



## **SARS-COV-2 From Veterinary Medicine Perspective**

An interview with

**Prof. Dr. Nicola Decaro**

Full Professor of Infectious Diseases of Animals

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[Alireza Sazmand] Today, there is a big and common problem in all around the world. An unprecedented crisis as result of a new viral infection, COVID-19. Over 3 million people got infected and more than 200,000 of them died. This virus again highlights the importance of zoonotic diseases, which are transmitted from animals to humans and vice versa.

Today I host Dr. Nicola Decaro, Full Professor of Infectious Diseases of Animals, from the Department of Veterinary Medicine, at the University of Bari, Italy. Dr. Decaro is an internationally recognized expert in Corona viruses. Professor Decaro welcome to our meeting!

[Nicola Decaro] Thank you Alireza. And I just would say hello to all Iranian colleagues and Iranian people. I remember that I just was in your county a couple of years ago, and it was a very important and amazing experience for me.

[Alireza Sazmand] Thank you. It was a great pleasure for us to have you here in Bu-Ali Sina University of Hamedan. But, we already know that in the last two decades there were at least two outbreaks related to coronaviruses, SARS and MERS, but they were not as extensive as COVID-19? What does make this virus different?

[Nicola Decaro] First of all, we must know that SARS-CoV-2 is not the first human coronavirus with an increase pathogenicity that was able to be transmitted from animals to humans to adapt to human species: we had two epidemics in the past, SARS and MERS that fortunately, they did not lead to pandemics.

SARS emerged in 2002 and the virus was eradicated in 2003, and MERS emerged in 2012, and some minor outbreaks are still running in Saudi Arabia and Middle East. These two epidemics were characterized by higher mortality rates. SARS had a fatality rate of about 12%, 11.6% to be more precise,



and MERS had 30% fatality rate, which means that infected patients who developed very severe respiratory disease had to be hospitalized and they sometimes died and this is important to understand why SARS-CoV and MERS-CoV did not become pandemic viruses while SARS-CoV-2 became a global concern.

SARS-CoV-2 is characterized by low fatality rates, maybe less than 2% because we should know that the official reports do not take into account the real number of infected people because for example in Italy and I suppose also in Iran not all suspected people are sampled to do PCR test, since we have a limited quantity of reagents and of people working in labs and this of course limits the number of samples that can be processed every day, so maybe our fatality rate is not so high and in the epidemiology of SARS-CoV-2 there is an important role of asymptomatic people, a lot of people may get infected but they do not develop symptoms of the disease and they show low clinical signs.

This is the way how the virus can circulate and make the virus difficult to eradicate, because if I get sick I am forced to stay at home or sometimes to be hospitalized, but if I am asymptomatic, I can go around and infect a lot of other people; so the success of this new virus is related to its lower pathogenicity with respect to SARS and MERS.

Of course all these three viruses originated from animals and we know for example that SARS-CoV originated from bats through an intermediate host which was represented by wild carnivores included palm civets and also, raccoon dogs, while MERS-CoV emerged from bats and it adapted to humans through an intermediate host which was represented by dromedary camels, and now we have this very important pandemic to fight against and we have to concentrate all our efforts to fight this pandemic.

[Alireza Sazmand] Dr. Decaro, let's talk more about animals' role. There are some reports about isolation of the SARS-CoV-2 from dogs, cats, minks and even tigers. It is possible that some pet owners decide to get rid of their pet animals, because people may be afraid of carriage of the virus by them.

Should we worry about transmission of SARS-CoV-2 from animals to humans, in particular pets? What is the responsibility of pet owners in this situation?



[Nicola Decaro] Unfortunately, unjustified alarmism was generated by some reports of sporadic infections of dogs and cats throughout the world and at the moment with the last cat case in Paris which was yesterday we have just 8 pets infected with SARS-CoV-2, at least confirmed to be infected with SARS-CoV-2, with respect to more than 3 million people that were infected and in all these cases of pet infection there was a close contact with infected human patients.

So, we believe that cats and dogs may be sporadically infected by the virus, but they should not represent a real threat to humans nor have any important role, at least based on current knowledge, in transmission of the virus to human beings. The first cases were reported in Hong Kong, there were two dogs, a 17-year-old Pomeranian and a 2-year-old German shepherd dog and these dogs were living in a close contact with their infected owners. Then, we had another dog case in the US, North Carolina. The first two cases in Hong Kong were completely asymptomatic, while the case in North Carolina was symptomatic and displayed some respiratory signs.

The situation is more important for cats. To date, we have a couple of cases in New York, a cat in Hong Kong, a new cat case in Paris, France, another cat case, the first one in Brussels, Belgium. These cases were characterized by some clinical respiratory signs, so unlike dogs, cats seem to show some respiratory signs and respiratory distress, but these cats all recovered from the disease and more importantly with respect to dogs, cats are able to shed higher viral titers through their respiratory secretions. There was also an experiment in China. This experimental infection demonstrated that dogs are infected by SARS-CoV-2 experimentally inoculated, but they do not develop clinical signs, they shed very low titers, so they cannot infect other animals and humans, while cats not only get infected but they can display some respiratory signs and more importantly they are able to shed higher viral titers with their respiratory secretions and in some instances these infected cats were able to transmit the infection to in-contact cats. So, this is a problem.

And apart from cats and dogs, we had an outbreak in a zoo in New York among tigers and lions. Maybe there was a tiger, which was an index case, and it was exposed to a human guardian who was infected by the virus and maybe the tiger was able to transmit the infection to some of the in-contact tigers and lions.



More recently, we had two important outbreaks in farmed mink in the Netherlands, and we do not know so much about these outbreaks but we can imagine that they were important outbreaks since very important restriction measures were taken by the authorities to control these outbreaks.

In conclusion, what I can say now is that, yes some of animals and pets can be infected by the virus, but to the best of our current knowledge they cannot play an important role in the transmission of the infection to humans. This virus is completely adapted to humans and is able to be transmitted from human to human via the respiratory route, so that this virus has no need to use an alternative host.

[Alireza Sazmand] Can the virus infect pet birds or there is no worry about it?

[Nicola Decaro] No, it is unlike that the virus can infect pet birds or avian species. Birds have their own coronaviruses that belong to coronavirus genera which are very distantly related to the new one, which is a beta-coronavirus and we should just remember that the natural reservoirs for coronaviruses are bats and birds, but bats are reservoirs for alphacoronavirus and betacoronaviruses, while birds are reservoirs for gammacoronavirus and deltacoronaviruses circulating among wild birds.

The most known virus of birds is infectious bronchitis virus of poultry, a gammacoronavirus which has been known for more than a century, while deltacoronaviruses were recently discovered in wild birds and they are circulating in wild birds, but there were some spillover events from wild birds to mammals. For example, there is a porcine deltacoronavirus, which derived from an avian deltacoronavirus, but birds can be unlikely infected by this new virus because it is completely different from bird coronaviruses.

[Alireza Sazmand] As the last question, would you please tell us how veterinarians can play a positive role in this outbreak?

[Nicola Decaro] Veterinarians can play an important role in the context of One Health medicine. We have known coronaviruses for a long time with respect human medicine. I told you that the first animal coronavirus to be known, was infectious bronchitis virus of poultry. Another important virus at the veterinary level is feline infectious peritonitis (FIP) virus, which is able to cause an important fatal disease in cats.



These viruses or at least the diseases caused by these viruses have been known since more than one century and we have a lot of experiences with vaccines and antivirals used against coronavirus infections. For example, for infectious bronchitis virus of poultry we have very effective vaccines available.

They are usually modified live vaccines that in some circumstances are also used through spray administration to chickens just after their birth and this gives us an important lesson, since for coronaviruses that are able to infect the respiratory mucosa like SARS-CoV-2 or avian coronaviruses (IBV) or the intestinal mucosa like swine enteric coronavirus, canine and feline coronavirus, the most important immune response is mediated by the mucosal immunity.

Antibodies of the IgA class represent the first barrier against the virus and block the virus, preventing virus entry into the cells and vaccines against IBV are able to induce very high amount of IgA and the same is for experimental vaccines that were developed in veterinary medicine against canine coronavirus or for example swine coronavirus, but these vaccines are not available in the market.

Another important lesson from veterinary medicine is that coronaviruses are very particular viruses in term of their immunogenicity. Usually they are not good immunogenic viruses and sometimes they can induce a particular phenomenon which is known as ADE (antibody dependent enhancement). Due to this phenomenon sometimes vaccines are not only not effective, but they can be also dangerous.

For example, we know this phenomenon for FIP. We do not have vaccine available in the market, because the experiment that was carried out in the past demonstrated that vaccinated cats developed subneutralising antibodies that were cryophilic and in case of contact with the virus these antibodies are not able to neutralize the virus, but they help the virus entry into the target cells so enhancing and exacerbating the disease caused by the virus.

A similar situation occurred with SARS coronavirus vaccine, the virus related to the 2002 epidemic, for which researchers were not able to develop an effective and safe vaccine, because this phenomenon, the antibody dependent enhancement, occurred even with SARS vaccines when these vaccines were tested in animals especially in non-human primates.



Another lesson from veterinary medicine is the use of antivirals; of course there are a lot of experimental trials with antivirals with FIP which is the most important disease caused by coronaviruses in cats and the experience of veterinary medicine tell us that there are some antivirals that could be effective against coronavirus diseases.

For example, there are some protease inhibitors which are related to the human drugs Lopinavir, and these protease inhibitors are able to block the so-called 3C-like protease, which is essential for the virus to cleave the polyprotein produced during the first phase of replication. These protease inhibitors were found to be effective against FIP but more recently there are another drug class which was found to be effective against FIP and also against SARS-CoV-2 and these are the nucleoside analogs.

The nucleoside analog drug in human medicine is called Remdesivir, and is able to replace the natural nucleosides during the synthesis of novel genomic RNA, so that the RNA replicase, an RNA dependent-RNA polymerase, is able to incorporate this wrong nucleotide into the new RNA molecule and in this case the synthesis of genomic RNA is blocked. We had very recently good results for FIP, but human doctors are having good results with Remdesivir which is the human drug for these nucleotide analogues.

So, we should think about One Health Medicine: in this context the health of humans, animals and environment is considered interconnected. We should speak about the One Health concept also for the measures that should be taken to prevent future pandemics caused by coronaviruses because we know that this pandemic occurring in the last decades were originated by the transmission of viruses from a wild animal host to humans and this was likely even for SARS-CoV-2.

I know that there are some conspiracy theories about the origin of the virus but, taking into account the experiences with SARS-CoV and MERS-CoV and other less pathogenic human coronaviruses that are now endemic in the human population, we know that coronaviruses are very prone to cross the species barriers and our behavior in the last decades has facilitated this jump because if we still have the wet markets in Asia and Africa, where you can see animals of different species that are sold dead or alive, and slaughtered at the place, this creates a fantastic situation for viruses, especially coronaviruses, to be transmitted among different animals and from animals to humans.



So, the first measure to take in this One Health concept is to ban these wet markets or at least to better regulate these markets and another thing is to reduce deforestation and anthropization of the environment, since in the last decades we have reduced the natural habitats for some wild species. This has facilitated closer contact between the wild species and human beings and this close contact is the key to understanding why we have coronaviruses that jumped cross barriers and are able to adapt to human species being, to be transmitted among human, so that is why the role of vets is important.

[Alireza Sazmand] Well, thank you Professor Decaro for speaking with us today, we highly appreciate that. Have a nice day!

[Nicola Decaro] I hope so Alireza, I hope so. So, my best wishes to all Iranian people. Bye. Bye-bye!

[Alireza Sazmand] Bye!

And thank you listeners out there for joining us.

I'm Alireza Sazmand for Bu-Ali Sina University of Hamedan, Iran.

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