

Coronaviruses – viruses marking the 21st century



Lorena Jemeršić*

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Summary

Coronaviruses are causative agents of respiratory, gastrointestinal and neurological infections in mammals and birds. The main characteristic of coronaviruses is a high mutation rate, resulting in possible changes in their pathogenicity, tissue tropism or in their host. Even though they have been known causes of disease for decades, they became interesting in the 21st century due to outbreaks of large epidemics in humans and causing serious economic losses in the animal production sector, primarily the pig industry. The outbreaks of the highest concern emerged in 2002 (Severe Acute Respiratory Syndrome – SARS) and in 2012 (Middle-East Respiratory Syndrome – MERS). Both diseases are of animal origin, and manifested with severe pneumonia in humans and a lethality of 11% and 36%, respectively. Today we

are confronted with one of the largest epidemics in the history of humankind, the COVID-19 pandemic. It is caused by a variant of the SARS coronavirus and transmitted through person to person contact, with no known animal vector. Until the time of press of this article the infection has been detected in over 4.8 million people and has been the cause of over 320,000 deaths. In Croatia, due to protective measures imposed by the National Civil Protection Headquarters, COVID-19 is still within linear case growth. This review provides insight into known coronavirus infections in animals and humans and shows that novel coronaviruses have already marked the 21st century and likely changed the world, as we know it, forever.

Key words: coronaviruses; animals; people; COVID-19

Introduction

Coronaviruses are the causative agents of mild to severe respiratory, gastrointestinal and neurological infections in mammals and birds. Most known coronaviruses have been detected in bats, swine and small mammals; however they can infect humans, horses, cattle, camels, cats, dogs,

rats, birds, whales, minks, ferrets and other wild animals (Monchatre-Leroy et al., 2017). The main characteristic of coronaviruses is a high mutation rate, resulting in possible changes of their pathogenicity, tissue tropism or host, and therefore strain transmission has been

Lorena JEMERŠIĆ*, DVM, PhD, Associate Professor, Scientific Advisor, (Corresponding author, e-mail: jemersic@veinst.hr), Croatian Veterinary Institute, Zagreb, Croatia

recorded amongst animal species, and from animals to humans. Though coronaviruses have been well known causes of infections for decades, they triggered scientific research worldwide in the 21st century due to epidemic outbreaks in both humans and animals caused by novel coronavirus strains. The most important public health infections recorded were the Severe Acute Respiratory Syndrome (SARS) in 2002, HKU1 (2003) and the Middle-East Respiratory Syndrome (MERS) in 2012. Today, we are confronted with a pandemic, the Coronavirus infectious disease 2019 (COVID-19) that is rapidly spreading globally and contributing to the development of infected, diseased, socially vulnerable and economically deteriorated communities.

Since 2000, there have been reports of novel coronavirus strains of higher virulence and pathogenicity spreading in animals, such as strains causing Pleural effusion disease in rabbits (2000), Canine respiratory coronavirus infection (2003), Porcine deltacoronavirus infection (2004), Equine coronavirus infection (2010), Swine acute diarrhoea syndrome (2016) and Porcine epidemic diarrhoea virus infection (2010, 2016).

This review describes the main coronavirus characteristics, and the most important coronavirus infections in animals and humans that have already marked the 21st century, changing the world as we know it.

Coronavirus aetiology

Coronaviruses belong to the realm *Riboviria*, order *Nidovirales*, suborder *Cornidovirinae*, family *Coronaviridae*, subfamily *Orthocoronavirinae*. The latter includes four genera: Alpha-, Beta-, Gamma- and Deltacoronavirus. The coronavirus origin is not well known; however, the mutual ancestor arose 8000 years BCE, while some evolution models estimate that the differentiation of *Orthocoronavirinae* took place

within the period from 3300 to 2400 BCE. Bats and birds are the main coronavirus reservoirs in the environment. Alpha- and betacoronaviruses are mostly found in bats, whereas delta- and gammacoronaviruses are most common in birds (de Groot et al., 2011).

Coronaviruses are pleomorphic, mostly spherical particles with a lipid bilayer envelope (Figure 1), approximately 120 nm in diameter. The name refers to their common characteristic, the appearance of a 'crown-like' or *corona*-like formation of the spike or S-proteins emerging from the envelope, as seen under two-dimensional electron microscopy. Within the envelope, the helical capsid serves to protect the viral genome, one of the largest (27-34 kb) known viral, single stranded, positive sense RNA molecules. The first two-thirds of the molecule contain an open reading frame that encodes a replicase/transcriptase polyprotein that is post-translationally auto-cleaved into smaller non-structural proteins engaged in viral replication. The remaining open reading frame (10 kb) of the coronavirus RNA encodes four structural proteins, the membrane (M), envelope (E), spike (S) and nucleocapsid (N) proteins (Fehr and Perlman, 2015). The M-protein plays an important role in virion formation during replication and induces the synthesis of neutralizing antibodies and α -interferon (Nguyen and Hogue, 1997). The S-protein is a glycoprotein peplomer that recognizes and attaches to the complementary protein on the host cell. Therefore, the structure of the S-protein defines the tissue tropism of a coronavirus. The majority of alphacoronaviruses attach to the aminopeptidase N, located on the cell surfaces in the small intestine. The exception is strain NL63, which, like most known betacoronaviruses, attaches to the angiotensin-converting enzyme 2 (ACE2), located on the surface of cells primarily in the lungs, but also in the arteries, heart, kidney, and intestines (Hofmann et al., 2005). On the other hand, the MERS coronavirus

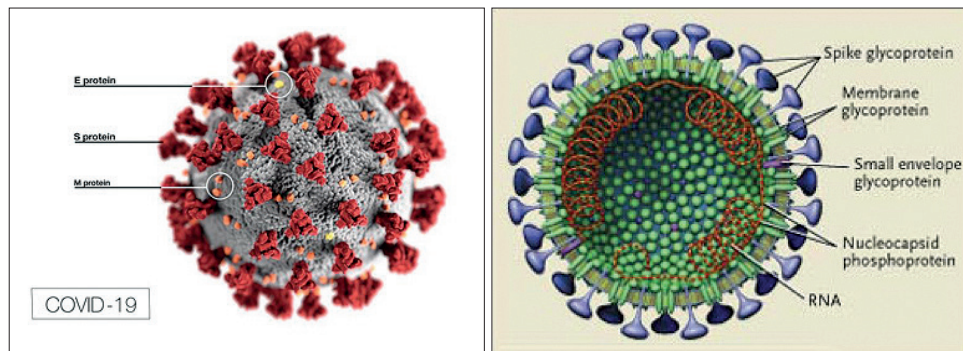


Figure 1. SARS CoV-2 projected by electron microscopy by the Center for Disease Control and Prevention, CDC [Ecker & Higgins, USA] and a schematic presentation of the coronavirus cross section (http://www.ph.ucla.edu/epi/bioter/graphics/sars_holmes2003.jpg).

is a betacoronavirus that attaches to dipeptidyl peptidase-4 receptors, a membrane glycoprotein of most human cells (Raj et al., 2013). Furthermore, S- protein induces the synthesis of neutralizing antibodies and plays a role in viral replication *in vitro* and attenuation *in vivo* (Sato et al., 2011). The function of the E-protein is not fully understood; however, it is involved in the formation of the virion during replication and exocytosis (Ruch and Machamer, 2012). The N-protein protects the viral RNA in the environment and is connected to the RNA in a helical complex that facilitates RNA release after entering the host cell (Sturman et al., 1980). Most betacoronaviruses contain an additional protein on their surface, hemagglutinin esterase (HE), which enables their attachment to sialic acid on host cells receptors. HE enhances neurovirulence in several betacoronavirus strains, such as certain strains of murine hepatitis coronavirus (Kazi et al., 2005; de Groot et al., 2011).

Important coronavirus infections of animals

Bovines

Bovine coronavirus (BCV) is a member of the betacoronavirus genus.

It was recognized as a causative agent of cattle infections in the late 18th century, following its differentiation from equine coronaviruses. It is responsible for causing severe enteritis in calves one week to three months of age, and it also participates in the development of enzootic pneumonia in calves and winter dysentery in cattle. Wild bovines are also susceptible to infections caused by BCV (Haitham, 2018). The infection can be transmitted horizontally, or via the faecal-oral or respiratory routes. A vaccine is commercially available and vaccination of gravid cows and heifers is recommended to prevent the disease in newborn calves. BCV has been reported in cattle in Croatia and has incurred significant economic losses in the cattle industry (Lojkić et al., 2009, 2015).

Swine

Swine have proven to be optimal 'incubators' for coronaviruses and the 21st century has already been marked by novel strains and genotypes that have resulted in the death of millions of swine worldwide, seriously affecting the pig industry. Coronaviruses in swine primarily cause gastrointestinal disorders that may have a lethal outcome, especially in piglets. Most infections are

caused by alphacoronaviruses. The first was described in 1943 and was named **Transmissible gastroenteritis of swine (TGE)**. All age groups can be affected, however the most susceptible are piglets with a lethality of almost 100%. In recent decades, the infection has been sporadic and the last case in Croatia was reported in 1972. The decrease in the number of outbreaks may be the result of the appearance of a novel coronavirus in 1986, the **Porcine respiratory coronavirus (PRC)**. PRC coronavirus has a lower virulence and pathogenicity and is antigenetically closely related to the TGE coronavirus, therefore it is possible that its global spread induced the synthesis of antibodies that ensure immunity against both viruses. The main difference between the TGE and PRV coronaviruses is within the genome region encoding the S-protein, resulting in differences in tissue affinity. During the 1970s, a new coronavirus was described in Europe: **Porcine epidemic diarrhea virus (PEDV)**. It caused clinical disorders similar to those resulting from TGE infection. Despite its global spread, until the appearance of a **novel and highly pathogenic strain** in China (2010), USA (2013) and Europe (2014), it did not arouse broader scientific interest (Wang et al., 2019). It was also recorded in Croatia in 2016 (Brnić et al., 2019, 2020). Implementation of strict biosecurity measures and vaccination with commercially available vaccines halted the spread of the infection. However, this did not end the occurrence of new coronaviruses in swine. During 2016, a new coronavirus was described in China as the causative agent of **Swine acute diarrhoea syndrome (SADS-CoV)**, which had a lethality outcome of 90% (Wang et al., 2019).

Swine are also susceptible to infections with beta- and deltacoronaviruses. One of the longest known infections of animals caused by a coronavirus is

the **Porcine hemagglutinating encephalomyelitis infection (PHE)**, which causes gastrointestinal disorders, and symptoms of the central nervous system. It was first described in 1957 and is still present in the pig industry today, primarily on farms with low biosecurity measures. The most recent outbreaks were recorded in 2001 and 2002 in Canada and 2006 in Argentina (Mora-Díaz et al., 2019). **Porcine deltacoronavirus infection (PDI)** is caused by a novel coronavirus strain described in Asia in 2009. Its effect on swine health was identified in 2014 in the USA when it was recognized as the cause of significant losses in the pig industry. Currently, it has been recorded in Asia, North America and Mexico (Wang et al., 2019). According to evolutionary parameters, it was transmitted from songbirds (*Passeriformes*) to swine, likely due to RNA recombination (Zhang et al., 2016). The susceptibility of birds towards the virus was confirmed by a successful challenge infection of Specific-Pathogen-Free (SPF) chicks. Even though PDI does not have a high lethality rate (less than 50%), due to its partial genome analogy with strains derived from humans, pigs and birds, its zoonotic potential and possibility of host change cannot be excluded (Jung et al., 2015).

Poultry

The first gammacoronavirus infection in poultry, **Infectious bronchitis in poultry (IBR)**, was described in chickens in 1931. The infection causes pathological changes within the upper respiratory tract and the epithelium of the oviduct, resulting in a rapid decrease of egg production (up to 70%). Some strains are nephropathogenic causing severe kidney disease accompanied by high lethality rates. The severity of the disease depends on the viral strain, ambient temperature, and the age, im-

mune status and general condition of chickens. Lethality ranges from 5% to 60%, depending on the occurrence of secondary bacterial infections. IBR is spread worldwide and is prevented by vaccination. However, due to the high mutation rate of the virus, and antigen variations, the efficacy of vaccination depends on the compatibility of the vaccine strain used (Jackwood and de Wit, 2019). At the end of the 1940s, a **gammacoronavirus infection in turkeys (TCoV)** was described in the USA. It was manifested by symptoms of acute atrophic enteritis, such as watery diarrhoea, inappetence and death (5 – 50%). It is also spread in Canada, Europe and Brazil, where it causes sporadic outbreaks that have been increasing in recent decades. Phylogenetic analysis has shown that TCoV has differentiated from the IBR coronavirus due to a recombination of the S-protein gene (Chen et al., 2015).

Cats

Feline coronavirus (FCoV) belongs to the alphacoronavirus genus and causes predominantly mild gastrointestinal infections in cats. It is spread via the faecal-oral route, and can remain infective in the environment. Therefore, most cats that are not kept indoors will be exposed to the virus sooner or later during their lifetime, though only a small number will actually develop symptoms of the disease. FCoV has a high mutation rate and in areas with a high density of cats, the occurrence of RNA recombination is more frequent. The most known FCoV 'mutant' causes **feline infectious peritonitis (FIV)**, a fatal disease of domestic and wild cats of all ages, even though the most sensitive to the infection are young cats up to three years of age. The disease can have an effusive (wet) or non-effusive (dry) form. The acute, wet form is character-

ized by breathing disorders and symptoms followed by the development of ascites, while the chronic, dry form lacks specific signs of disease, but is followed by general signs of infection, loss of sight and neurological disorders. The infection has been known from the 1950s but was officially reported in 1963 (Holzworth, 1963). FIV was described in Croatia in the 1970s and is still present among cats today (Hađina et al., 2015).

Dogs

Canine coronaviruses belong to different genera and vary in their properties, especially virulence. **Canine coronavirus enteritis (CCoV1)** is caused by an alphacoronavirus that shows a tropism towards the epithelium of the small intestine, especially in puppies. The infection is mostly mild, even sub-clinical, and it spreads through the faecal-oral route. It was recorded in 1972 in Germany, and today is spread worldwide. A vaccine is commercially available for the prevention of the disease. **Canine respiratory coronavirus (CCoV2)** was detected in Great Britain in 2003 as the cause of respiratory infections primarily described in puppies as 'kennel cough'. Currently, it is globally widespread. Phylogenetical analysis showed that the causative agent is a betacoronavirus that is genetically highly related (98.8%) to the bovine coronavirus and the human coronavirus strain OC43 (98.4%). Its relationship with CCoV1 is much lower (68.53%) (Erles et al., 2003).

Horses

Equine coronavirus (ECoV) belongs to the betacoronavirus genus and was described in 2010 in two-year-old horses showing general clinical signs of infection, gastrointestinal disorders, and neurological features. It is now known that the infection has a mild course and that all age categories of equines can be

affected. The disease has been reported in the USA, Japan and Europe (Pusterla et al., 2013).

Rabbits

Rabbit enteric coronavirus infection was described in the 1980s in rabbits six to eight weeks of age. The infection has a mild course and primarily affects the gastrointestinal tract. A more severe coronavirus disease in laboratory rabbits is **Pleural effusion disease**. The target organ of the virus is the heart, resulting in cardiomyopathic changes. It is assumed that the virus, an alphacoronavirus, was introduced iatrogenically into laboratories. Recently, a novel betacoronavirus has been detected in rabbits in China (Lau et al., 2012).

Murines

Murine coronavirus is a betacoronavirus (MCoV) that causes primarily hepatitis characterized by a high mortality rate in mice. Some strains may lead to progressive demyelinating encephalitis in laboratory mice. MCoV has been used as a model for coronavirus pathogenicity research and studies on viral replication. In human medicine, it has been used for decades as a model for multiple sclerosis research (Tirota et al., 2010).

Coronavirus infections in humans

Coronaviruses were first isolated from humans in the 1950s. Since then, they have caused mild infections of the upper or lower respiratory tract, with a seasonal character predominant in winter and early spring. The first described coronavirus in humans was **strain OC43** of the betacoronavirus genus. The strain is genetically highly related to bovine coronavirus. Currently, four genotypes have been recognized, the

original genotype A, genotypes B and C that differentiated in the 1980s, and genotype D that developed in the 1990s as a result of recombination of genotypes B and C. At the turn of the 21st century, a novel betacoronavirus was isolated from humans – **strain HKU1**, the cause of bronchitis that in some cases can lead to pneumonia. HKU1 was isolated from a patient in Hong Kong in 2005, though further investigation found the virus in an archive sample from a patient with severe pneumonia in 2003 (Lau et al., 2006). HKU1 was also detected in the USA where it was named HCoV-NH (New Haven), and in Europe (Esper et al., 2006). Phylogenetic analysis has shown high genetic relation with the murine coronavirus. Except betacoronaviruses, common colds in humans can also be the result of alphacoronavirus infections. The most frequent strain of the common cold is **strain 229E**, which is also derived from bats. In addition to mild respiratory infections, 229E can cause pneumonia. A similar pathogenicity has been observed in **strain NL63**. Recent research has shown a connection of strain NL63 with hoarseness and even Kawasaki disease in children (Fielding, 2011).

SARS

In 2002, a respiratory infection in humans was described in China that then spread throughout Eastern Asia (Chan-Yeung and Xu, 2003). Cases of the disease were subsequently reported in Canada (Toronto) and USA (New York, San Francisco). The causative agent of the disease was a betacoronavirus, SARS CoV-1. During the epidemic, 8442 people were infected with a fatal outcome in 916 cases (11%). Patients over the age of 50 years proved to be more susceptible to infection, whereas those under 30 years of age were more resistant. In June 2003, the World

Health Organization (WHO) declared the end of the epidemic. However, several sporadic cases of SARS caused by SARS CoV-1-like viruses have been reported since. The natural reservoir of the virus was found to be the horseshoe bat (*Rhinolophidae*). However, the virus was transmitted to humans by the Asian palm civet (*Paradoxurus hermaphroditus*). Retrospectively, SARS CoV-1 was isolated from raccoon dogs (*Nyctereuteus* sp.), ferrets (*Melogale* spp.) and domestic cats (Lau et al., 2006). The virus attaches to the ACE2 receptors of host cells, mainly the alveolar type II cells of the lungs, though it can also be detected in the epithelium of arteries, in the heart, kidney and small intestine. SARS is characterized by the development of fibrinous pneumonia, possible osteoporosis and femoral necrosis, with clinical manifestation similar to influenza. The incubation is four to six days, rarely one and a maximum of 14 days. The rapid disappearance of the disease astonished epidemiologists worldwide. Even so, SARS revealed the possibility of the appearance of novel strains of coronaviruses that may threaten all humanity.

MERS

MERS was recorded in Saudi Arabia in 2012, after which it spread throughout the Arabian Peninsula. It was also diagnosed in people travelling from the Arabian Peninsula to the USA, Africa, Europe and Asia (Zumla et al., 2015). The causative agent of the disease was discovered to be a betacoronavirus (MERS CoV). Nowadays, the virus is divided into two groups, the first isolated strains belong to group A, whereas novel strains belong to group B (Chu et al., 2014). MERS CoV is not genetically highly related to SARS CoV-1, though it shows high genetical analogy with strains isolated from bats, indicating

they are its natural reservoirs. Further research showed that the Arabian camel (*Camelus dromedarius*) was the source of infection for humans, even though the transmission route from camels to humans is still unknown. MERS CoV in camels causes the 'camel flu'. In humans, MERS is manifested by severe respiratory disorders, with a fatal outcome in one-third (36%) of infected patients. According to the available data, 2468 people were infected by MERS CoV, with 851 deaths (WHO, 2019). Less frequently, gastrointestinal disorders can also appear. Horizontal transmission (person to person) is very rare and is reported as a hospital acquired infection (Assiri et al., 2013). The lack of human transmission of MERS limits the spread of disease, and therefore MERS is not on the list of viral diseases that can threaten humanity. Currently, there are no available vaccines against SARS or MERS.

COVID-19

COVID-19 is a respiratory infection of humans caused by the betacoronavirus SARS CoV-2, a variant of the strain SARS CoV-1 (Zhu et al., 2020). The main reservoir of the virus is the bat, though no animal species have yet been recognized as the intermediate transmitter of SARS CoV-2 to humans. After the first report of the disease in Wuhan, China in December 2019, the WHO pronounced COVID-19 a Public Health Emergency of International Concern, and pronounced a pandemic on 11th of March 2020. At the time of press of this article, officially over 4.8 million people have been infected by SARS CoV-2, with an average lethality rate of 6.7%. The severity of the disease and its outcome largely varies depending on patient age, general condition and the presence of risk factors (hypertension, diabetes and heart diseases). Younger people are more re-

silent to infection, whereas in patients over 70 years of age, lethality increases up to 15% (Hui et al., 2020). SARS CoV-2 is easily transmitted from person to person, mostly due to aerosols and droplets released by coughing, and can also be transmitted indirectly through contact with contaminated materials and surfaces. The virus remains infective on copper surfaces for 18, cardboard for 55, stainless steel for 90 and plastic for 100 hours (van Doremalen et al., 2020). SARS CoV-2 has been detected in faeces in 54% of patients during the course of the disease, as well as in reconvalescents even after the virus is no longer detected in the nasopharyngeal mucosa, indicating the possibility of faecal-oral spread (Gu et al., 2020). Vertical transmission has not been confirmed (Chen et al., 2020). The incubation of COVID-19 is five to six days, maximum 14 days, though most subjects (97%) develop signs of the disease as late as 11.5 days post infection. About 20% of infected subjects will show no signs of the disease but are considered important carriers/transmitters (Bai et al., 2020). High population density in small areas, closed rooms, and public transport are considered risk factors of viral transmission. Therefore, personal protection measures (hand and body hygiene, required distances, auto-isolation, working from home, masks, etc.) and public protection measures (bans of social gatherings, public transport, closing schools and kindergartens, cancelling cultural events, intercity transport, etc.) are highly recommended and implemented. The aim is to flatten the epidemic curve as much as possible to prevent a rapid increase of the number of infected persons and their contacts in a limited timeframe. Only by constraining movement will viral transmission be reduced from $R_0=2.35$ to $R_0=1.05$ (Kucharski et al., 2020).

Clinically, COVID-19 is similar to influenza, accompanied by gastroin-

testinal and cardiovascular disorders. Other symptoms, such as anosmia, have been reported (Iacobucci, 2020). Severe cases describe laboured breathing, chest pain and hypoxia. Spontaneous coagulation disorders and cytokine storm can occur. Following progressive pneumonia, acute respiratory distress syndrome (ARDS) and multi-organ failure can arise, resulting in death (Hui et al., 2020). The seroconversion dynamics have not yet been fully elucidated, though a challenge infection and re-infection in Macaque monkeys resulted in the occurrence of active immunity. COVID-19 diagnosis is based on the epidemic situation, clinical signs, X-ray and CT scans, blood testing and detection of the viral RNA in nasopharyngeal swabs by Reverse Transcription Polymerase Chain Reaction (PCR) methodology. The recommended methods for diagnosing are real time PCR protocols (Centers for disease control and prevention, CDC, 2020). Recently, quick tests for detecting COVID-19 have been approved by WHO. Commercially available serological tests have also been developed. Previously, there were no specific prevention methods or therapies listed for COVID-19. Even if a vaccine were to be developed soon, its active administration would not be possible before 2021. However, extreme scientific capacities are involved in investigating different models of inactivated and genetically modified vaccines based primarily on the S-protein. Due to the lack of an effective vaccine, the focus of current scientific research is investigating known or novel chemotherapeutics for treating the disease. Four have already been used in clinical trials: remdesivir (nucleotide analogue used for Ebola, Marburg fever, SARS and MERS), chloroquine and hydroxychloroquine (anti-malarial drugs), lopinavir/ritonavir (anti-HIV treatment) and lopinavir/ritonavir combined with β -in-

terferon (Kupferschmidt and Cohen, 2020). Recently, ACE2 receptor inhibitors are being investigated for the prevention or treatment of COVID-19. Another option investigated is the use of passive immunization by convalescent sera that showed good results in SARS treatment.

To date, there has been no evidence of SARS CoV-2 naturally infecting animals; however, ACE2 receptors with similar configuration as human ACE2 receptors are found in some animal species, theoretically raising the question of possible susceptibility (Wan et al., 2020). This hypothesis should be challenged, since SARS CoV-2 RNA was detected in two dogs in Hong Kong, a cat in Belgium and a tiger from a zoo in New York. The owners of the dogs and cat, and the tiger trainer all tested positive for SARS CoV-2 (WHO, 2020). Therefore, even though no reasonable connection was found, a thorough investigation of animals as potential virus carriers is needed. Until then, COVID-19 positive owners of animals should be cautious because they can transmit SARS CoV-2 to their pets or contaminate them. Due to the initiative of the Croatian Ministry of Agriculture, Directorate for Animal Health and Food Safety, in collaboration with the Croatian Veterinary Institute and Veterinary Faculty, University of Zagreb, an Action Plan has been developed to ensure preparedness in case testing of animals is needed.

COVID-19 has altered our comprehension of society in general. Countries that have been struck by the disease have reported the appearance of xenophobia, coronophobia, depression and despair due to loneliness and the feeling of hopelessness. COVID-19 has also negatively impacted the economy. The consequences of the pandemic will be calculated and visible only after it ends.

In conclusion, coronavirus infections, especially COVID-19, have changed the

perception of life and the world marking the 21st century, forever.

References

1. ASSIRI, A., M. C. GEER, A. PERL et al. (2013): Hospital outbreak of Middle East respiratory syndrome coronavirus. *N. Engl. J. Med.* 369, 407–416.
2. BAL, Y., L. YAO, T. WEI, F. TIAN, D. Y. JIN, L. CHEN and M. WANG (2020): Presumed asymptomatic carrier transmission of COVID-19. *JAMA*. Doi:10.1001/JAMA.2020.2565.
3. BRNIĆ, D., I. ŠIMIĆ, I. LOJKIĆ, N. KREŠIĆ, A. JUNGIĆ, D. BALIĆ, M. LOLIĆ, D. KNEŽEVIĆ and L. B. HEN (2019): The emergence of porcine epidemic diarrhoea in Croatia: molecular characterization and serology. *BMC Vet. Res.* 15, 249.
4. BRNIĆ, D., I. ŠIMIĆ, A. KOVAČEVIĆ and N. KREŠIĆ (2020): Viral gastroenteritis in pigs: current knowledge and challenges. *Vet. stn.* 51, 53–66. (In Croatian).
5. CENTERS FOR DISEASE CONTROL AND PREVENTION (2020): Real-Time RT-PCR Panel for Detection 2019-nCoV. 29 January 2020.
6. CHAN-YEUNG, M. and R. H. XU (2003): SARS: epidemiology. *Respirology (Carlton, Vic.)* 8, Suppl: 9–14.
7. CHEN, Y.-N., W. CHING and L. TSANG (2015): Turkey coronavirus: an updated review. *Taiwan Vet. J.* 41, 1–10.
8. CHEN, H., J. GUO, C. WANG, F. LUO et al. (2020): Clinical characteristics and intrauterine vertical transmission potential of COVID-19 infection in nine pregnant women: a retrospective review of medical records. *Lancet* 395, 809–815.
9. CHU, D. K. W., L. M. POON, M. M. G. GOMAA et al. (2014): MERS Coronaviruses in Dromedary Camels, Egypt. *Emerg. Inf. Dis.* 20, 1049–1053.
10. DE GROOT, R. J., S. C. BAKER, R. BARIC et al. (2011): Family Coronaviridae. King, A., Lefkowitz, E., Adams, M. J., Carstens E. B. (Eds.), *Virus Taxonomy, Ninth Report of the International Committee on Taxonomy of Viruses*, Elsevier, pp. 806–828.
11. ESPER, F., C. WEIBEL, D. FERGUSON, M. L. LANDRY and J. S. KAHN (2006): Coronavirus HKU1 Infection in the United States. *Emerg. Inf. Dis.* 12, 775–779.
12. ERLES, K., C. TOOMEY, H. W. BROOKS and J. BROWNLIE (2003): Detection of a group 2 coronavirus in dogs with canine infectious respiratory disease. *Virology* 310, 216–223.
13. FIELDING, B. C. (2011): Human coronavirus NL63: a clinically important virus? *Fut. Microbiol.* 6, 153–159.
14. FEHR, A. R. and S. PERLMAN (2015): Coronaviruses: an overview of their replication and pathogenesis. *Meth. Mol. Biol.* 1282, 1–23.
15. GU, J., B. HAN and J. WANG (2020): COVID-19: Gastrointestinal manifestations and potential fecal-oral transmission. *Gastroenter.* doi:10.1053/j.gastro.2020.02.054.

16. HAĐINA, S., A. BECK, V. STEVANOVIĆ i sur. (2015): Zarazni peritonitis mačaka (Feline infectious peritonitis). *Hrv. vet. vjesnik* 23, 51–60.
17. HAITHAM, M. A. (2018): Bovine-like coronaviruses in domestic and wild ruminants. *Anim. Health Res. Rev.* 19, 113–124.
18. HOFMANN, H., K. PYRC, L. VAN DER HOEK, M. GEIER, B. BERKHOUT and S. POHLMANN (2005): Human coronavirus NL63 employs the severe acute respiratory syndrome coronavirus receptor for cellular entry. *Proceedings of the National Academy of Sciences of the United States of America*, 102, 7988–7993.
19. HOLZWORTH, J. (1963): Some important disorders of cats. *Cornell Vet.* 53, 157–160.
20. HUI, D. S., I. E. AZHAR, T. A. MADANI et al. (2020): The continuing 2019-nCoV epidemic threat of novel coronaviruses to global health – The latest 2019 novel coronavirus outbreak in Wuhan, China. *Int. J. Infect. Dis.* 91, 264–266.
21. IACOBUCCI, G. (2020): Sixty seconds on anosmia. *B. M. J.* 368, m1202. doi:10.1136/bmj.m1202.
22. JACKWOOD, M. W. and S. DE WIT (2019): Infectious Bronchitis. Eds.: David E. Swayne Martine Boulianne Catherine M. Logue Larry R. McDougald Venugopal Nair David L. Suarez Sjaak de Wit Tom Grimes Deirdre Johnson Michelle Kromm Teguh Yodiantara Prajitno Ian Rubinoff Guillermo Zavala. *Diseases of Poultry*, 14th Edition. 2020 by John Wiley & Sons, Inc. <https://doi.org/10.1002/9781119371199.ch4>.
23. JUNG, K., H. HU, B. EYERLY, Z. LU, J. CHEP-NGENO and L. J. SAIF (2015): Pathogenicity of 2 porcine deltacoronavirus strains in gnotobiotic pigs. *Emerg. Infect. Dis.* 21, 650–654.
24. KAZI, L., A. LISSEBERG, R. WATSON, R. J. DE GROOT and S. R. WEISS (2005): Expression of hemagglutinin esterase protein from recombinant mouse hepatitis virus enhances neurovirulence. *J. Virol.* 79, 15064–15073.
25. KUCHARSKI, A. J., T. W. RUSSELL, C. DIAMOND et al. (2020): Early dynamics of transmission and control of COVID-19: a mathematical modelling study. *Lancet Inf. Dis.* doi:10.1016/S1473-3099(20)30144.
26. KUPFERSCHMIDT, K. and J. COHEN (2020): WHO launches global megatrial of the four most promising coronavirus treatments. *Science AAAS*. Retrieved 23 March 2020.
27. LAU, S. K. P., P. C. Y. WOO, C. C. Y. YIP et al. (2006): Coronavirus HKU1 and Other Coronavirus Infections in Hong Kong. *J. Clin. Microb.* 44, 2063–2071.
28. LAU, S. K. P., P. C. Y. WOO, C. C. Y. YIP et al. (2012): Isolation and Characterization of a Novel Betacoronavirus Subgroup A Coronavirus, Rabbit Coronavirus HKU14, from Domestic Rabbits. *J. Virol.* 86, 10, 5481–5496.
29. LOJKIĆ, I., T. BEDEKOVIĆ, Ž. ČAČIĆ i M. LOJKIĆ (2009): Dokaz i izdvajanje goveđeg koronavirusa uzročnika neonatalnog proljeva teladi. *Vet. strn.* 40, 257–262.
30. LOJKIĆ, I., N. KREŠIĆ, I. ŠIMIĆ and T. BEDEKOVIĆ (2015): Detection and molecular characterisation of bovine corona and toroviruses from Croatian cattle. *BMC Vet. Res.* 11, 202.
31. MONCHATRE-LEROY, E., F. BOUÉ, J. M. BOUCHER, C. RENAULT, F. MOUTOU, M. A. R. GOUILH and G. UMHANG (2017): Identification of Alpha and Beta Coronavirus in Wildlife Species in France: Bats, Rodents, Rabbits, and Hedgehogs. *Viruses* 9, 12.
32. MORA-DÍAZ, J. C., P. E. PIÑEYRO, E. HOUSTON, J. ZIMMERMAN and G. GIMÉNEZ-LIROLAL (2019): Porcine Hemagglutinating Encephalomyelitis Virus: A Review. *Front. Vet. Sci.*, doi.org/10.3389/fvets.2019.00053.
33. NGUYEN, V. P. and B. G. HOGUE (1997): Protein interactions during coronavirus assembly. *J. Virol.* 71, 9278–9284.
34. PUSTERLA, N., S. MAPES, C. WADEMAN, A. WHITE, R. BALL, K. SAPP, P. BURNS, C. ORMOND, K. BUTTERWORTH, J. BARTOL and K. G. MAGDESIAN (2013): Emerging outbreaks associated with equine coronavirus in adult horses. *Vet. Microb.* 162, 228–231.
35. RAJ, V. S., V. S. H. MOU, S. L. SMITS et al. (2013): Dipeptidyl peptidase 4 is a functional receptor for the emerging human coronavirus-EMC. *Nature* 495, 251–254.
36. RUCH, T. R. and C. E. MACHAMER (2012): The coronavirus E protein: assembly and beyond. *Viruses* 4, 363–382.
37. SATO, T., N. TAKEYAMA, A. KATSUMATA, K. TUCHIYA, T. KODAMA and K. KUSANAG (2011): Mutations in the spike gene of porcine epidemic diarrhea virus associated with growth adaptation in vitro and attenuation of virulence in vivo. *Vir. Gen.* 43, 72–78.
38. STURMAN, L. S., K. V. HOLMES and J. BEHNKE (1980): Isolation of coronavirus envelope glycoproteins and interaction with the viral nucleocapsid. *J. Virol.* 33, 449–462.
39. TIROTTA, E., K. S. CARBAJAL, C. S. SCHAUMBURG, L. WHITMAN and T. E. LANE (2010): Cell replacement therapies to promote remyelination in a viral model of demyelination. *J. Neuroim.* 224, 101–107.
40. VAN DOREMALEN, N., T. BUSHMAKER, D. H. MORRIS et al. (2020): Aerosol and Surface Stability of SARS-CoV-2 as Compared with SARS-CoV-1. *N. Engl. J. Med. Massach. Med. Soc.*, doi:10.1056/nejmc200497.
41. WAN, Y., J. SHANG, R. GRAHAM, R. S. BARIC and F. LI (2020): Receptor recognition by novel coronavirus from Wuhan: an analysis based on decade-long structural studies of SARS. *J. Virol.*, doi: 10.1128/JVI.00127-20.
42. WANG, Q., A. N. VLASOVA, S. P. KENNEY and L. J. SAIF (2019): Emerging and re-emerging coronaviruses in pigs. *Curr. Opin. Virol.* 34, 39–49.

43. WORLD HEALTH ORGANIZATION (2019): Middle East Respiratory Syndrome Coronavirus (MERS-CoV). Archived from the original on 2019-10-18. Datirano 2019-12-10.
44. WORLD HEALTH ORGANIZATION (2020): Coronavirus disease 2019 (COVID-19): situation report, 29. hdl:10665/331118.
45. ZHANG, J. (2016): Porcine deltacoronavirus: Overview of infection dynamics, diagnostic methods, prevalence and genetic evolution. *Vir. Res.* 226, 71–84.
46. ZHU, N., D. ZHANG, W. WANG et. al. (2020): A Novel Coronavirus from Patients with Pneumonia in China. *N. Engl. J. Med.* 382, 727–733.
47. ZUMLA, A., D. S. HUI and S. PERLMAN (2015): Middle East respiratory syndrome. *Lancet* 386, 995–1007.

Koronavirusi – virusi koji obilježavaju 21. stoljeće

Dr. sc. Lorena JEMERŠIĆ, dr. med. vet., znanstvena savjetnica, naslovna izvanredna profesorica, Hrvatski veterinarski institut, Zagreb, Hrvatska

Koronavirusi su uzročnici respiratornih, gastrointestinalnih i neuroloških infekcija u sisavaca i ptica. Značajka je koronavirusa visoka mutacijska stopa koja može rezultirati promjenom patogenosti, tkivnog tropizma i/ili domaćina. Premda su znanstvenoj javnosti poznati već desetljećima, potakli su posebno zanimanje istraživača tek u 21. stoljeću nakon pojave emergentnih koronavirusnih infekcija epidemijskih razmjera u ljudi, ali i životinja, naročito svinja. Najznačajnije su emergentne infekcije u ljudi teški akutni respiratorni sindrom (SARS) koji je obilježio 2002. godinu i srednje-istočni respiratorni sindrom (MERS) koji se pojavio 2012. godine. Obje su infekcije životinjskog podrijetla, a očituju se teškom pneumonijom u ljudi s letalitetom od 11 % (SARS) i 36 % (MERS). Danas smo suočeni s jednom od najvećih

epidemija u povijesti čovječanstva, pandemijom COVID-19. Uzročnik je koronavirus, inačica virusa uzročnika SARS, a prenosi se izravno s čovjeka na čovjeka. Nije poznato je li u transmisiji virusa na ljude sudjelovala i životinja. Do dana tiskanja ovog članka je infekcija ustvrđena u više od 4,8 milijuna ljudi sa smrtnim ishodom u preko 320 000 ljudi. U Hrvatskoj je zahvaljujući Nacionalnom stožeru civilne zaštite za COVID-19 i mjerama koji je stožer preporučio i uveo, infekcija još uvijek u granicama mogućnosti pružanja potrebite skrbi. Ovaj članak opisuje koronavirusne infekcije u životinja i ljudi te prikazuje kako su novi sojevi koronavirusa već sada obilježili 21. stoljeće i možda zauvijek promijenili svijet.

Ključne riječi: *koronavirusi, životinje, ljudi, COVID-19*