Coronaviruses in Veterinary Medicine

Subjects: Respiratory System

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Coronaviruses (CoVs) are known in veterinary medicine affecting several species, and causing respiratory and/or enteric, systemic diseases and reproductive disease in poultry. Animal diseases caused by CoVs may be considered from the following different perspectives: livestock and poultry CoVs cause mainly "population disease"; while in companion animals they are a source of mainly "individual/single subject disease". Therefore, respiratory CoVs diseases in high-density, large populations of livestock or poultry may be a suitable example for the current SARS-CoV-2/COVID-19 pandemic.

Keywords: coronavirus ; SARS-COV-2/COVID-19 ; animals ; airborne ; diffusion ; biosecurity ; air filtration

1. Introduction

CoVs are known in veterinary medicine affecting several species, and causing respiratory and/or enteric, systemic disease in mammals and reproductive disease in poultry. Indeed, companion animals, dogs, cats, horses, and ferrets may have CoVs infections, as well as cattle and pigs among livestock, and poultry (chicken, turkey). Other important reservoirs for CoVs are wild or semi-wild animals, and these latter ones were confirmed to be the source for SARS-CoV and MERS-CoV [1], and a probable source for SARS-CoV-2/COVID-19 [2]. The latter was demonstrated as able of reverse spill-over from humans to other animals like dogs and cats, then able of further intraspecies spread as recently demonstrated in farmed fur-minks in several EU countries and in the USA [3].

Table 1 summarizes coronaviruses and animal diseases of usual veterinary interest.

Table 1. Coronaviruses and animal diseases of veterinary interest (from [2], modified). The four genera apparently have a common ancestor dating 10,000 years back (from [4], modified).

Order: Nidovirales, Family: *Coronaviridea* (RNA Viruses; Enveloped; Single Stranded; Positive Sense), Sub-Families: *Ortho Coronavirinea*					
Animal Population	**Animal Species**	**Genera**			
		Alphacoronavirus	**Betacoronavirus**	**Gammacoronavirus**	**Deltacoronavirus**
Livestock	***pig***	**Transmissible Gastro Enteritis; Porcine Respiratory CoV; Porcine Epidemic Diarrhea; Severe Acute Diarrhea Syndrome;**	**Porcine Hemagglutinating Encephalomyelitis;**		**Porcine delta enteric coronavirus (PDCoV);**
	cattle		**Neonatal calf diarrhea; Bovine Respiratory CoV;**		
Companion	***dog***	**Canine Enteric CoV;**	**Canine Respiratory CoV;**		
	cat	**Feline Infective Peritonitis; Feline Enteric CoV;**			
	horse		**Equine CoV;**		

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		Alphacoronavirus	**Betacoronavirus**	**Gammacoronavirus**	**Deltacoronavirus**
Avian	***chicken***			**Infectious Bronchitis CoV;**	**wild; farmed game; enteric/respiratory Delta-CoVs**
	turkey			**Turkey Enteric CoV;**	

2. Biosecurity Measures

Biosecurity implicates a set of management and physical measures designed to reduce the risk of the introduction, establishment and spread of diseases, infections or infestation to, from and within a population. Biosecurity measures aim at preventing the introduction (external biosecurity or bio-exclusion), managing the stability and reducing the spread (internal biosecurity) of disease. Segregation, cleaning and disinfection represent the basic principles of biosecurity in every population (farm, residency, etc.).

Biosecurity plans should identify potential pathways for the introduction and spread of disease in a zone or compartment, and should describe the measures that will be used to mitigate the risk of disease. When considering the risk of occurrence of an infectious disease, the likelihood of its occurrence, the likely magnitude, the biological and economical consequences, should be considered. Veterinary medicine is familiar with biosecurity concepts and the implementation of biosecurity measures. Biosecurity is an integral part of any successful poultry and livestock production; it represents the set of rules and measures taken to prevent the incursion and spread of disease. These have been divided into the following three categories [5]: conceptual, which includes the location for a farm or a population; structural, which covers the physical facilities; and operational, which covers the procedures to be followed by the farm staff and visitors. Biosecurity aims to prevent the introduction of the potential pathogen through external bio exclusion measures; to manage the stability of internal biosecurity once a pathogen has been introduced into a population (see Porcine Reproductive and Respiratory Virus, PRRSV, for example); to manage/limit the spread of the pathogen from the infected population.

2.1. Biosecurity in Animal and Human Populations

Relatively to respiratory CoVs, the experience gained in veterinary medicine could be of interest for human medicine as well. Direct contact, airborne transmission, people (personnel, visitors, or suppliers), fomites, and pests (birds, bats, rodents), may represent a cluster of biosecurity issues in which veterinary medicine has already developed references. The design of an effective biosecurity plan hinges on an understanding of how disease-causing organisms are introduced and spread, and the identification of any pathogens that might be already present. The best biosecurity plan must be based on understanding the risks to the considered population. While the classical biosecurity principles of population segregation; thoroughly cleaning of tools and materials; disinfection, constitute the basic principles of any biosecurity plan, further considerations must be done when dealing with airborne pathogens. In facts, biosecurity should not be about targeting some few possible risks factors and hoping having done the right choice, rather understanding and controlling the whole series of critical points (https://www.cidlines.com/en-US/cid-lines-nieuw, 2021) which could contribute to pathogen introduction and diffusion.

2.2. Preventing Introduction (External Biosecurity; Bio-Exclusion)

The airborne spread of CoVs and other RNA viruses was confirmed in both human and animal diseases, with PRCV demonstrated to spread airborne, live and vital, up to 1,6 km in areas of high population density, while shedding from nasal secretions was demonstrated between 10 to 14 days post-exposure [2][6][7][8][9]; simple air change/extraction did not prevent the spread of some CoVs [10] between sensible animal populations kept 30 mt apart in separate buildings. Air filtration or air treatment systems can be an effective way to prevent the aerosol transmission of viruses. The efficacy of filtration is generally measured by the percentage of reduction in dust, droplets and aerosol of different sizes, which may carry viruses and/or bacteria.

2.3. Managing the Risks of Disease Entering a Population of Elderly Residency/Nursing Homes

While it is difficult for the authors to enter into the details of SARS-CoV-2/COVID-19 pandemic tolls at private homes, hospitals and nursing homes, it looks less difficult to examine some characteristics of the main populations involved: the elderly residency/nursing home population and long-term hospitalized population. The elderly residency/nursing home population is at high risk. The SARS-CoV-2/COVID-19 pandemic data show that mortality rates are higher within nursing homes (30–39%) which total population in western countries is estimated 2% to 5%. Aerogenic spread of CoVs between animal populations has already been demonstrated [7][8][9][11], but there are also evidences for the current pandemic. Indeed, a neighborhood with a high population density (≥5000 individuals/km^2) was associated with higher SARS-CoV-2/COVID-19 mortality with respect to a low population density (<150 individuals/km^2) in elderly people living at their own home [12]. Data relative to association between PRCV diffusion within a population and population size were demonstrated already in the '90s [8][13]. PRCV was also demonstrated as regularly reintroduced in farms during colder seasons [13]. Similar data relative to seasonality of bacterial concentration in aerosol (higher concentration in winter; lower in summer) and not related to farm dimension or population size, induce thinking about air or ventilation role in microorganisms [14] diffusion by means of aerosols Therefore, the approach based on air filtration or air treatment may represent a very efficient preventive measure, as already shown, for example, with Porcine Reproductive and Respiratory Virus (PRRSV), a tiny RNA virus, in veterinary medicine [15]. The objective should be to prevent the introduction of the virus by means of outdoor sourced air, at positive-pressure, through HEPA 17–20 or MERV 16 (no less) (ISOPM1) filtration systems, which demonstrate 95% to 99,97% efficacy in trapping particles <0.3 µm diameter.

2.4. Bio-Surveillance; Bio-Containment

In the case of epidemics, a total strict confinement can be imposed on all the most fragile and susceptible population, with a no-entry and no-leave policy, even for a relatively long time. Procedural barriers should be put in place, effective in excluding potentially asymptomatic spreaders entering or leaving: SARS-CoV-2/COVID-19 tests should be carried out on elderly residency/nursing home populations. Positive individuals, regardless of their health status, should be immediately removed from shared areas, isolated or hospitalized. In parallel with this strategy, strict internal biosecurity measures for personnel and visitors are highly necessary.

Biocontainment means managing the risks of the disease spreading within a population; many hospitals were equipped with intensive care units (ICU) for SARS-COV-2/COVID-19 patients. These hospitals presented at least two sub-populations, as follow: SARS-COV-2/COVID-19-positive, and "other patients". The objective should be to control the endemic situation within the structure between different compartments and different sub-populations, which means avoiding the spread of the virus from SARS-CoV2/COVID-19 areas. This result may be obtained by a negative-pressure pre-filtered air system in place at ICUs, then a HEPA 17–20 or MERV 16 filtration system, in exhausted air, with very high efficiency in trapping particles of <0.3 µm diameter , with no-recirculation. Aerosol particles of <0.5 µm diameter exhaled from human patients with respiratory infections were shown carrying different pathogens, both bacteria and viruses [16].

2.5. Personal Protective Equipment (PPE)

These equipment have their parallel in preventive PPE recommended when approaching in livestock infections, and they are of high importance in reducing the spread of infections [17]. Masks and hand sanitization, together with social distancing, constituted for around one year the main protective measures suggested and implemented at the population level. Lockdown, curfews have been used in several countries, with different schedules and durations. The efficacy and impact of these approaches on global population health should be carefully assessed to be prepared in the case of a new pandemic [18][19][20].

Recommendations, such as distancing (1–2 meters according to most countries); "sneezes protection"; "towels and scarfs"; up to "masks" and other generical indications, have a questionable rational and their usefulness is also arguable. In most of the cases, people used "face masks" or "surgical masks" supplied by pharmacies and/or general stores, or self-made "community masks", or even "fashion masks". ". Dealing with airborne pathogens, masks should be intended – at the least - to protect the wearer from splashes and large droplets, and minimize the particles expelled by the wearer himself; in such a perspective, they should be at least surgical type 2 masks. In general, infectious particle sizes less than 10 µm tend to have more serious health implications as they are able to penetrate into lower respiratory tract and establish infection [9]. Indeed the CoV responsible for PEDV, while it demonstrated an higher concentration in droplets with size 3.3 µm to > 9 µm ($4.5x10^7$ to $3.5x10^8$ geometric mean of RNA copies/m^3 of air samples), in aerosols particle sizes of 0.4 µm to 0.7 µm diameters, still demonstrated a concentration of $1.3x10^6$ RNA copies/m^3. These data strongly suggest for the adoption of highest filtration ability masks. Generic or face masks do not provide adequate protection against airborne contaminants. Respiratory protection is required to prevent transmission via the airborne route. Seals tighter than those of surgical masks are needed around the nose and mouth to prevent inhalation of some airborne particles. N95/FPP2 - N95/FPP3 respiratory masks, properly worn, provide proper tight seal to the face and small particles (0.3 µm) filtration (>94% to ≥99%). Use of FFP2 and FFP3 masks by hospital's personnel, in order not to increase the risk of infection, was recently adopted in some EU Countries [21].

2.6. Herd/Population Immunity

In veterinary medicine, disease control is based on both trying to prevent the exposure of animals to pathogens and/or, when possible, inducing an immune response in susceptible populations through vaccination. In companion animals, the implementation of vaccination plans and the relative isolation within domestic walls—especially in cats—look effective to the purpose.

Veterinary medicine has good experience with the population vaccination concept and herd immunity. In a veterinary approach, the whole susceptible population is generally vaccinated; vaccination schedules may change according to age, passive immunity interference or productive phase (i.e., pregnancy). “Population or herd immunity” represents the result of the susceptible population vaccination; for example, rinderpest (now eradicated) required a 70%–90% population/herd immunity, while foot and mouth disease requires an 80%. It means that following the vaccination of 100% of susceptible subjects, we expect that an immune response will develop in a significant part of the population (70%–90%), resulting in the protection of the entire population, generally from the disease rather than the infection. The significant reduction in “susceptible/available guests” in which the pathogen can multiplicate and diffuse, will cause it to vanish.
The objective, quite simply from a veterinary point of view, is to administer the most appropriate vaccine at the most appropriate stage of life and/or production; this is generally possible when dealing with and managing an endemic situation. In course of outbreaks or epidemic/pandemic situation, the whole population should be vaccinated. When vaccination cannot be implemented due to an illness situation or risk of being impaired by the immunological status in some subjects, it should be postponed until the first suitable moment; in such a situation, fragile individuals should possibly be isolated. Modified Live Vaccines (MLV) can pose some risks to some categories of animals; in such a situation, however, it should be considered if a virulent virus poses a greater risk than vaccinal virus In veterinary medicine, short-term postponing of vaccination in sick animals (often isolated in a “sick-bay”), or in pregnant livestock very close to calving/farrowing, is routinely implemented. These subjects will be included in the vaccination program as soon as the situation allows, unless they are removed from the farm. When implementing vaccination plans in animal populations, the objective is that no one is left behind. In veterinary population medicine it sounds simply unthinkable to keep non vaccinated subjects (whatever the species) in contact with the population susceptible to disease. The impact of some unvaccinated subjects on the spread of the disease and on the time needed to have a population immunity is unforeseeable. Not only these could be subject to the disease, but incomplete population vaccination will compromise the elimination time-frame of a disease and/or will require further vaccinations and efforts to obtain the expected results.

Relative to the CoVs of veterinary interest, only few vaccines are available, as follow: against canine enteric CoV; feline infective peritonitis; neonatal calf diarrhea; transmissible gastroenteritis in pigs; and avian infectious bronchitis.

Puppies and kittens are vaccinated on a regular basis in almost all western countries, but it is a matter of fact that living as pets, relatively isolated from other conspecifics, makes the burden of strict biosecurity easier, unless in epidemic episodes in kennels.

Strict biosecurity measures and scheduled vaccinations of the whole pregnant heifer/cow or gilt/sow populations are implemented respectively to control and reduce the damages induced by neonatal calf diarrhea and porcine transmissible gastroenteritis CoVs, even if these are not considered as airborne.

Infectious bronchitis virus (IBV) may represent an example of difficulties and constraints related to airborne CoVs. The control and reduction in the damages induced by IBV request strict biosecurity protocols and intense vaccination schedules [22], which include the whole population, both egg-layers and/or broilers. Mass vaccinations are executed on the 1st day of age in broilers, or even “in-ovo” during incubation; hens request multiple vaccinations in their life [23]. The emergence of new serotypes and variants continually occurs [23], challenging poultry productions. IBV teaches us about the difficulties in controlling a disease induced by an airborne CoV and its attitude to generate variants. Again, the available strategies for its control remain strict biosecurity, mass vaccination, and the development of new vaccines.

3. Conclusions

Coronaviruses have been known for a long time in veterinary medicine, in different animal species. The airborne spread ability of coronaviruses and RNA viruses in general is also already known. In livestock production, prevention or mitigation measures against virus spread within susceptible populations are already in place, including alternative systems of air-flow management and filtration. Biosecurity in veterinary medicine is an integral part of any successful production, representing the set of rules and measures taken to prevent the incursion and spread of disease; some of these rules and measures may be taken into consideration in the current human pandemic. Susceptible populations, especially sedentary populations, should be protected against viral spread through ventilation/air-flow control and the blocking of spreaders. The interpersonal spread of the virus should be abated or mitigated through the use of recognized appropriate and effective PPE, without leaving to improvisation and self-made solutions. Population vaccination and population/herd immunity are also well-known concepts in veterinary medicine, including specific experiences against coronaviruses and/or RNA/airborne spread viruses. In the current pandemic, vaccination of the entire susceptible population is also an important measure to reduce the potential spread of the virus within a susceptible/fragile population.

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