Review

OVERVIEW OF THE MOST SIGNIFICANT CORONAVIRUS INFECTIONS IN VETERINARY MEDICINE

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Abstract

Background. Coronaviruses (CoVs) have been recognized in veterinary virology for a long time and comprise a large group of RNA viruses responsible for enteric, respiratory, hepatic, and neurologic diseases in a variety of animal species and humans. These viruses are very adaptable considering their highly error-prone replication process and recombination ability, resulting in remarkable mutability and efficient expansion of their host range and tissue tropism.

Scope and Approach. In the recent past, after the outbreaks caused by SARS-CoV in 2002 and MERS-CoV in 2012, CoVs became a research focus in the scientific community. Moreover, the ongoing SARS-CoV-2 pandemic raised more questions concerning the threats posed by these viruses. Several significant examples of coronaviruses jumping the species barrier and changing their tropism have been reported in the past, and novel viruses of both animals and humans have appeared as a consequence. This paper reviews some of the examples of CoV mutability and the most notable animal coronaviruses of veterinary relevance.

Key Findings and Conclusions. There is still no proof that the novel virus SARS-CoV-2 can be transmitted to humans from domestic animals, and its recent cross-species jump is currently being intensively researched. Intensified and diverse human activities that lead to the disruption of ecosystems contribute to the increased risk of contact with animals that might represent virus reservoirs. The need for constant surveillance of CoVs and expanded studies of their virological traits, mutation mechanisms, diversity,

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prophylactic and therapeutic measures highlight the key role of both veterinarians and medical doctors in order to preserve the health of the human population.

Key Words: animals**,** coronavirus, veterinary

INTRODUCTION

Coronaviruses (CoVs) have been recognized in veterinary virology for a long time and comprise a large group of RNA viruses responsible for enteric, respiratory, hepatic, and neurologic diseases in a variety of mammalian and avian species (Saif, 2004; Wege et al. 1982). The *Coronaviridae* family is divided into *Orthocoronavirinae* and *Letovirinae* subfamilies, and based on serological cross-reactivity and genetic differences, the *Orthocoronavirinae* subfamily is further divided into four following genera: *Alphacoronavirus*, *Betacoronavirus*, *Gammacoronavirus*, and *Deltacoronavirus* (ICTV, 2020; Brownlie, 2017; Woo et al., 2012). The genus *Alphacoronavirus* mainly encompasses viruses of carnivores (e.g., dogs, cats, ferrets and minks), transmissible gastroenteritis virus of swine (TGEV), porcine epidemic diarrhoea virus (PEDV), porcine respiratory coronavirus (PRCoV), the human coronaviruses 229E and NL63, and many viruses found in bats (Brownlie, 2017; Nišavić and Milić, 2017; Woo et al., 2005). Equine coronavirus (ECoV) is located within the genus *Betacoronavirus* along with bovine coronavirus (BCoV), canine respiratory coronavirus (CRCoV), porcine hemagglutinating encephalomyelitis virus (PHEV), human OC43 (HCoV-OC43) and HKU1 coronaviruses, human severe acute respiratory syndrome coronavirus (SARS-CoV), horseshoe bat coronaviruses, Middle East respiratory syndrome coronavirus (MERS-CoV) from both humans and camels, etc. (Brownlie, 2017; Nišavić and Milić, 2017). Gammacoronaviruses mainly contain avian coronaviruses such as infectious bronchitis virus (IBV) and turkey coronavirus (TCoV), as well as new viruses from wild birds and marine mammals (Nišavić and Milić, 2017; Woo et al., 2014). The recently established genus *Deltacoronavirus*, in addition to CoVs from birds, also includes porcine deltacoronavirus (PDCoV), which is clinically indistinguishable from TGEV or PEDV (Brownlie, 2017; Woo et al., 2012). The diversity of coronaviruses is explained by a model of CoV evolution, according to which bats are the gene source of alphacoronaviruses and betacoronaviruses, whilst birds are the gene source of gammacoronaviruses and deltacoronaviruses (Woo et al., 2009).

Coronaviruses are the largest enveloped single-stranded RNA viruses, and their genome is packed inside a helical capsid located within the viral envelope. The nucleocapsid (N) protein is a phosphoprotein that modulates the synthesis of viral RNA and creates a helical nucleocapsid by binding to it. Trimers of the spike protein form peplomers embedded in the viral envelope, so accordingly, the CoV virions have a characteristic crown-like morphology (*corona* means crown in Latin) (Nišavić and Milić, 2017; Li, 2016). There are at least three structural glycoproteins with multiple roles in the viral replication cycle associated with the viral envelope: the membrane (M) protein and envelope (E) protein are crucial for virus assembly, and the spike

(S) protein mediates virus entry into host cells (Li, 2016). The S protein is also responsible for viral host range and tissue tropism, thus initiating the generation of virus-neutralizing antibodies (Brownlie, 2017; Li, 2016). Interestingly, CoV genomes also encode different accessory proteins (eight in the SARS coronavirus) that are not vital for their *in vitro* replication but increase virus potency *in vivo*. For example, the envelope-associated haemagglutinin-esterase protein (HE) is a particular feature of some betacoronaviruses (Brownlie, 2017; Li, 2016; Cheng et al., 2007).

CORONAVIRUS EVOLUTION AND DIVERSITY

Coronaviruses are highly adaptable, given their highly error-prone replicative scheme and recombination capabilities that result in marked mutability, and hence, efficient change and expansion of their host range and tissue tropism (Graham and Baric, 2010; Lorusso et al., 2008; Vijgen et al., 2005; Pratelli et al., 2003; Herrewegh et al 1998). Prior to the emergence of SARS-CoV, only 12 animal and human coronaviruses were described. In the recent past, after the outbreaks caused by SARS-CoV in 2002 and MERS-CoV in 2012, coronaviruses became the subject of increased interest in the scientific community (Graham and Baric, 2010; Cheng et al., 2007; Lau et al., 2005; Guan et al., 2003). Both SARS-CoV and MERS-CoV originated in animals, and their reservoirs were in close contact with the human population (Dawson et al., 2019; Graham and Baric, 2010; Lau et al., 2005). The detection of SARS-related coronaviruses in palm civets and a racoon dog from live animal markets in China was the first indicator of the occurrence of interspecies transmission (Guan et al., 2003). However, further study showed these animals were incidental hosts, and various horseshoe bat species are now suspected to be the ultimate reservoir of SARS-related CoV (Lau et al., 2005; Li et al., 2005; Song et al., 2005). The evolution of MERS-CoV in camels included the exchange of genetic elements among viruses either in bats, or most probably within the camels as a mixing vessel (Dawson et al., 2019; Corman et al., 2014).

The S protein is considered to be the principal mediator for the emergence of coronaviruses in new hosts, since both of its subunits (S1 and S2) have nucleotide substitution abilities (Li, 2016; Graham and Baric, 2010; de Haan et al., 2006). The adaptive possibilities of coronaviruses are portrayed by investigations related to SARS-CoV S protein receptor-binding domains (RBDs), which are virus-specific regions within the S1 subunit that engage with the host cell receptor angiotensin-converting enzyme 2 (ACE2) (Li, 2016; Graham and Baric, 2010; Cheng et al., 2007). Notably, the RBD has been shown to evolve under the selective pressure of neutralizing antibodies, and it is stated that one or a few mutations in viral RBDs can cause serious epidemic outcomes (Li, 2016). Additionally, coronaviruses have a sophisticated system for receptor recognition. It is known that CoVs from different genera bind to the same receptor protein, though CoVs from the same genus recognize diverse receptors (Li, 2016). For example, within the genus *Betacoronavirus*, SARS-CoV specifically binds

to ACE2, whilst MERS-CoV recognizes dipeptidyl peptidase 4 (DPP4). It must be emphasized that DPP4 protein displays high amino acid sequence conservation across different animal species, thus representing a low barrier against cross-host transmission (Raj et al., 2013). The multihost potential of a *Deltacoronavirus* was recently documented in a study showing that porcine deltacoronavirus (PDCoV) uses the phylogenetically conserved catalytic domain of aminopeptidase N as a host cell entry receptor and also efficiently infects cells of a broad species range, which might enable it to jump the species barrier (Li et al., 2018).

Several significant examples of coronaviruses jumping the species barrier as well as of their tropism changes have been reported in the past. Important diseases of both animals and humans have appeared as a consequence. Human coronavirus OC43 is thought to be the most commonly encountered human coronavirus in respiratory tract infections. However, this virus shares a nucleotide identity of approximately 96% with BCoV and emerged from a zoonotic transmission from bovines (Vijgen et al., 2005). The potential of BCoV to infect other species was also shown after the genetic analysis of a closely related virus (human enteric coronavirus – HEC-4408), previously isolated from the faeces of a diarrhoeic child (Zhang et al., 1994). Furthermore, it was suggested that canine respiratory coronavirus (CRCoV) is of bovine origin, since pups can be successfully experimentally infected with BCoV (Kaneshima et al., 2007). Genetic recombination amongst coronaviruses that infect different animal species is known to give rise to new viral strains as happened with the emergence of feline coronavirus (FCoV) type 2. This particular recombination event occurred between the S gene regions of FCoV type 1 and canine coronavirus (CCoV) (Pedersen, 2014; Herrewegh et al., 1998). Since CCoV and FCoV are closely related viruses, it practically diminishes the borders for their interspecies circulation (Benetka et al., 2006; Pratelli et al., 2003). A cross-species jump also occurred with the adaptation of CCoV type 2 from dogs to pigs and the emergence of TGEV characterized by inactivation and loss of specific open reading frames (ORFs) in the viral genome (Lorusso et al., 2008). Furthermore, the change in viral tropism from enteric to respiratory tract receptors, attributed to nucleotide deletions in the S1 domain of TGEV, led to the emergence of porcine respiratory coronavirus (PRCoV) (Laude et al., 1993; Rasschaert et al., 1990).

CORONAVIRUSES OF UNGULATES

Bovine coronavirus (BCoV)

Bovine coronavirus is a member of the genus *Betacoronavirus* and causes enteric and respiratory disease in cattle with documented spillovers to small ruminants (Burimuah et al., 2020). Three different clinical syndromes are related to BCoV infections in susceptible animals: calf diarrhoea, winter dysentery characterized by haemorrhagic diarrhoea in adult animals, and respiratory infections, most notably the shipping fever of feedlot cattle (Boileau and Kapil, 2010; Saif, 2010; Tsunemitsu and Saif, 1995).

Bovine coronavirus infection is mostly subclinical, a consequence of its ubiquitous presence in the cattle population, and the virus is shed by the faecal-oral and respiratory routes under various stressful conditions (Nišavić and Milić, 2017; Saif, 2010). The clinical manifestations also depend on factors such as secondary infections, stress, the animals' overall immunologic status and environmental temperature (Saif, 2010; Tsunemitsu and Saif, 1995). The wide tropism of BCoV is a result of the fact that its host cell receptor is sialic acid, found in enterocytes of the intestinal tract and in the epithelium of the upper and lower respiratory tract (Brownlie, 2017; Saif, 2010).

Shedding of BCoV is of short duration, thus requiring timely sample collection, i.e., within the first week after the transport of affected animals (Saif, 2010). Bovine viral infections can be diagnosed by detection of the virus, viral antigen, viral genomic RNA or specific antibodies in adequate samples from infected animals (Nišavić et al., 2018; Nišavić and Milić, 2017; Veljović et al., 2016; Milić et al., 2010). Virus isolation (VI) is most successfully performed in cells of bovine origin or human colorectal adenocarcinoma cell cultures (HRT-18). However, cell culture techniques are time-consuming and some viral strains fail to grow (Radalj et al., 2018; Saif et al., 2010). For this reason, sensitive molecular methods such as reverse transcription polymerase chain reaction (RT-PCR) or real time RT-PCR assays are most often used (Nišavić and Milić, 2017; Saif, 2010). Because BCoV antibodies are widespread in cattle, paired acute and convalescent serum samples are needed for serologic diagnosis of BCoV infections by virus neutralization, immunofluorescence assay, haemagglutination-inhibition (HI) or enzyme-linked immunosorbent assay (ELISA) tests (Burimuah et al., 2020; Brownlie, 2017; Saif, 2010). Serum antibodies play an important protective role against BCoV infections. Since no respiratory BCoV vaccines have been developed yet, intranasal vaccination using attenuated enteric strains has been proposed to reduce the risk of BCoV-associated pneumonia, whilst several vaccines, both attenuated and inactivated types, have been developed against BCoV enteric disease (Tizzard, 2020; Brownlie, 2017; Nemoto et al., 2017; Saif, 2010).

Coronaviruses of swine

Transmissible gastroenteritis virus belongs to the genus *Alphacoronavirus*, and since its first detection in the United States in 1946, it has been reported worldwide as causing a highly contagious enteric disease of economic importance to the swine industry (Vlasova et al., 2020; Brownlie, 2017). Piglets are especially susceptible to infection since their gastric acidity levels are lower than in adults, whilst milk-based nutrition further protects the virus within the stomach, enabling its passage to the intestine. The virus is spread by the oral uptake of faeces from infected pigs, and it replicates within the villus enterocytes, leading to their destruction, along with maldigestion and malabsorption, with diarrhoea as a direct consequence (Brownlie, 2017; Nišavić and Milić, 2017).

Porcine respiratory coronavirus (PRCoV) was derived from TGEV after specific genetic deletions. It is spread by respiratory droplets (with limited faecal shedding)

and replicates in the tonsils, the epithelium of the upper and lower respiratory airways, as well as in pneumocyte types I and II (Vlasova et al., 2020; Laude et al., 1993; Rasschaert et al., 1990). Infection by PRCoV occurs in piglets of all ages and causes mild respiratory disease if uncomplicated by other pathogens (Brownlie, 2017). It was documented that the rising prevalence of PRCoV suppressed the occurrence of TGEV (Chen et al., 2019).

Since TGEV and PEDV are indistinguishable based on clinical symptoms in affected animals and are often found in mixed infections, multiplex real-time RT-PCR for their simultaneous detection and quantification was developed (Kim et al., 2007). Similar diagnostic methods are used for the detection of PRCoV, with a difference in sampling requirements since it is a respiratory pathogen. Both TGEV and PRCoV, as well as other significant swine viruses, can be isolated in cell lines of pig origin. However, this method might require several blind passages after primary isolation of field strains (Nišavić and Milić, 2017; Lukač et al., 2016; Miković et al., 2016). Considering the declining TGEV prevalence, the need for vaccines has also reduced, although both modified live and inactivated products are available. No vaccines have been developed against PRCoV since it causes mild infections (Tizzard, 2020; Brownlie, 2017).

Porcine epidemic diarrhoea virus (PEDV) is another representative of the genus *Alphacoronavirus*, and it is presumed that PEDV was introduced into the pig population from bats (Nišavić and Milić, 2017; Huang et al., 2013). Since 2013, this virus has caused major epizootic episodes resulting in vast economic damage to the pig industry in the United States with the loss of 10% of the United States pig population (Tizzard, 2020; Stevenson et al., 2013). Porcine epidemic diarrhoea is an acute and highly contagious disease characterized by profuse diarrhoea, dehydration, anorexia and high mortality rates of 1- to 7-day-old piglets, even though animals of all age groups can manifest various clinical symptoms (Brownlie, 2017; Stevenson et al., 2013). Recently, a recombinant TGEV/PEDV virus denominated swine enteric coronavirus (SeCoV) emerged in Europe (Vlasova et al., 2020). It is suggested that tests that differentiate PEDV infections from TGEV, SeCoV, and PDCoV be used. Since SeCoV is a recombinant virus of TGEV with PEDV's S protein, a discriminatory assay is required (Vlasova et al., 2020). Multiple PEDV vaccines have been developed, including both inactivated and modified live products that can be combined with TGEV and rotavirus vaccines, and vaccination of sows is the most widely employed protective procedure (Tizzard, 2020; Brownlie, 2017).

Porcine deltacoronavirus (PDCoV) is a member of the genus *Deltacoronavirus*, and was first identified in 2012 in China and subsequently in several other Asian countries, the United States, and Canada (Vlasova et al., 2020; Woo et al., 2012). The observed clinical signs of PDCoV-induced disease are similar to other intestinal coronaviruses, but with a lower mortality rate (Vlasova et al., 2020; Brownlie, 2017). PDCoV-specific RT-PCR is currently the diagnostic method of choice, since VI in cell cultures is not always successful (Zhang, 2016).

Porcine hemagglutinating encephalitis virus (PHEV) is the only porcine *Betacoronavirus* and causes either encephalomyelitis or a vomiting and wasting condition in piglets deprived of maternal immunity (Vlasova et al., 2020; Mora-Diaz et al., 2019; Brownlie, 2017). It is a highly neurotropic virus that is spread by aerosols and multiplies in the airways, tonsils, and intestine, with consequent spread to the central nervous system via peripheral nerves (Brownlie, 2017). Diagnosis is based on the haemagglutination (HA) and haemagglutination inhibition (HI) tests or by RT-PCR, and there currently are no available vaccines (Mora-Diaz et al., 2019; Brownlie, 2017).

Swine acute diarrhoea syndrome virus (SADS CoV) is a novel *Alphacoronavirus* that has only recently been discovered in pigs in China. It is assumed to have emerged from the interspecies transmission of bat CoVs to pigs, since SADS-related CoVs were detected in horseshoe bats (Zhou et al., 2018).

Equine coronavirus (ECoV)

Equine coronavirus is classified within the genus *Betacoronavirus* due to its relatedness to BCoV (Brownlie, 2017). Clinical symptoms associated with ECoV disease in affected horses include diarrhoea, fever, anorexia, and lethargy, with the number of clinical cases being higher during autumn and winter (Pusterla et al., 2017; Nemoto et al., 2014; Pusterla et al., 2013). Clinically apparent infection is mostly seen in adults and it is presumed that the pathogenicity of ECoV is linked with the horse's age, i.e., the presence of passive colostral immunity (Pusterla et al., 2018; Pusterla et al., 2013). Some adult horses also remain asymptomatically infected with concurrent shedding of ECoV in their faeces (Pusterla et al., 2013). Transmission of ECoV occurs predominantly by the faecal-oral route, while the significance of nasal shedding remains to be determined (Nemoto et al., 2014). Horses with manifest disease shed ECoV in their faeces for several weeks and up to three months, but asymptomatic animals are also a significant source of the disease (Goodrich et al. 2020; Pusterla et al, 2018; Pusterla et al., 2013). Isolation of ECoV is possible in HRT-18 cells, but viral detection is predominantly performed by faecal real-time RT-PCR (Brownlie, 2017; Pusterla et al., 2017; Miszczak et al., 2016). A vaccine for ECoV remains unavailable. However, given the antigenic relatedness between the two viruses, BCoV vaccine does provide horses with antibodies against ECoV. Nonetheless, the efficacy of BCoV vaccine against ECoV needs to be investigated (Nemoto et al., 2017).

CORONAVIRUSES OF CARNIVORES

Canine coronavirus (CCoV)

Canine coronavirus (CCoV) from the genus *Alphacoronavirus* is a common enteric pathogen of dogs that has a worldwide distribution (Nišavić and Milić, 2017). Two distinct genotypes of this virus are recognized, namely CCoV type I (CCoV-I) and

CCoV type II (CCoV-II). This latter type is further divided into CCoV-IIa and CCoV-IIb, which is a result of the recombination with TGEV (Decaro and Buonavoglia, 2008). Canine coronavirus I is genetically similar to FCoV type I in the spike and membrane genes and causes gastroenteritis in affected dogs (Benetka et al., 2006). It is known that CCoV-IIa is divided into two different biotypes: classical, which is known to cause enteritis with mild diarrhoea, and pantropic, which was isolated from dead pups in Italy and can been detected in various organs (Decaro et al., 2010; Buonavoglia et al., 2006). Canine coronavirus is transmitted through the faecal-oral route, and prolonged viral shedding for a period of several months has been previously documented (Pratelli et al., 2001). Molecular methods are used for the rapid detection of CCoV in clinical specimens, and moreover, a recently established multiplex PCR method for simultaneous detection of the most significant viruses associated with canine enteric diseases has proved to be useful (Hao et al., 2019; Nišavić and Milić, 2017). Inactivated and modified live vaccines against CCoV are available, but their protective values are debatable, in part due to the emergence of new CCoV genotypes and pathotypes in dogs (Tizzard, 2020; Decaro and Buonavoglia, 2008).

Canine respiratory coronavirus (CRCoV)

Aside from affecting the gastrointestinal system, canine coronaviruses also induce respiratory disease in dogs. The *Betacoronavirus*, canine respiratory coronavirus (CRCoV), was first detected in 2003 and is genetically unrelated to CCoV (Erles and Brownlie, 2008). Canine respiratory coronavirus spreads rapidly by aerosol among kennelled dogs and causes mild respiratory symptoms, occurring more frequently during autumn and winter (Brownlie, 2017; Erles and Brownlie, 2008). Diagnosis of CRCoV can be performed by VI in HRT-18 cells, although RT-PCR is the preferred method, and previous exposure can be serologically detected (Brownlie, 2017; Erles and Brownlie, 2008). Antibodies against CCoV are not cross-protective and vaccines against canine respiratory pathogens do not include CRCoV. Instead, these infections can be controlled by the segregation of animals (Tizzard, 2020; Brownlie, 2017; Decaro and Buonavoglia, 2008).

Feline coronavirus (FCoV)

Feline coronavirus is a member of the *Alphacoronavirus* genus and is a common pathogen of both domestic and wild felids, causing fatal granulomatous peritonitis (Nišavić and Milić, 2017). This virus is known to exist in two pathotypes, resulting in either subclinical to mild enteric disease (feline enteric coronavirus – FECV) or progressive, debilitating and lethal disease (feline infectious peritonitis virus – FIPV) (Nišavić and Milić, 2017; Pedersen, 2014). The two pathotypes cannot be differentiated serologically, and it was proposed that genetic mutations might result in altered pathogenicity of FCoV (Pedersen, 2014). Aside from the pathotype differentiation, FCoVs are separated into two serotypes, FCoV types 1 and 2. However, these two

divisions are not in correlation with illness, other than the consideration that type 1 FCoVs are the leading cause of feline infectious peritonitis (FIP) since they are more prevalent in the field (Sharif et al., 2010). The animals are infected at an early age after the decline of maternal immunity but stay healthy and become susceptible to the development of FIP in stressful or immunosuppressive conditions (Brownlie, 2017). The more virulent FCoV genetic variants rapidly replicate within macrophages, specifically those with an affinity for the endothelia of venules in the serosa, omentum, pleura, and meninges (Brownlie, 2017; Pedersen, 2014). Feline infectious peritonitis clinically presents as either as the classical effusive (wet), or the non-effusive (dry) forms. Both forms result in the appearance of focal pyogranulomas of multiple internal organs and serous membranes (Pedersen, 2014). The effusive form is rapidly progressive and characterized by abdominal dissention due to the accumulation of fluid in the peritoneal cavity associated with pyogranuloma formation (Brownlie, 2017; Nišavić and Milić, 2017). FCoV type 1 strains are very difficult to grow in cell culture as opposed to type 2 FCoVs. Rapid and sensitive RT-PCR tests are commonly used for faecal or other clinical samples, but interpretation of results must be in accordance with clinical findings (Sharif et al., 2010; Herrewegh et al., 1998). Since the development of antibodies stimulates the virus uptake by macrophages, this further complicates vaccine development, and the only commercially available FIP vaccine is applied to the nasal mucosa, inducing a local IgA response, but has limited efficacy (Tizzard, 2020).

AVIAN CORONAVIRUSES

Avian infectious bronchitis virus

Avian infectious bronchitis virus (IBV) is considered to be the prototype of the genus *Gammacoronavirus* and causes one of the most important and contagious viral diseases in chickens of all ages worldwide (Ramakrishnan and Kappala, 2019). The constant emergence of new variants occurs as a consequence of mutations in the hypervariable regions of the S gene, and even though some are unable to replicate or survive, others become economically important worldwide or in certain geographic areas (Sjaak de Wit et al., 2011). IBV infects the upper airway epithelium, causing respiratory distress, but more virulent strains show tropism for kidney cells, the oviduct and the gastrointestinal tract (Nišavić and Milić, 2017; Ignjatovic and Sapats, 2000). Characteristically, the damage to the reproductive system caused by this infection is a decrease of egg production in laying hens, and the eggs become uncalcified, and differ in size, colour and shape (Brownlie, 2017). IBV spreads by aerosol and faecal-oral routes, but indirect transmission through contaminated equipment, especially during the colder months when prolonged viral shedding occurs, is also a considerable risk (Ramakrishnan and Kappala, 2019; Ignjatovic and Sapats, 2000). Preferred samples for VI are tracheal swabs or whole trachea tissues from suspected animals (Brownlie, 2017). Embryonated chicken eggs are used for VI and, upon infection with IBV, show dwarfism, congestion of the main blood vessels in the chorioallantoic membrane and

death. Definitive identification of the agent is most commonly performed by serologic methods, immunofluorescence or RT-PCR (Ramakrishnan and Kappala, 2019). Since VI is time-consuming and often requires successive passaging, the use of genotype-specific RT-PCR assays is preferred, and methods such as multiplex real-time RT-PCR for simultaneous detection of several avian viruses are useful in a laboratory setting (Laamiri et al. 2018). Commercial poultry are vaccinated against IBV, and both inactivated and modified live vaccines are used in different regimes to induce maternal immunity that protects chicks (Tizzard, 2020; Sjaak de Wit et al., 2011). It is advisable to optimize protection against different viral variants that circulate in a given area (Tizzard, 2020; Sjaak de Wit et al., 2011).

Turkey coronavirus (TCoV)

Turkey coronavirus (TCoV) belongs the genus *Gammacoronavirus* along with IBV, but these two viruses have very different S proteins, so TCoV can be considered a recombinant coronavirus (Nišavić and Milić, 2017; Hughes, 2011). This virus was identified in the United States during the 1970s as one of the agents responsible for the acute enteric disease most often named bluecomb; it is present throughout the world where turkeys are raised (Brownlie, 2017). Even though TCoV infects animals of all ages, intestinal disorders occur mostly within the first three weeks of life and involve loss of appetite, watery diarrhoea, dehydration and hypothermia, as well as atrophy of the thymus and the bursa of Fabricius, thus contributing to secondary infections (Nišavić and Milić, 2017; Guy, 2013). Only one TCoV serotype exists, but there are no licenced vaccines available (Brownlie, 2017).

CONCLUSION

The role of veterinary virologists has been increasingly important over the past years since there has been abundant proof of the zoonotic potential of animal coronaviruses. Accordingly, the field of the discovery of new CoVs, and studies regarding their constant evolution and pathogenesis in different hosts has significantly expanded. The most recent and ongoing severe acute respiratory syndrome in humans, the coronavirus 2 (SARS-CoV-2) pandemic, has once again raised questions concerning the threats posed by coronaviruses from the aspect of their high mutability and frequent host switching capabilities. It is currently known that the genome of SARS-CoV-2 shares around 96% identity to the bat coronavirus, BatCoV RaTG13 (Zhou et al., 2020). Nevertheless, many important questions remain unanswered, one of which is if and how this cross-species jump occurred. Several dogs and cats, and a tiger, which all had been in close contact with infected humans, have recently tested positive for SARS-CoV-2. However, further studies are required to better understand animal susceptibility to this virus. Nevertheless, to date, there is no evidence that infected animals play a role in the spread to humans of this virus, which is transmitted by person-to-person contact (OIE, 2020). Human activities such as deforestation,

disruption of ecosystems, urbanization due to population expansion, increased consumption, access to new technologies, intensified tourism, and many others have contributed to the increased risk of contact with some animal species that might be virus reservoirs. Having that in mind, as well as the known fact that coronaviruses have zoonotic potential, reinforces the need for constant surveillance and intensive research with close cooperation between veterinarians and medical doctors, as both are responsible for the preservation of human health.

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Authors' contributions

JN: participated in the design of the study, conceived the study, and participated in its design and coordination and helped to draft the manuscript. NM: participated in the design of the study. AR: participated in the design of the study, participated in its design and coordination and helped to draft the manuscript. All authors read and approved the final manuscript.

Competing interests

The authors declare that they have no competing interests.

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PREGLED NAJZNAČAJNIJIH INFEKCIJA KORONAVIRUSIMA IZ VETERINARSKE PERSPEKTIVE

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Kratak sadržaj

Uvod. Koronavirusi se u okviru veterinarske virusologije izučavaju već dugi niz godina i predstavljaju veliku grupaciju RNK virusa odgovornih za gastrointestinalna, respiratorna i neurološka oboljenja velikog broja životinja i ljudi. Navedeni virusi su visoko adaptibilni s obzirom na njihov jedinstven mehanizam replikacije i sposobnost mutiranja, pri čemu dolazi do česte transmisije koronavirusa među različitim vrstama, kao i promena u njihovom tropizmu.

Cilj i pristup. U skorijoj prošlosti su zabeležene epidemije izazvane virusima SARS-CoV 2002., odnosno MERS-CoV 2012. godine, nakon kojih su koronavirusi postali tema mnogih ispitivanja. Nove nepoznanice i pitanja vezana za pretnju koju koronavirusi predstavljaju izazvala je trenutna pandemija izazvana virusom SARS-CoV-2. Postoji veliki broj značajnih primera koronavirusa koji su preskočili barijeru vrste i posledično doveli do pojave novih oboljenja kako životinja, tako i ljudi. U ovom radu su opisani neki od najznačajnih primera koji oslikavaju sposobnost mutacije koronavirusa, kao i osnovne karakteristike koronavirusnih infekcija koje su od velike važnosti za veterinarsku medicinu.

Ključni nalazi i zaključak. Do danas ne postoje dokazi da se novootkriveni virus SARS-CoV-2 prenosi sa domaćih životinja na ljude, a mehanizam kojim je došlo do prelaska navedenog virusa na ljude se intenzivno ispituje. Sve učestalije aktivnosti čoveka koje dovode do narušavanja ekosistema doprinose povećanju rizika od kontakta sa divljim životinjama koje mogu predstavljati rezervoare virusa. Potreba za kontinuiranim nadzorom nad pojavom infekcija izazvanih koronavirusima, podrobnijim ispitivanjima u poljima virusologije i vakcinologije, kao i za pronalaskom efikasne terapije ovih oboljenja predstavljaju ključnu i zajedničku ulogu veterinara i lekara u cilju očuvanja zdravlja ljudi.

Ključne reči: životinje, koronavirus, veterina