[17], P[23], P[30], P[31], P[35], P[37], P[38], P[39], P[56]) RVA genotypes have been discovered in avian hosts to date (Hatcher et al., 2017; RCWG, 2023). Conversely, the scarcity of RVD gene sequences restricts its classification into different genotypes (Deol et al., 2017).

Epidemiology

Most natural AvRV enteric infections have been described in turkeys, chickens, pheasants, partridges, and ducks (Dhama et al., 2015). Turkey poults are generally more susceptible to AvRV infection than chickens (Yason and Schat, 1987), followed by the observation that RVD was the most commonly found rotavirus in turkeys (McNulty and Reynolds, 2008; Dhama et al., 2015). Furthermore, the occurrence of RVD in apparently healthy asymptomatic chickens was reported (Bezerra et al., 2012). A higher occurrence of AvRVs has been reported in flocks with high bird density, a known stressor in poultry that magnifies the risk of AvRV dissemination (Silva et al., 2013; Pauly et al., 2017). Avian excrement is most often the source of infection since horizontal transmission occurs by the faecal-oral route or via direct contact. After efficient infection and replication, birds excrete progeny virions via faeces within 2 to 5 days (McNulty, 2003). Thus far, there are no reports of vertical transmission of RVs in poultry, and evidence of AvRV carrier birds is lacking to date (Dhama et al., 2015). Concerning the pigeon population, reassortment and intercontinental spread reportedly led to the emergence of novel RVA variants, which may threaten animal welfare and the health of domestic pigeon populations worldwide (Rubbenstroth et al., 2018). Natural AvRV infections are most common under the age of six weeks in turkeys, chickens, pheasants, partridges, and ducks (Dhama et al., 2015). Birds younger than 14 days are reported to be the most susceptible to high mortalities, especially broiler chickens (Yurika Tamehiro et al., 2003). Moreover, Gallego et al. reported a detection rate of RVD and RVF as statistically higher in the seven- to nine-day old age group, whilst RVA was detected only in chicks between 13 to 14 days old (Gallego et al., 2022). An outbreak of diarrhoea associated with RV infection in commercial laying hens between 32 and 92 weeks of age was detected, thus confirming that all age groups can be affected (McNulty, 2003) despite higher susceptibility in younger birds. Regarding seasonality, AvRV infection in broiler chickens most often appears in winter (Dhama et al., 2015), though in Southeast Asia, it has been recorded mainly in the summer (Karim et al., 2007). The presence of AvRVs in faecal material and their extreme resistance have paved the way for the persistent presence of this disease in poultry environments where they remain infectious for prolonged periods. They can survive in poultry manure for nearly 60 days (Guy, 1998) and up to six months

in the environment (Dhama et al., 2015). They are also relatively heat-stable and resistant to ether, chloroform, and sodium deoxycholate, while glutaraldehyde has a greater inactivating capacity than sodium hypochlorite and iodine-based disinfectants (McNulty, 2003). However, AvRVs have proved sensitive to phenol and formaldehyde (Dhama et al., 2015). After establishing a few whole-genome constellations of RVs in birds, conclusions about interspecies transmission could be drawn. The first acquired whole genome sequence of AvRVs was the RVA PO-13 strain derived from a pigeon, characterised as genotype G7P[17] (Ito et al., 2001), followed by the whole-genome of the chicken-derived RVA Ch-2G3 strain with G19P[30] genotype (Trojnar et al., 2009). Also, complete genomes of RVA were sequenced from pheasant, turkey (Trojnar et al., 2013), common gull (Fujii et al., 2022a), and velvet scoter (Fujii et al., 2022b), revealing entirely different genotype constellations than those found in mammals. Some examples of RVA genotypes similar to mammalian RVAs found in birds are bovine G8 and porcine G5 and G11 genotypes detected in broilers and layers (Bessera et al., 2014). A typical bovine rotavirus G6P[1] genotype (Asano et al., 2011) has also been found in turkeys, and bovine genotypes G6P[1] and G10P[1] were found in faecal samples of ostriches (Silva et al., 2012). In experimental conditions, it has been confirmed that it is possible to infect a mammal using AvRVs, as Mori et al. (2001) demonstrated a successful clinically visible infection in mice infected with the pigeon RVA PO-13 isolate. Moreover, an RVA with high sequence similarity to AvRVs was isolated from a calf with diarrhoea, indicating that rotavirus transmission from avian to mammalian hosts can occur in field conditions (Brüssow et al., 1992; Rohwedder et al., 1995). Busi et al. (2017) reported another example of heterologous infection: an avian RVA strain that displayed high sequence similarity to the avian PO-13 strain isolated from the brain of a red fox with encephalitis. Likewise, mammalian-like RVs have been detected in chickens (Wani et al., 2003). Transmission is also possible between different avian species. For instance, the chicken RVA Ch2 isolate is most closely related to those of turkeys, which may indicate an interspecies transmission of the virus from turkeys to chickens (Schumann et al., 2009). Nonetheless, zoonotic transmission of AvRVs to people has not yet been detected (MSD Manual, 2022).

Pathogenesis

The RVs present in the environment enter the body through ingestion. Mammalian and AvRVs target mature enterocytes and enteroendocrine cells located at both the tip and middle regions of the intestinal villi epithelium in the small intestine (McNulty, 2003). In birds, besides the small intestine, viral replication has also been observed in the colon and caecum (McNulty, 2003). Experiments on the MA104 cell line demonstrated that AvRVs use sialic acid-containing glycans for cell attachment (Sugiyama et al., 2004). The RV particle undergoes cleavage, splitting its outer capsid VP4 into VP5 and VP8 proteins upon exposure to trypsin. VP8 interacts with cell membrane receptors, facilitating viral entry via endocytosis. During replication, the RV particle sheds its outer layer, undergoes transcription and translation in the cytoplasm, forms viroplasms from lipid droplets, and assembles progeny viral particles. Finally, new RV particles mature in the rough endoplasmic reticulum before being released via cell lysis or vesicular transport

into the intestinal lumen (Crawford et al., 2017). Through cell damage and death of the mature enterocytes, immature enterocytes migrate more rapidly from the intestinal crypts to the surface of the villi, while still not being able to absorb, causing the shortening of the intestinal villi (Crawford et al., 2017). However, experimental infections in turkeys and chickens demonstrated less prominent shortening of the villi in comparison with RV-infected calves and piglets (Yason and Schat, 1987). Consequently, chloride, sodium, potassium, and water malabsorption occurs, leading to rapid osmotic watery diarrhoea with a loss of electrolytes and dehydration (Crawford et al., 2017). Another diarrhoea-inducing mechanism of RVs is through the NSP4 enterotoxin protein, which has similar activity in mammals and birds, despite significant amino acid differences observed between the NSP4 of RVs and AvRVs (Dhama et al. 2015). Finally, with nutrient malabsorption reducing the food conversion ratio and dehydration possibly leading to death, the poultry industry faces severe economic impacts (McNulty, 2003). Apart from targeting the GI tract, RVs also affect other tissues (Dian et al., 2021). The presence of avian RVA in the tissue outside the GI tract was discovered in the pancreas and spleen of broilers; however, the ability of RVs to cause viremia was hypothesised as a reason (Nunez et al., 2016). There is no supporting evidence for similar processes due to RVD (Deol et al., 2017).

Clinical signs

Variations in virulence and severity of clinical signs associated with different RV strains have been reported (Dhama et al., 2015). Enteric diseases related to RVs in commercial poultry can range from clinically unnoticeable to severe, substantially impacting the industry due to slowed growth and increased death rates in flocks (Otto et al., 2006; Falcone et al., 2015). The impact of RV-induced disease is often increased by simultaneous or subsequent mixed agent infections due to a weakened immune system in infected birds. Improper handling procedures can exacerbate the situation, potentially leading to higher disease spread and worsening outcomes (Dhama et al., 2015). Falcone et al. sampled poultry flocks experiencing clinical manifestations and lesions associated with enteric diseases. Clinical signs mainly included diarrhoea, dehydration, reduced food intake with anorexia, cachexia, weight loss, nervous signs, and increased mortality. They reported multiple AvRVs of different species present in a high number of samples (95%) from diseased flocks (Falcone et al., 2015). Previous research supports these findings, stating that other than diarrhoea and enteritis, RV diseases may also be associated with anorexia and malabsorption in field conditions (McNulty, 2003; Yurika Tamehiro et al., 2003). Other clinical signs include unrest, litter ingestion, and wet litter (Barnes, 1997). Furthermore, Otto et al. reported that RVA and RVD caused diarrhoea, growth retardation, and/or RSS in chickens and turkeys (Otto et al., 2012). Noticeable variations in the severity of RV infections might be attributed to the varying virulence of RV strains, the presence of other infectious agents, environmental stressors, or management-related issues (McNulty, 2003). Except in the commercial poultry industry, AvRVs also present significant issues in all classes of domestic pigeons, with hepatic necrosis as an outstanding clinical manifestation. The first report of an AvRV-associated hepatic necrosis in any avian species was in fancy pigeons in Australia, caused by previously undescribed RVA G18P[17] (McCowan et

al., 2018). This genotype was also detected in fatally diseased pigeons in Europe clinically presenting with anorexia, vomiting, pasty diarrhoea, emaciation, and crops filled with water and seeds (crop stasis). At the same time, respiratory or neurologic signs or diphtheroid mucosal lesions have rarely been reported (Rubbenstroth et al., 2018). The reported RVA prevalence of 50%, 80%, or even 90% at pigeon pageants points to such gatherings as a risk factor for the disease spread (Harzer et al., 2020). The disease outbreaks typically had a high flock morbidity (even 100%) and varying mortality (7-45%), presenting with clinical signs for 12-48 hours: severe depression, weakness, extreme thirst, regurgitation, anorexia, and diarrhoea (Schmidt et al., 2021).

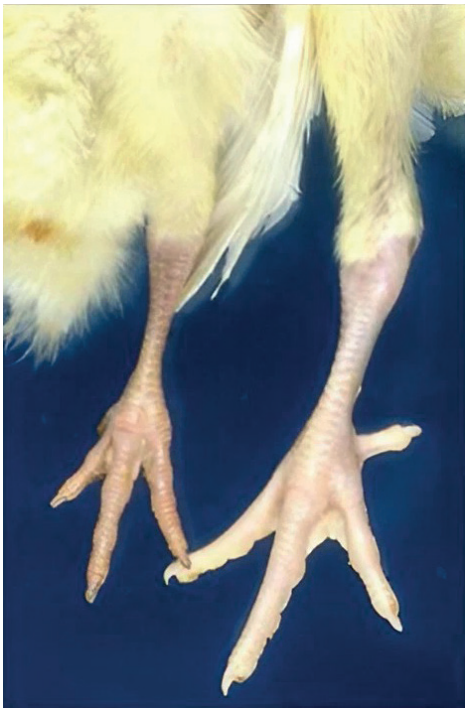

Figure 1. Dehydrated poult (left) with a darker shank characteristic for dehydration and a normal poult (right) (AAAP, 2013)

Gross and pathohistology findings

The most prominent gross findings include intestinal lesions in affected birds, meaning frothy contents, paleness, and thinning of the intestinal walls, resulting in pale and slender intestines filled with undigested food (Day et al., 2007). Microscopic examination reveal blunted intestinal villi responsible for poor nutrient absorption. The extent to which AvRVs contribute to RSS-affected birds on their own has not been entirely resolved. Nonetheless, RVD is considered to play a significant role in flocks with severe villous atrophy (Otto et al., 2006). In pigeons, the most consistent findings on postmortem examination were variably congested, mottled, and enlarged livers and spleens. Microscopically, mild to severe hepatic necrosis was observed with variable bile duct hyperplasia, sinusoidal congestion, hemosiderosis, and portal lymphoplasmacytic inflammation (Blakey et al., 2019). The absence of blood in diarrhoea or intestinal content can also be used as an indicator; however, none of these signs is pathognomonic for AvRV infection and can only raise suspicion.

Diagnostics

AvRV infection can be differentiated from other conditions causing diarrhoea only in laboratory conditions, since clinical signs and pathology findings are not pathognomonic. When evaluating molecular detection tools for RVA, reverse transcription-polymerase chain reaction (RT-PCR) is considered the best option since it is rapid and very sensitive (Otto et al., 2006; Schumann et al., 2009; Trojnar et al., 2009). Nevertheless, protocols for AvRV detection differ from those of mammalian RVs, and different RT-PCR and real-time

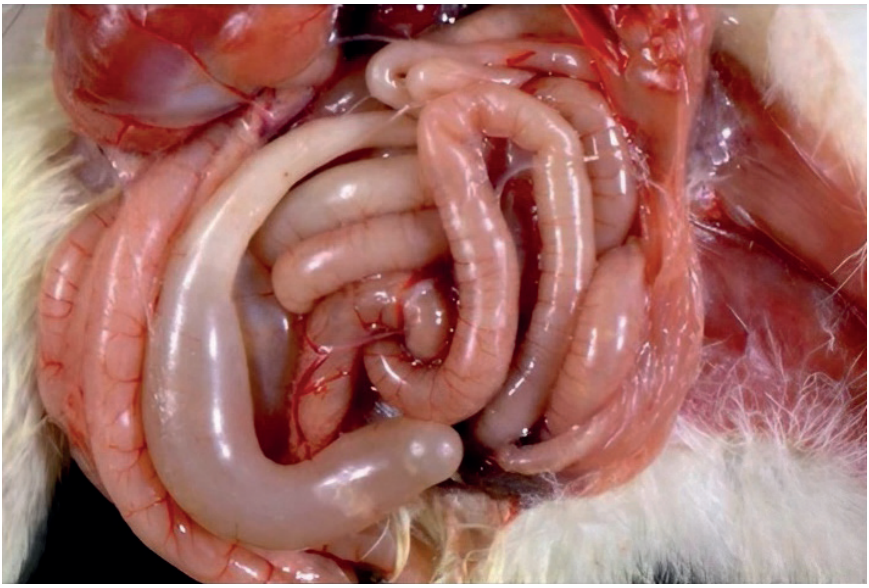

Figure 2. Thin-walled and dilated small intestines filled with fluid and gas (AAAP, 2013).

RT-PCR protocols have been developed for detecting NSP3, NSP4, and VP6 gene segments (Dhama et al., 2015). However, successful surveillance of AvRVs requires that primer pairs are updated regularly to account for detection failures stemming from genetic drift causing nucleotide changes at the primer binding sites (Oni et al., 2018). Moreover, next-generation sequencing (NGS) as a new research tool has up-levelled the investigation of viruses since it can provide whole genome sequencing and a metagenomic approach to reveal complex microbiome communities (Dhama et al., 2015; Qiu et al., 2019). As Performance Efficiency Index scores in flocks exhibit a substantial reliance on overall health, the significance of comprehending the microbiome becomes increasingly pronounced (Gallego et al., 2022). NGS also surpasses the primer binding issue, enabling the most comprehensive diagnostic process. Polyacrylamide gel electrophoresis and electron microscopy (EM), although capable of identifying RVs, are rarely employed for routine diagnostics (McNulty, 2003). To continue, screening tools include enzyme-linked immunosorbent assays (ELISA) for antigen detection, and immunochromatographic assays for qualitative detection of RVA in faeces, such as the FASTest® ROTA Strip (Megacor Diagnostik, Austria). These can be used as screening tools for proclaiming and monitoring the status of specific-pathogen-free flocks (McNulty, 2003). Commercial ELISAs are widely employed for detecting RVA in mammalian and avian faeces. ELISAs for RVD, RVF, and RVG detection are yet to be developed (Dhama et al., 2015). Moreover, the diagnosis of RV infection through virus isolation in cell cultures is only feasible for RVA. This is due to the fact that the RVD, RVF, or RVG species have not yet been successfully isolated and adapted to grow in traditional RV cell culture systems (Otto et al., 2015). Due to the prevalent occurrence of AvRVs other than RVA, especially RVD, relying solely

on serological methods or cell culture isolation developed for RVA may result in false negatives, and as such, these diagnostic techniques are not recommended (McNulty, 2003; Dhama et al., 2015).

Immune response and passive immunisation therapy

As for passive immunity, maternally derived antibodies to rotavirus are passively transferred to the avian embryo through the egg yolk. They progressively decline in titre in the serum and are undetectable at 3-4 weeks of age (Yason and Schat, 1986). Interestingly, maternal antibodies in the serum had no apparent effect on the susceptibility of chickens and turkeys to experimental RVA infection (Yason and Schat, 1986). In chickens experimentally infected with RVA, rotavirus-specific IgM, IgG, and IgA were detected in serum, whereas the intestinal antibody response consisted almost entirely of IgA (Myers et al., 1989). The research from Myers and Schat (1990) observed that intestinal IgA alone was a mediator for recovery. These findings collectively suggest the crucial role of mucosal antibodies in AvRV infection. On the other hand, natural killer cell-like activity was demonstrated in chickens' intestinal leukocytes against RV-infected target cells (Myers and Schat, 1990). Historically, therapeutic IgY effects in poultry were investigated in experimentally infected chickens, where oral administration of immunoglobulins was shown to prevent the development of RV-induced gastroenteritis (Dhama et al., 2015), along with alleviating clinical signs in poultry caused by a multitude of other pathogens (Gadde et al., 2015). Over the years, pathogen-specific IgY has garnered attention for its potential in passive immunisation against infectious diseases in humans and animals. This is attributed to several advantages, including benefits to animal welfare, safety, and the absence of drug resistance issues associated with IgY derived from the egg yolks of immunised chickens (Dai et al., 2013). The same authors also reported that the dual P-VP8*-induced IgY could block norovirus and RVs binding to HBGA receptors and neutralise RV replication in cell cultures. These findings suggest a substantial potential for passive IgY immunisation, not only in enhancing poultry health but also in benefiting other species. This holds importance within the One Health initiative.

Vaccination

To date, the development of vaccines proved to be difficult largely due to the high antigenic variation of AvRVs and the fact that AvRVs are difficult to grow in cell culture (Dhama et al., 2015; Otto et al., 2015; Patzina-Mehling et al., 2020). Nevertheless, cell-culture-adapted AvRVs are eligible for future investigation and the development of diagnostic tools and vaccines (Patzina-Mehling et al., 2020). When vaccination with inactivated RVA was tested, it led to the conclusion that maternally derived antibodies in the progeny of vaccinated turkeys and pheasants are unlikely to provide significant protection against a field challenge with RVs, as detected antibody titres in sera were not high enough to guarantee protection (McNulty, 2003). Therefore, egg-derived IgY antibodies from immunised hens administrated orally may be a less expensive and more practical alternative (Sarker et al., 2001). On the other hand, in the pigeon population, two types of vaccines are currently used in Germany: autogenous RVA vaccines, and the commercial inactivated RVA vaccine Colvac RP (PHARMAGAL-BIO, Nitra, Slovakia) licensed in 2019. The commercial vaccine

contains RVA genotype G18P[17] and pigeon paramyxovirus 1. The manufacturer states that the vaccine can reduce mortality and the frequency and severity of clinical signs caused by RVA infection, and sequencing the vaccine strain revealed high similarity to circulating pigeon RVA strains (Harzer et al., 2021). Protective vaccines for domestic birds are not yet commercially available.

Biosecurity measures and disease treatment

As mentioned earlier, flocks with higher bird density are at an increased risk for AvRV infection, so strict biosecurity measures must be followed to prevent the disease from spreading from one flock to another (Silva et al., 2013; Pauly et al., 2017). Regularly removing litter and meticulously cleaning poultry areas before introducing a new group of birds can mitigate the risk of disease. In cases where serious issues occur, it is advised to eliminate the litter, thoroughly sanitise the premises and equipment, and perform formaldehyde fumigation before introducing a new flock (McNulty, 2003). Participation in poultry/pigeon pageants and all similar mass accumulations of birds from different backgrounds in the same places are associated with a significantly increased risk of infection with different pathogens, including AvRVs (Harzer et al., 2021). Therefore, enforcement of biosecurity measures is crucial for disease control at such events. Treatment options are limited; however, during the acute phase, it is beneficial to include an oral electrolyte solution to avoid dehydration, increase dwelling temperature, improve ventilation, and add fresh litter. Antibiotics may be used to treat secondary bacterial infections (MSD Manual, 2022).

Conclusion

Avian rotaviruses pose a considerable health threat in the poultry industry, causing enteric diseases and substantial production losses and significant economic impact. Most documented natural AvRV infections occur in avian species, including turkeys, chickens, pheasants, partridges, and ducks. Notably, RVA and RVD species, particularly associated with gastrointestinal tract infections in chickens and turkeys, contribute to conditions such as RSS, with RVD exhibiting a higher prevalence. While RVA affects both mammal and avian species, the species RVD, RVF, and RVG have been exclusively identified in birds. Concurrently, coinfections with other viral agents like adenoviruses, astroviruses, and enteroviruses are common, amplifying the severity of clinical signs and disease outcomes. Consequently, clinical signs, including diarrhoea, dehydration, anorexia, cachexia, and increased mortality are observed, though none are considered pathognomonic. Implementing strict biosecurity measures and adopting proper sanitation practices are crucial for preventing disease spread, particularly in densely populated poultry dwellings and pigeon pageants. Currently, RT-PCR stands as the most optimal diagnostic option. The development of vaccines for AvRVs is challenging due to high antigenic variation and difficulties in cultivating RVs in cell culture. However, passive immunisation through orally administered egg-derived antibodies has demonstrated significant protective potential in experimental conditions, not only in regards to poultry health, but also in animal husbandry and human medicine. Therefore, antigen-specific IgY could be considered a comprehensive One Health prophylactic and therapeutic approach for RV infections across diverse species, warranting further exploration.

References

1. AMERICAN ASSOCIATION OF AVIAN PATHOLOGIST (AAAP) (2013): Poult Malabsorption / Runting-Stunting Syndrome, In: Avian Disease Manual. Seventh Edition, Ed: M. Boulianne; Available online: https://aaap.memberclicks.net/avian-disease-manual-old-edition, accessed on 19th January, 2024.
2. ASANO, K. M., F. GREGORI, S. P. SOUZA, D. ROTAVA, R. N. OLIVEIRA, L.Y. VILLARREAL, L. J. RICHTZENHAIN and P. E. BRANDÃO (2011): Bovine rotavirus in turkeys with enteritis. Avian Dis. 55, 697-701. 10.1637/9765-041911-ResNote.1
3. BARNES, H. J. (1997): Virology of enteric infections. Diseases of poultry. 10th Edition. Ames: Iowa State University Press (685-686).
4. BERGELAND, M. E., J. P. MCADARAGH and I. STOTZ (1977): Rotaviral enteritis in turkey poults. In: Proceedings of the 26th Western Poultry Diseases Conference. Davis (CA): University of California, pp. 129-130.
5. BESERRA, L. A. R., B. R. P. BARBOSA, N. T. C. G. BERNARDES, P. E. BRANDÃO and F. GREGORI (2014): Occurrence and characterization of rotavirus A in broilers, layers, and broiler breeders from Brazilian poultry farms. Avian Dis. 58, 153-157. 10.1637/10626-080513-ResNote.1
6. BEZERRA, D. A., R. R. SILVA, J. H. L. KAIANO, R. V. SILVESTRE, D. DE SOUZA OLIVEIRA, A. C. LINHARES, Y. B. GABBAY and J. D. MASCARENHAS (2012): Detection of avian group D rotavirus using the polymerase chain reaction for the VP6 gene. J. Virol. Methods 185, 189-192. 10.1016/j.jviromet.2012.07.017
7. BISHOP, R. F., G. P. DAVIDSON, I. H. HOLMES and B. J. RUCK (1973): Virus particles in epithelial cells of duodenal mucosa from children with acute non-bacterial gastroenteritis. Lancet 302, 1281-1283. 10.1016/S0140-6736(73)92867-5
8. BLAKEY, J., B. CROSSLEY, J. K. ROSENBERGER, et al. (2019): Rotavirus A Associated with Clinical Disease and Hepatic Necrosis in California Pigeons (Columba livia domestica). Avian Dis. 63, 651-658. 10.1637/aviandiseases-D-19-00114
9. BRÜSSOW, H., O. NAKAGOMI, G. GERNA and W. EICHHORN (1992): Isolation of an avian-like group A rotavirus from a calf with diarrhea. J. Clin. Microbiol. 30, 67-73. 10.1128/jcm.30.1.67-73.1992
10. BUSI, C., V. MARTELLA, A. PAPETTI, et al. (2017): Group A rotavirus associated with encephalitis in red fox. Emerg. Infect. Dis. 23, 1535-1538. 10.3201/eid2309.170158
11. CRAWFORD, S. E., S. RAMANI, J. E. TATE, et al. (2017): Rotavirus infection. Nat. Rev. Dis. Primer 3, 17083. 10.1038/nrdp.2017.83
12. CRAWFORD, S. E., D. G. PATEL, E. CHENG, Z. BERKOVA, J. M. HYSER, M. CIARLET, M. J. FINEGOLD, M. E. CONNER and M. K. ESTES (2006): Rotavirus Viremia and Extraintestinal Viral Infection in the Neonatal Rat Model. J. Virol. 80, 4820-4832. 10.1128/JVI.80.10.4820-4832.2006
13. DAI, Y. C., X. F. ZHANG, M. TAN, P. HUANG, W. LEI, H. FANG, W. ZHONG and X. JIANG (2013): A dual chicken IgY against rotavirus and norovirus. Antiviral. Res. 97, 293-300. 10.1016/j.antiviral.2012.12.011
14. DAY, J. M., E. SPACKMAN and M. PANTIN-JACKWOOD (2007): A multiplex RT-PCR test for the differential identification of turkey astrovirus type 1, turkey astrovirus type 2, chicken astrovirus, avian nephritis virus, and avian rotavirus. Avian Dis. 51, 681-684. 10.1637/1933-5334(2007)2[e13:AMRTFT]2.0.CO;2
15. DEOL, P., J. J. KATTOOR, S. SIRCAR, S. GHOSH, K. BÁNYAI, K. DHAMA and Y. S. MALIK (2017): Avian group D rotaviruses: Structure, epidemiology, diagnosis, and perspectives on future research challenges. Pathogens 6, 53. 10.3390/pathogens6040053
16. DHAMA, K., M. SAMINATHAN, K. KARTHIK, R. TIWARI, M. Z. SHABBIR, N. KUMAR, Y. S. MALIK and R. K. SINGH (2015): Avian rotavirus enteritis - an updated review. Vet. Q. 35, 142-158. 10.1080/01652176.2015.1046014
17. DIAN, Z., Y. SUN, G. ZHANG, Y. XU, X. FAN, X. YANG, Q. PAN, M. PEPPELENBOSCH and Z. MIAO (2021): Rotavirus-related systemic diseases: clinical manifestation, evidence and pathogenesis. Crit. Rev. Microbiol. 47, 580-595. 10.1080/1040841X.2021.1907738
18. ESTES, M. K. and H. B. GREENBERG (2013): Rotaviruses. In: Fields Virology. 6th edition. Eds. Knipe, D. M. and P. M. Howley (Philadelphia, PA: Lippincott Williams and Wilkins) (1347-1401).
19. ESTES, M. K. and A. Z. KAPIKIAN (2007): Rotaviruses. In: Fields Virology. 5th edition. Eds. Knipe, D. M., Howley, P. M., Griffin, D. E., Lamb, R. A., Martin, M. A., Roizman, B., Straus, S. E., Philadelphia, P. A: Lippincott Williams and Wilkins (1917-1974).
20. FALCONE, E., C. BUSI, A. LAVAZZA, M. MONINI, M. BERTOLETTI, E. CANELLI, E. VIGNOLO, F. M. RUGGERI and M. B. BONIOTTI (2015): Molecular characterization of avian rotaviruses circulating in Italian poultry flocks. Avian Pathol. 44, 509-515. 10.1080/03079457.2015.1096011
21. FITZGERALD, S. D. (2008): Adenovirus infections. In: Diseases of Poultry. 12th edition. Eds. Saif, Y. M., Fadley, A. M., Glission, J. R., McDougald, L. R., Nolan, L. K., Swayne, D. E., Blackwell Publishing Professional, Ames, IA, USA (251-252).
22. GADDE, U., T. RATHINAM and H. S. LILLEHOJ (2015): Passive immunization with hyperimmune egg-yolk IgY as prophylaxis and therapy for poultry diseases-A review. Anim. Health Res. Rev. 16, 163-176. 10.1017/S1466252315000195
23. GALLEGO, J. C., D. LORENCENA, J. L. DE MELLO, R. R. DELAI, M. R. DE MATOS, A. DE MARCO VIOTT, E. LORENZETTI, A. ALFIERI, S. R. FERNANDES and E. TAKIUCHI (2022): Investigation of avian rotavirus infections in broiler chicks from commercial flocks with different

performance efficiency indexes. Vet. Res. Commun. 46, 853-858. 10.1007/s11259-022-09910-x
24. GUY, J. S. (1998): Virus infections of the gastrointestinal tract of poultry. Poult. Sci. 77, 1166-1175. 10.1093/ps/77.8.1166
25. HARZER, M., K. HEENEMANN, M. SIEG, T. VAHLENKAMP, M. FREICK and A. RÜCKNER (2021): Prevalence of pigeon rotavirus infections: animal exhibitions as a risk factor for pigeon flocks. Arch. Virol. 166, 65-72. 10.1007/s00705-020-04834-w
26. HATCHER, E. L., S. A. ZHDANOV, Y. BAO, O. BLINKOVA, E. P. NAWROCKI, Y. OSTAPCHUCK, A. A. SCHAFFER and J. RODNEY BRISTER (2017): Virus Variation Resource-improved response to emergent viral outbreaks. Nucleic Acids Res. 45, 482-490. Available online: https://www.ncbi.nlm.nih.gov/genomes/VirusVariation/Database/nph-select.cgi?taxid=28875, accessed on 20th October, 2023. 10.1093/nar/gkw1065
27. INTERNATIONAL COMMITTEE ON TAXONOMY OF VIRUSES (ICTV) (2023): Rotavirus Taxonomy. Available online: https://ictv.global/, accessed on 20th October, 2023.
28. ITO, H., M. SUGIYAMA, K. MASUBUCHI, Y. MORI and N. MINAMOTO (2001): Complete nucleotide sequence of a group A avian rotavirus genome and a comparison with its counterparts of mammalian rotaviruses. Virus Res. 75, 123-138. 10.1016/S0168-1702(01)00234-9
29. JONES, C. (2008): Reovirus infections. In: Diseases of Poultry. 12th edition. Eds. Saif, Y. M., Fadley, A. M., Glission, J. R., McDougald, L. R., Nolan, L. K., Swayne, D. E., Blackwell Publishing Professional, Ames, IA, USA (309-328).
30. KARIM, M. R., F. I. RUME, M. M. ALAM and M. U. AHMED (2007): Molecular epidemiologic study on avian rotavirus prevailing in Bangladesh. J. Vet. Med. 5, 43-48. 10.3329/bjvm.v5i1.1308
31. MATTHIJNSSENS, J., M. CIARLET, M. RAHMAN, et al. (2008): Recommendations for the classification of group a rotaviruses using all 11 genomic RNA segments. Arch. Virol. 153, 1621-1629. 10.1007/s00705-008-0155-1
32. MCCOWAN, C., S. CRAMERI, A. KOCAK, et al. (2018): A novel group A rotavirus associated with acute illness and hepatic necrosis in pigeons (Columba livia) in Australia. PLoS One 13 (9), e0203853. 10.1371/journal.pone.0203853
33. McNULTY, M. S. (2003): Rotavirus infections. In: Diseases of poultry. Eds. Saif, Y. M., Barnes, H. J., Glisson, J. R., Fadly, A. M., McDougald, L .R., Swayne, D. E. Ames (IA): Iowa State Press (308-317).
34. McNULTY, M. S. and D. L. REYNOLDS (2008): Rotavirus infections. In: Diseases of poultry. 12th edition. Eds. Saif, Y. M., Fadley, A. M., Glission, J. R., McDougald, L. R., Nolan, I. K., Swayne, D. E. Ames (IA): Blackwell Publishing Professional (338-350).
35. METTIFOGO, E., L. F. N. NUÑEZ, J. L. CHACÓN, S. H. SANTANDER PARRA, C. S. ASTOLFI-FERREIRA, J. A. JEREZ, R. C. JONES and A. J. PIANTINO FERREIRA (2014): Emergence of enteric viruses in production chickens is a concern for avian health. The Sci. World J. 2014, 450423. 10.1155/2014/450423
36. MORI, Y., M. A. BORGAN, N. ITO, M. SUGIYAMA and N. MINAMOTO (2002): Sequential analysis of non-structural protein NSP4s derived from Group A avian rotaviruses. Virus Res. 89, 145-151. 10.1016/S0168-1702(02)00112-0
37. MSD VETERINARY MANUAL (2022): Rotavirus Infections of Poultry. Merck & Co., Inc., Rahway, N. J., USA. Available at: https://www.msdvetmanual.com/poultry/viral-enteritis/rotavirus-infections-of-poultry, accessed on 1st December, 2023.
38. MYERS, T. J., K. A. SCHAT and A. P. MOCKET (1989): Development of immunoglobulin class-specific enzyme-linked immunosorbent assays for measuring antibodies against avian rotavirus. Avian Dis. 33, 53-59. 10.2307/1591067
39. MYERS, T. J. and K. A. SCHAT (1990): Natural killer cell activity of chicken intraepithelial leukocytes against rotavirus-infected target cells. Vet. Immunol. Immunopathol. 26, 157-170. 10.1016/0165-2427(90)90064-Y
40. NUÑEZ, L. F. N., S. H. SANTANDER PARRA, C. S. ASTOLFI-FERREIRA, C. CARRANZA, D. I. D. DE LA TORRE, A. C. PEDROSO and A. J. P. FERREIRA (2016): Detection of enteric viruses in pancreas and spleen of broilers with runting-stunting syndrome (RSS). Pesqui. Vet. Bras. 36, 595-599. 10.1590/S0100-736X2016000700006
41. ONI, O. O., A. A. OWOADE and C. A. O. ADEYEFA (2018): Design and evaluation of primer pairs for efficient detection of avian rotavirus. Trop. Anim. Health Prod. 50, 267-273. 10.1007/s11250-017-1425-2
42. OTTO, P. H., E. M. LIEBLER-TENORIO, M. ELSCHNER, J. REETZ, U. LOHREN and R. DILLER (2006): Detection of rotaviruses and intestinal lesions in broiler chicks from flocks with runting and stunting syndrome (RSS). Avian Dis. 50, 411418. 10.1637/7511-020106R.1
43. OTTO, P. H., M. U. AHMED, H. HOTZEL, P. MACHNOWSKA, J. REETZ, B. ROTH, E. TROJNAR and R. JOHNE (2012): Detection of avian rotaviruses of groups A, D, F, and G in diseased chickens and turkeys from Europe and Bangladesh. Vet. Microbiol. 156, 8-15. 10.1016/j.vetmic.2011.10.001
44. OTTO, P. H., J. REETZ, W. EICHHORN, W. HERBST and M. C. ELSCHNER (2015): Isolation and propagation of the animal rotaviruses in MA-104 cells-30 years of practical experience. J. Virol. Methods 223, 88-95. 10.1016/j.jviromet.2015.07.016
45. PAULY, M., O. O. ONI, A. SAUSY, A. A. OWOADE, C. A. O. ADEYEFA, C. P. MULLER, J. M. HUBSCHEN and C. J. SNOECK (2017): Molecular epidemiology of avian rotaviruses group A and D shed by different bird species in Nigeria. Virol. J. 14, 111. 10.1186/s12985-017-0778-5
46. PATZINA-MEHLING, C., A. FALKENHAGEN, A. K. GADICHERLA, J. GRÜTZKE, S. H. TAUSCH and R. JOHNE (2020): Whole genome sequence

analysis of cell culture-adapted rotavirus A strains from chicken. Infect. Genet. Evol. 81, 104275. 10.1016/j.meegid.2020.104275

47. PINHEIRO, M. S., J. B. L. DIAS, M. P. PETRUCCI, C. E. P. F. TRAVASSOS, G. S. MENDES and N. SANTOS (2023): Molecular Characterization of Avian Rotaviruses F and G Detected in Brazilian Poultry Flocks. Viruses 15, 1089. 10.3390/v15051089
48. QIU, Y., S. WANG, B. HUANG, H. ZHONG, Z. PAN, Q. ZHUANG, C. PENG, G. HOU and K. WANG (2019): Viral infection detection using metagenomics technology in six poultry farms of eastern China. PLoS One 14 (2), e0211553. 10.1371/journal.pone.0211553
49. REYNOLDS, D. L., Y. M. SAIF and K. W. THEIL (1987): A survey of enteric viruses of turkey poults. Avian Dis. 31, 89-98. 10.2307/1590779
50. REYNOLDS, D. L. and S. L. SCHULTZ-CHERRY (2008): Astrovirus infections. In: Diseases of Poultry. 12th edition. Eds. Saif, Y. M., Fadley, A. M., Glission, J. R., McDougald, L. R., Nolan, L. K., Swayne, D. E., Blackwell Publishing Professional, Ames, IA, USA (351-355).
51. ROHWEDDER, A., K. I. SCHÜTZ, N. MINAMOTO and H. BRÜSSOW (1995): Sequence analysis of pigeon, turkey, and chicken rotavirus VP8* identifies rotavirus 993/83, isolated from calf feces, as a pigeon rotavirus. Virology 210, 231-235. 10.1006/viro.1995.1338
52. Rotavirus Classification Working Group (RCWG) (2023): Available online: https://rega.kuleuven.be/cev/viralmetagenomics/virus-classification/rcwg, accessed on accessed on 20th October, 2023.
53. RUBBENSTROTH, D., E. PEUS, E. SCHRAMM, et al. (2019): Identification of a novel clade of group A rotaviruses in fatally diseased domestic pigeons in Europe. Transbound. Emerg. Dis. 66, 552-561. 10.1111/tbed.13065
54. SAIF, Y. M. (2008): Viral enteric infections. In: Diseases of Poultry. 12th edition. Eds. Saif, Y. M., Fadley, A. M., Glission, J. R., McDougald, L. R., Nolan, L. K., Swayne, D. E., Blackwell Publishing Professional, Ames, IA, USA, (329-365).
55. SARKER, S. A., T. H. CASSWALL, L. R. JUNEJA, E. HOQ, I. HOSSAIN, G. J. FUCHS and L. HAMMARSTROM (2001): Randomized, placebo-controlled, clinical trial of hyperimmunized chicken egg yolk immunoglobulin in children with rotavirus diarrhea. J. Pediatr. Gastroenterol. Nutr. 32, 19-25. 10.1002/j.1536-4801.2001.tb07200.x
56. SCHMIDT, V., M. KÜMPEL, K. CRAMER, M. SIEG, M. HARZER, A. RÜCKNER and K. HEENEMANN (2021): Pigeon rotavirus A genotype G18P[17]-associated disease outbreaks after fancy pigeon shows in Germany - A case series. Tierarztliche Praxis Ausgabe K: Kleintiere - Heimtiere 49, 22-27. 10.1055/a-1339-0366
57. SCHUMANN, T., H. HOTZEL, P. OTTO and R. JOHNE (2009): Evidence of interspecies transmission and reassortment among avian group A rotaviruses. Virology 386, 334-343. 10.1016/j.virol.2009.01.040
58. SILVA, L. C., A. A. SANCHES, F. GREGORI, P.E. BRANDÃO, A. A. ALFIERI, S. A. HEADLEY and J. A. JEREZ (2012): First description of group A rotavirus from fecal samples of ostriches (Struthio camelus). Res. Vet. Sci. 93, 1066-1069. 10.1016/j.rvsc.2011.12.007
59. SILVA, R. R., D. A. M. BEZERRA, J. H. L. KAIANO, et. al. (2013): Molecular epidemiology of avian rotavirus in fecal samples of broiler chickens in Amazon Region, Brazil, from August 2008 to May 2011. Rev. Pan-Amaz. Saude 4, 55-62. 10.5123/S2176-62232013000200007
60. SUGIYAMA, M., K. GOTO, H. UEMUKAI, Y. MORI, N. ITO and N. MINAMOTO (2004): Attachment and infection to MA104 cells of avian rotaviruses require the presence of sialic acid on the cell surface. J. Vet. Med. Sci. 66, 461-463. 10.1292/jvms.66.461
61. TODD, D. and M. S. MCNULTY (1986): Electrophoretic variation of avian rotavirus RNA in polyacrylamide gels. Avian Pathol. 15, 149-159. 10.1080/03079458608436274
62. TROJNAR, E., P. OTTO and R. JOHNE (2009): The first complete genome sequence of a chicken group A rotavirus indicates independent evolution of mammalian and avian strains. Virology 386, 325-333.10.1016/j.virol.2009.01.034
63. TROJNAR, E., J. SACHSENRÖDER, S. TWARDZIOK, J. REETZ, P. H. OTTO and R. JOHNE (2013): Identification of an avian group A rotavirus containing a novel VP4 gene with a close relationship to those of mammalian rotaviruses. J. Gen. Virol. 94, 136-142. 10.1099/vir.0.047381-0
64. TROEGER, C., I. A. KHALIL, P. C. RAO, et. al. (2018): Rotavirus Vaccination and the Global Burden of Rotavirus Diarrhea among Children Younger Than 5 Years. JAMA Pediatr. 172, 958-965. 10.1001/jamapediatrics.2018.1960
65. WANI, S. A., M. A. BHAT, S. M. ISHAG, M. A. ASHRAFI, A. S. BUCH and M. HAQ (2003): Detection of a mammalian-like group A rotavirus in diarrheic chicken. Vet. Microbiol. 94, 13-18. 10.1016/S0378-1135(03)00079-8
66. YASON, C. V. and K. A. SCHAT (1986): Pathogenesis of rotavirus infection in turkey poults. Avian Pathol. 15, 421-435. 10.1080/03079458608436304
67. YASON, C. V. and K. A. SCHAT (1987): Pathogenesis of rotavirus infection in various age groups of chickens and turkeys: clinical signs and virology. Am. J. Vet. Res. 48, 977-983.
68. YURIKA TAMEHIRO, C., A. FERNANDES, A., KERLEY, C. MÉDICI and A. A. ALFIERI (2003): Segmented double-stranded genomic RNA viruses in fecal samples from broiler chicken. Braz. J. Microbiol. 34, 349-353. 10.1590/S1517-83822003000400013

Zdravstvene posljedice ptičjih rotavirusa za perad i uzgojne golubove

Valentina KUNIĆ, dr. med. vet., asistentica, Hrvatski veterinarski institut, Zagreb, Hrvatska; dr. sc. Željko GOTTSTEIN, izvanredni profesor, Veterinarski fakultet Sveučilišta u Zagrebu, Hrvatska; Marina PRIŠLIN, dr. med. vet., asistentica; dr. sc. Vladimir SAVIĆ, znanstveni savjetnik, docent, Centar za peradarstvo, Hrvatski veterinarski institut, Zagreb, Hrvatska; dr. sc. Dragan BRNIĆ, dr. med. vet., viši znanstveni suradnik, Hrvatski veterinarski institut, Zagreb, Hrvatska

Multikauzalne bolesti probavnog sustava predstavljaju značajne izazove za globalnu peradarsku industriju, što dovodi do znatnih ekonomskih gubitaka. Ovaj pregledni članak usredotočuje se na ulogu ptičjih rotavirusa (AvRV) u enteritisu peradi i sindromu zaostajanja u rastu (RSS) koji pogađaju domaće vrste peradi, a ističe i važnost međuvrsnog prijenosa. Rotavirusi ptica, posebno vrste *Rotavirus A* (RVA) i *Rotavirus D* (RVD), potencijalni su uzročnici enteritisa u peradi, doprinoseći složenosti kliničkih znakova povezanih s koinfekcijama različitim patogenima. Virion rotavirusa primarno se umnožava u zrelim enterocitima u tankom crijevu, što dovodi do malapsorpcije, skraćenja crijevnih resica i vodenastog proljeva. Horizontalni prijenos fekalno-oralnim putem ili prijenos izravnim kontaktom dio su složene epidemiologije infekcija ptičjim rotavirusima. Velika gustoća jata i okolišna otpornost AvRV-a doprinose njihovom perzistiranju u okolišu peradi. Zabilježena su i izbijanja AvRV infekcija na izložbama golubova što se dovodi u vezu s teškim kliničkim manifestacijama, uključujući nekrozu jetre i abnormalnosti probavnog sustava. Prevalencija AvRV-a u golubova na takvim događanjima može doseći čak 90 %. Primijećen je i međuvrsni prijenos između ptica i sisavaca, iako do sada nije zabilježen zoonotski prijenos AvRV-a. Laboratorijske dijagnostičke metode, poput RT-PCR-a, imaju ključnu ulogu u prepoznavanju AvRV infekcija s obzirom na odsutnost patognomoničnih kliničkih znakova. Razvoj cjepiva izazovan je zbog značajnih antigenskih varijacija, ali obećavajuće alternative, poput oralne primjene IgY protutijela dobivenih iz jajeta, pokazuju potencijal za profilaksu i terapiju. Mjere biosigurnosti i mogućnosti liječenja, uključujući oralne otopine elektrolita i antibiotike za sekundarne bakterijske infekcije, ključni su u kontroli mortaliteta prouzročenim AvRV infekcijama. Unatoč izazovima, napredak u molekularnoj dijagnostici i inovativne strategije profilakse nude obećavajuće načine za ublažavanje utjecaja AvRV-a na zdravlje peradi.

Ključne riječi: *Rotavirus A, Rotavirus D, perad, uzgojni golub, međuvrsni prijenos, sindrom zarazne kržljavosti*