



SARS-CoV-2 in Animals-Evolution and Associated Risks

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Abstract

It is emphasized that the medical staff is subject to a maximum risk, and so it is. Due to permanent contact with potentially contaminated patients, carriers may be infected or carry the virus. In this context, it is highlighted that veterinarians may have a high risk of infection. In the world literature, and international epizootic forums, it reports and publishes information on the presence of COVID19 in animals. Some animals have been confirmed with this virus, generally pets that come from families where there have been several carrier members. Pets that tested positive showed clinical signs of dyspnea, fever, impaired general condition, difficulty breathing. The International Office of Epizootics cites a few scattered cases in which they tested positive in laboratory tests, but their study led to some findings essential for understanding the epidemiology of the new disease. Obviously, in the case of dogs and cats found positive, the SARS-CoV-2 infection was linked to the situation of the owners, who were also positive. The thorough investigations revealed that in fact dogs and cats had not been the source of infection of the owners, but, they contracted the infection from their owners. And more clearly, it was not humans who turned out to be victims of animals, but vice versa. Among pets, cats and ferrets are the most blamed, they were also present in clinical manifestations and may possibly transmit the disease to other cats. Dogs don't seem to be as sensitive. Veterinary medicine is in this situation caught in the middle: on the one hand it is obliged to investigate the possible source of animal infection, using its own and specific means of investigation, but on the other hand it has the professional duty to defend the innocence of some animal species, unjustly suspected and possibly incriminated. Let's not forget that Covid 19 is a syndrome not a specific disease, and therefore clinical confusions are not impossible.

Keywords: Animal Health; COVID-19; Cured or Denied; Veterinary Association

Introduction

This paper is a review of the current literature and of the officially reported data of the main institutions responsible for the evolution of the Covid pandemic19.

The national and international associative structures of veterinarians actively monitor the evolution of the COVID-19 pandemic and the effects it has on human society as a whole. Thus, the Federation of European Veterinarians (FVE) is in regular contact with WHO, OIE, ECDC and the EU, and

the World Veterinary Association (WVA) and the World Organization for Animal Health (OIE) draw attention to the roles and responsibilities of the veterinary profession for public health.

It is known that infections with viruses of the family coronavirale animals are a common practice in general to the company.

Veterinarians and auxiliary veterinary staff working

with animals and their secretions and by-products, and given the suspected animal origin of SARS-CoV-2, it is relevant to review all literature currently available relating to the role of animals in infection and transmission of SARS-CoV-2, particularly in the context of reproduction, and assess the potential role of reproductive material in transmission.

All veterinary medical organizations and institutions emphasize during this period the importance of veterinary activities, which are essential to ensure a continuum in the field of food safety, disease prevention and emergency management.

General Information, and from the Point of View of the Authorities, Regarding the Evolution of the Coronavirus Family in Animals [1]

In the public space, there are and will be publications describing the infection of pets and farm animals, but also studies currently available in the international scientific community, the World Health Organization (WHO), the International Organization for Animal Health (OIE), the Center for Disease Prevention and Control USA (CDC), Food and Drug Administration USA (FDA), Food Safety Agency for People and Animals of France (ANSES), Veterinary Association of the United States (AVMA), European Food Safety Authority (EFSA), regarding the possible transmission of the virus to humans by farm or pet animals, the National Sanitary Veterinary and Food Safety Authority makes certain clarifications:

- Coronaviruses are an extremely large viral family; some coronaviruses induce disease in humans, others in certain animal populations;
- Coronaviruses that infect humans can rarely infect animals;
- The genetic structure of the SARS-CoV-2 virus suggests that the original source was of animal origin; however, following the analysis of currently available data, transmission of the SARS-CoV-2 virus from humans to other animal species is very unlikely;
- SARS-CoV-2 virus binds to certain specific cellular receptors, allowing access to host cells; although these receptors have been identified in domestic animal species and appear to be able to interact with the human virus, the mere presence of receptors is not a sufficient condition for the animals to become infected; this is explained by the fact that the virus uses not only cellular receptors, but also other cellular components to replicate inside the cell;
- At present, the international scientific community has prioritized the investigation of the possibility of transmitting the virus between animals and humans, through food and through contact with the environment,

and there are numerous studies initiated in this regard;

- Animals as a source of primary infection, when the infection passes from animals to other animals of the same species, from another naturally receptive species or to humans, by 1) direct contact or 2) by interposing the contaminated environment called secondary source of infection
- Animals as a source or reservoir of infection, when the infection is perpetuated in a closed circuit for a long period of time, on a population of animals of a certain species, in a certain area, until a certain moment when, due to a complex of circumstances not always identified, passes to another species of animals or humans, after which the infection can be perpetuated by animal-animal, animal-human or interhuman infection.
- However, there is also the possibility that a new epidemic may not occur by taking over as such from another population of the same species or from another species, constituted as a source or source of infection, but through one of the genetic mechanisms of minor mutations, called antigenic drift, or deep genomic mutations, called antigenic shift. The resulting microbial population will belong to a new type or variant, is antigenically different and can evade the action of antibodies induced by the initial microbial population.

Name, Taxonomy

Whenever a new human epidemic of unknown origin occurs, the question automatically arises as to whether the source or source of infection is animals, because sometimes it is, (www.oie.int, www.cdc.gov, www.who.int, www.asas.ro) [2-5].

The International Taxonomy Committee finally gave the name in February of this year to the virus that causes the new coronavirus epidemic, SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2), and the name of the disease is Covid 19 (Coronavirus disease 2019).

Coronaviruses belong to the family Coronaviridae. Alpha- and beta-coronaviruses usually infect mammals, while gamma and delta coronaviruses usually infect birds and fish. Canine coronaviruses, which can cause mild diarrhea, and feline coronaviruses, which can cause feline infectious peritonitis (FIP), are both alpha-coronaviruses. These coronaviruses are not associated with the current coronavirus outbreak.

Until the advent of SARS-CoV-2, which belongs to beta-coronaviruses, there were only six known coronaviruses capable of infecting humans and producing respiratory diseases, including severe acute respiratory syndrome

with SARS-CoV coronavirus as a pathogen (identified in 2002/2003) and Middle East respiratory syndrome with MERS-CoV coronavirus as a pathogen (identified in 2012).

SARS-Cov-2 is genetically more related to SARS-CoV than to MERS CoV, but both are beta-coronaviruses originating in bats. Although it is not known whether COVID-19 will behave in the same way as SARS and MERS, information on both previous coronaviruses may provide recommendations for COVID-19.

The role of Veterinary Medicine

Of course, even in the case of this pandemic, the question of its origin was asked; the first direction investigated being the animal source. Veterinary medicine is in this situation caught in the middle: on the one hand it is obliged to investigate the possible source of animal infection, using its own and specific means of investigation, but on the other hand it has the professional duty to defend the innocence of some animal species, unjustly suspected and possibly incriminated. Let's not forget that Covid 19 is a syndrome not a specific disease, and therefore clinical confusions are not impossible.

Unfortunately, for the time being, given the novelty of this epidemic, knowledge in this field is very little and is based more on random observations than on experimental studies.

That is why it is somewhat understandable that the first thought of infected animal owners is sometimes if the source of infection is not even their own pets. In this sense, in the USA, France, Great Britain, Russia, Japan, China, etc. there have been several requests from pet owners to veterinary offices to have their animals, more frequently dogs and cats, tested for Covid-19 Infection.

And indeed, the International Office of Epizootics cites a few scattered cases in which they tested positive in laboratory tests, but their study led to some findings essential for understanding the epidemiology of the new disease.

Obviously, in the case of dogs and cats found positive, the SARS-CoV-2 infection was linked to the situation of the owners, who were also positive. The thorough investigations revealed that in fact dogs and cats had not been the source of infection of the owners, but, they contracted the infection from their owners.

And more clearly, it was not humans who turned out to be victims of animals, but vice versa. Among pets, cats and ferrets are the most blamed, they were also present in clinical manifestations and may possibly transmit the disease to

other cats. Dogs don't seem to be as sensitive.

For the time being, the OIE recommends that SARS-CoV-2 suspicious or positive individuals limit contact with all domestic and captive wild animals for as long as they are positive.

It is recommended that owners declared infected keep all known rules of preventive hygiene and other people take care of their animals until the tests are cured or denied.

Only if an animal shows suspicious symptoms of Covid 19 in the event that its owners have also been diagnosed as infected, there is the problem of taking samples from the animal in order to establish the diagnosis. The suspicious animal should be isolated immediately before the laboratory result.

O.M.S. has developed a series of documents regulating the personal hygiene measures of pet owners, veterinarians of carers, food industry workers and all contacts, in order to avoid infection. These measures are now well known.

The FAO has also developed instructions on how to prevent and avoid infecting the population with potentially contaminated food.

Spread between Animals and People

At this time, the risk of COVID-19 spreading from animals to people is considered to be low.

It appears that the virus that causes COVID-19 can spread from people to animals in some situations. CDC is aware of a small number of pets worldwide, including cats and dogs, reported to be infected with the virus that causes COVID-19, mostly after close contact with people with COVID-19, (www.cdc.gov) [6].

In April and May, 2020, Hong Kong has tested more than 29 dogs and 17 cats from households with human COVID-19 cases or close contacts of cases, and was diagnosed two dogs and one cat [7].

A survey of 24 stray cats in the proximity of the mink farms found seven with antibodies against SARS-CoV-2 and one cat with positive viral RNA on an oropharyngeal swab sample [8]. This suggests that environmental transmission has likely occurred in this instance and may also present a hazard to humans. Following this initial outbreak in two mink farms, a further nine mink farms in the Netherlands have become infected.

In a serological survey of 1914 samples from 35 different species of animals, 1 using a double antigen sandwich ELISA,

all tested negative for antibodies against SARS-CoV-2, leading the authors to conclude that all of the animal species included in the study could not act as intermediate hosts [9]. The ELISA test was validated for specificity using samples from pig, mouse and rabbit, and sensitivity using samples from ferrets, but was not validated in all 35 of the animal species. It is not clear where some of the animals were sourced from or whether they could have had contact with a COVID-19 patient, except for one dog, who was owned by a COVID-19 patient and tested negative [9].

During the validation process of Idexx SARS-CoV-2 RealPCR Test, more than 3500 canine, feline and equine specimens from the United States of America and South Korea were tested, with no positive results. By mid-April more than 5000 samples from Europe, Canada, USA and South Korea had been tested, with no positive results [10].

Experimental infection under laboratory conditions demonstrated that SARS-CoV-2 replicates poorly in dogs, pigs, chickens and ducks. Animals were inoculated with 10⁵ PFU of samples of SARS-CoV-2 intranasally [11]. Five inoculated beagles housed with two uninoculated beagles resulted in detection of viral RNA in rectal swabs of the inoculated dogs but no infectious virus detected [11]. Two inoculated dogs seroconverted, but the rest were antibody negative by ELISA, demonstrating that dogs were not efficiently infected and did not transmit the virus [11]. The experiment was replicated for pigs, chickens and ducks, all of which tested negative for viral RNA and anti-SARS-CoV2 antibodies on day 14, leading to the same conclusion [11].

Evidence of SARS-CoV-2 in semen or embryos Currently, there is no literature published related to the presence of SARS-CoV-2 in animal germplasm; however, there are some studies in human COVID-19 patients assessing the potential effects of SARSCoV-2 on sexual transmission and reproductive function [12].

Infection and transmission during reproductive techniques There is no literature that specifically relates to the transmission of SARS-CoV-2 in animal germplasm or the risks of exposure associated with veterinary reproductive techniques.

History, Appearance and Evolution

Preface: In December of 2019, many cases of undiagnosed pneumonia in people became apparent in Wuhan city, Hubei region, China. It was determined that this emerging disease was caused by a novel coronavirus, SARS-CoV-2, causing the disease COVID-19. Since then, the virus has spread to more than 213 countries around the world, with almost 3 million confirmed cases, and over 202,000 deaths attributed to

COVID-19 worldwide, as of April 28, 2020, WHO [13].

Background: • On December 31, 2020, the World Health Organisation (WHO) was notified by Chinese authorities of cases of pneumonia in people linked with a seafood and live animal “wet” market in Wuhan city, Hubei region of China [13]. • On January 9, 2020, WHO identified that the causal pathogen for the cases of pneumonia was a new emerging coronavirus. This coronavirus was temporarily labelled 2019-nCoV (novel coronavirus) [13]. • On February 11, 2020, the novel coronavirus was officially labelled SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) by WHO. The subsequent disease was labelled COVID-19 disease (coronavirus disease) [13]. • On January 30, 2020, due to the large scale of the spread of the disease, WHO declared it to be a Public Health Emergency of International Concern. • On March 11, 2020, as global spread became apparent, SARS-CoV-2 was labelled a pandemic [12]. • Coronaviruses are enveloped, single-stranded, positive-sense RNA viruses that infect a wide variety of species, including humans, livestock and companion animals. • Coronaviruses are classified in four genera—Alphacoronavirus, Betacoronavirus, Gammacoronavirus and Deltacoronavirus. Alpha- and Betacoronaviruses usually infect mammals, and Gamma- and Deltacoronaviruses usually infect birds and fish. • SARS-CoV-2 is classified as a Betacoronavirus. • Zhou [14] reported that 2019-nCoV (now named SARS-CoV-2) shares 79.6% sequence identity with SARS CoV and shares 96.2% sequence identity at a whole-genome level to Bat CoV RaTG13, which was previously detected in *Rhinolophus affinis* (horseshoe bats) from Yunnan province, China. To date, this provides the most substantial evidence that SARS-CoV-2 originated from an animal reservoir, a bat. • Additionally, it was found that SARS-CoV-2 likely uses the same cell entry receptor, angiotensin converting enzyme 2 (ACE2), as SARS-CoV [14,12].

Evidence of Infection and Evolution in Animals

Initial, there have been a few isolated reports of natural infection with SARS-CoV-2 in animals, which have been associated acontact with a human diagnosed. The majority of reports infection in animals has been experimental studies in laboratory conditions [12].

Natural conditions: The following are reports from the World Organisation for Animal Health (OIE 2020) [15]:

- February 29, 2020 – **Hong Kong, China** – A Pomeranian dog owned by a confirmed COVID-19 patient showing no clinical signs of COVID-19 tested positive to SARS-CoV-2 with qRT-PCR on nasal and oral swabs. Virus isolation negative.
- March 18, 2020 – **Belgium, Netherlands** – One cat

owned by a confirmed COVID-19 patient presented with clinical respiratory and gastrointestinal signs and tested positive to SARS-CoV-2 by PCR.

- March 20, 2020 – **Hong Kong** – A German Shepherd dog, one out of two dogs owned by a confirmed COVID-19 patient, neither showing any clinical signs, tested positive to SARS-CoV-2 with qRT-PCR and virus isolation.
- March 31, 2020 – **Hong Kong** – One cat owned by a confirmed COVID-19 patient, showing no specific clinical signs, tested positive to SARS-CoV-2 with qRT-PCR.
- April 6, 2020 – **Bronx, New York, USA** – Tiger – Three lions and five tigers presented with a dry cough and wheezing, and had presumed exposure to an asymptomatic zoo employee with COVID-19. One tiger and one lion were tested; both were positive for SARS-CoV-2 with qRT-PCR.
- April 15, 2020 – **Richmond, New York, USA** – Dogs – One out of two German shepherd dogs from a household with known COVID-19-affected inhabitants showed respiratory illness and tested positive to SARS-CoV-2 with PCR. Virus neutralizing antibodies were detected in both the clinically affected and clinically unaffected dog.
- April 19 and 20, 2020 – **Netherlands** – Two mink farms had mink showing respiratory disease and increased mortality rates. Epidemiological investigations and viral sequencing revealed that the mink were infected with SARS-CoV-2 through two separate introductions into the two farms, most likely from contact with infected farm workers [8]. Workers were confirmed COVID-19.
- April 22, 2020 – **New York, USA** – Two cats from separate households, owned by confirmed COVID-19 patients, presented with respiratory signs, tested positive to SARS-CoV-2 with qRT-PCR and had virus neutralizing antibodies (reported on April 29, 2020).
- April 30, 2020 – **Paris, France** – One cat owned by a suspected COVID-19 patient with mild respiratory and digestive signs tested positive to SARS-CoV-2 on rectal swab but negative on nasopharyngeal swab [16].
- May 18, 2020 – **Russia** – One cat tested positive to SARS-CoV-2 with RT-PCR of throat and nasal swabs, currently, the animal is quarantined at the place of keeping.
- May 19 and 20, 2020 – **Illinois and Minnesota, USA** – In two separate incidences, one cat from a household with known COVID-19-affected inhabitants showing respiratory signs tested positive to SARS-CoV-2 with PCR.
- Jun 2, 2020 **Richmond County, Richmond, New York** – A pet German Shepherd dog from a household with known COVID-19 affected inhabitants was sampled for respiratory illness. Clinical signs included severe lethargy, diagnosed as hemolytic anemia. The dog tested positive for SARS-CoV-2, by PCR. Virus neutralizing antibody was detected in follow-up samples from the affected dog as well as a second pet German shepherd dog in the household who showed no clinical signs of disease and tested negative by PCR. The first dog is progressively recovering [17].
- Jun 3, 2020 **Carver, Minnesota** – A domestic cat from a household with known COVID-19 affected inhabitants was sampled for respiratory illness. Clinical signs included depression, fever, and harsh lung sounds. The cat tested positive for both mycoplasma felis and SARS-CoV-2 at the initial testing laboratory. Infection with SARS-CoV-2 was confirmed based upon molecular testing (PCR and sequencing). Both the cat and owners have reportedly recovered.
- Jun 10, 2020 **Cook, Illinois** – A domestic cat from a known positive COVID-19 household was sampled for respiratory illness. Clinical signs included fever, oral lesions and ulcerations on the tongue. The cat tested negative by feline respiratory panel, FIV and FeLV, and positive by feline coronavirus serologic test, a common finding. The initial testing laboratory also conducted a SARS-CoV-2 test. Infection with SARS-CoV-2 was confirmed at NVSL based upon molecular testing (PCR and sequencing). The cat is reportedly recovering.
- July 21, 2020, **Sheung Wan, Hong Kong** – A cat was placed under quarantine after confirmation of a human case from the same household. Following veterinary examination nasal, oral and rectal swab samples were taken after the cat's admission to the quarantine facility. The oral sample was tested positive for SARS-CoV-2. The cat has not exhibited any specific clinical signs. Mammalian pets from household with confirmed human cases will be collected for testing of SARS-CoV-2 as appropriate [18-20].
- July 2, 2020 **Berrien, Georgia** – A domestic dog from a known positive COVID-19 household was confirmed positive for SARS-CoV-2 at the National Veterinary Services Laboratories based upon molecular testing (PCR and sequencing). The affected dog was showing neurological signs and was euthanized. At necropsy a pituitary tumor was identified, which is thought to be the cause of the dog's neurological signs. Serum from a second dog in the household, which has not shown clinical signs of illness, tested negative for SARS-CoV-2 virus neutralizing antibodies.
- Jul 9, 2020 **SUA - California (CA)**: A domestic cat from a known positive COVID-19 household was confirmed positive for SARS-CoV-2 at the National Veterinary Services Laboratories based upon molecular testing (sequencing). The cat first showed clinical signs of difficulty breathing and was later hospitalized for tachypnea, hypothermia and heart murmur. Further diagnostics revealed abnormalities consistent with hypertrophic cardiomyopathy [21]. The cat's condition worsened and it died, likely due to its cardiac condition. The cat tested positive for both mycoplasma felis and SARS-CoV-2 at the initial testing laboratory. A second

pet cat in the household has shown no clinical signs of disease. Texas **(TX)**: A domestic dog from a known positive COVID-19 household was confirmed positive for SARS-CoV-2 at the National Veterinary Services Laboratories based upon molecular testing (PCR and sequencing). The dog has shown no clinical signs of illness and was initially tested because it was leaving a COVID-19 positive household and entering a veterinary facility for boarding [22].

- Jul 16, 2020 - **South Carolina (SC)**: A domestic dog from a known positive COVID-19 household was confirmed positive for SARS-CoV-2 at the National Veterinary Services Laboratories based upon molecular testing (PCR and sequencing). The affected dog, which had a chronic health condition, exhibited mild respiratory clinical signs. When the animal's condition worsened, it was euthanized [23-25].
- Jul 23, 2020 **USA- Arizona (AZ)**: A domestic dog from a known positive COVID-19 household was confirmed positive by PCR. The affected dog exhibited respiratory clinical signs, but has since reportedly recovered. Texas **(TX)**: A domestic cat was confirmed. The cat showed no clinical signs and continues to be asymptomatic. Two dogs residing in the same household have remained asymptomatic and tested negative by PCR. Samples for this case were collected as part of planned and targeted active surveillance of a specific animal, with known or suspected exposures to a person with COVID-19 or other exposure to SARS-CoV-2, to better understand risk factors for SARS-CoV-2 transmission. Virus neutralizing antibodies in the absence of other positive test results have been detected in the following animals (listed by state): 1. 4 cats and 2 dogs from four households **(UT)**. 2. 2 dogs from different households **(WI)**. 3. 1 dog **(NC)**. As of 23 Jul 2020, total number of animals with detections of virus neutralizing antibody only: 12 *Animal had exposure to a probable or confirmed human with COVID-19 [26].

Conclusion

Pets are with priority / possibly the only animals that have been infected so far with Covid19. Certainly the infected animals are more, but they are not tested, they are not reported. The data presented are the official ones and are visible on the OIE.

The symptoms of infected animals may be absent (asymptomatic carriers), there are signs of dyspnea fever, appetite - as in human cases. No cases of infection have been reported in large animals, possibly due to the biosecurity specific to production farms [27].

The current evidence shows that the only animals that

have been demonstrated to develop infection with SARS-CoV-2 either naturally or experimentally are members of the families Felidae, Canidae and Mustelidae and golden Syrian hamsters in two experimental papers [17,28]. There are very few isolated cases of natural infection in companion animals (cats, dogs), zoo animals (big cats), and mink, which all have evidence of contact with a human with COVID-19; however, it is not clear whether horizontal transmission was possible or occurred in any of these cases.

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