The contribution of veterinary public health to the management of the COVID-19 pandemic from a One Health perspective

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ABSTRACT

The human coronavirus disease 2019 (COVID-19) pandemic represents one of the greatest public health crises in recent history, which has caused unprecedented and massive disruptions of social and economic life globally, and the biggest communication challenges for public information-sharing. While there is strong evidence that bats are the animal source of SARS-CoV-2, the causative agent of COVID-19, there are many uncertainties around the epidemiology, the intermediate animal species, and potential animal routes of SARS-Cov-2 transmission to humans. While it has also long been known that coronaviruses circulate among different animal species, including SARS-CoV and MERS-CoV, responsible for the pandemics of severe acute respiratory syndrome and Middle East respiratory syndrome endemic in Middle Eastern countries in 2002–2003 and 2012 respectively, the way this pandemic is being managed tends to downplay or neglect the veterinary contribution, which is not in line with the One Health approach, if we consider that the genesis of the COVID-19 pandemic, likewise SARS and MERS lies on a close and interdependent links of humans, animals and the environment. To overcome this flaw, and to better operationalize the One Health approach, there are several lines of contributions the veterinary profession might provide to manage the COVID-19 pandemic in the framework of interventions jointly concerted in the veterinary and medical domains, notably: the experience in dealing with past animal epidemics, the skills in conducting wildlife surveillance targeting emerging pathogens at risky hot spots, and with the aim to predict and prevent future pandemics, the laboratory support for the diagnosis and molecular characterization of SARS-CoV-2 and human samples testing, and animal import risk assessment to define COVID-19 risk strategy for international air travel. The veterinary profession presents itself ontologically with a strong One Health accent and all the related valuable knowledge can be properly integrated within centralised multidisciplinary task-forces set up at the national and international level, with a renewed role in the management and monitoring structures required for managing the COVID-19 pandemic.

1. Introduction

The novel infection COVID-19, caused by severe acute respiratory syndrome coronavirus type 2 (SARS-CoV-2), which emerged in China in late 2019, has marched relentlessly across the world, causing unequaled disruption of the social structure and related human interactions, wreaking havoc on the world economy and overstretching global health care systems beyond their capacity [1]. As of 11 January 2021, in accordance with the applied case definitions and testing strategies in the affected countries, there have been almost 90,742,460 confirmed cases of COVID-19 reported worldwide, with 1944, 209 deaths (https://www.worldometers.info/coronavirus/). US, India and Brazil have the highest case loads. The European Center for Disease Prevention and Control (ECDC) reports continuing community transmission in most EU/EEA countries, EU candidate and potential candidate countries and the UK, with second or third waves of observed cases and large localised outbreaks [2]. Despite the massive research efforts of the scientific community around the globe, there are still many uncertainties, including the identity of the original animal source of SARS-CoV-2 [3], the intermediate animal host [4], the routes and dynamics of virus transmission to humans [5], the broad range of animal hosts that are affected in the field [6], the virus mutations and their impacts on pathogenicity

[7], the efficiency and durability of antibody response and reinfection, [8] the effectiveness of therapeutic regimes, current vaccines and vaccination strategies [9] [10]. Clearly, although the pandemic is the result of rapid and effective person-to-person spread of the virus in an enormous immunologically-naïve population, the fact that animals are involved in the genesis of COVID-19 and possibly even the maintenance of SARS-CoV-2 in the human population argues for a multidisciplinary and multilateral One Health coalition [11] and a much stronger implementation of the One Health Berlin Principles [12]. The findings of SARS-CoV-2 in cases of respiratory disease and sudden deaths in farmed mink in the Netherlands, Denmark and a number of other countries around the world identifies a highly-sensitive animal host. SARS-CoV-2 strains with the same genetic characteristics as affected mink have been isolated from in-contact farm workers with respiratory disease and other signs of COVID-19. This definitively shows the zoonotic capability of this virus. The direction of first transmission will have been human-to-animal, but subsequent multiplication and dissemination of the virus has been animal-to-human. The effective management of COVID-19 and future pandemics caused by animal-emergent pathogens requires the overcoming of the dichotomy between the veterinary and human medical professions by developing synergies and methodological integration. The relevance of veterinary experience, especially in the diagnosis of emerging diseases, elucidation of disease dynamics and establishment of effective collaborative control and disease management at national and regional levels is a good reason to break down the interdisciplinary barriers that still separate human from veterinary medicine and both from ecological, evolutionary, and environmental sciences. There is a prevalent attitude to downplay or neglect the contribution of veterinary virologists, epidemiologists and public health experts to the monitoring and management of COVID-19. However there are only a few European countries where veterinarians are lead persons in centralised COVID multidisciplinary task-forces and work together with human public health colleagues. This is the case of Ireland, where the COVID-19 team is chaired by a veterinary epidemiologist [13], and the United Kingdom [14]. One Health is very relevant to the current pandemic and much can be anticipated and prevented if the One Helath approach is operationalized by the wider mobilization of veterinary skills within national and international task forces set up within the public health system.

2. Coronaviruses and the novel SARS-CoV-2

SARS-CoV-2 is a small RNA virus, diameter 65–125 nm, with an outer envelope bearing an array of characteristic spike proteins (S-proteins), containing a linear positive-sense single-stranded and large genome of nearly 30kD. It has 82% sequence identity with SARS-CoV. It belongs to the family *Coronaviridae,* subfamily *Coronavirinae,* and is a member of the *Betacoronavirus* group, along with the viruses of SARS and MERS, as well as low-pathogenicity endemic human coronaviruses such as HCoV (Human Coronavirus)-OC43 and HCoV-HKU1 [15]. The *alphacoronavirus* group includes CCoV, canine coronavirus, responsible for enteric and respiratory disease, FCoV, the feline coronavirus that causes feline infectious peritonitis (FIP), as well as HCoV-NL63 and HCoV-229E [16], which globally contribute to about one third of the common cold infections in humans [17]. Infections by any of the HCoV types can sometimes cause life-threatening pneumonia and bronchiolitis especially in the elderly, children, and immunocompromised patients [18]. Pigs are infected by porcine deltacoronavirus, which appears species-specific, and a recently-emerged alphacoronavirus SADS-CoV responsible for Swine acute diarrhoea syndrome and most closely related to bat coronavirus HKU2 [19]. Of concern, recombinant rSADS-CoV can replicate efficiently in several primary human lung and intestinal cell types, indicating it might become higher-risk for humans in the future [20]. Recent work on the phylogenetic analysis of CoVs has clarified the origins of the groups and the evolutionary lines among animal species [21]. Coronaviruses are distinguished by their remarkable complexity and high genetic variability, as a result of high rates of mutation and recombination [22]. SARS-CoV-2, compared to other RNA viruses, has an overall 10-fold lower mutation rate, due to internal proofreading by the non-structural protein 14 (nsp14) that cuts out mutated genes as they are synthesized by RNA dependent RNA polymerase (RdRp) [23]. The mutations that have been detected so far in SARS-CoV-2 genomes are linked to the genes encoding the S (spike) protein present on the surface or envelope of the virus and are used to track virus spread and evolution with the goal to aid COVID-19 epidemiological understanding and improve pandemic response [24]. The S protein has the main function of recognizing and locking onto the ACE2 receptor (angiotensin 2 conversion enzyme) expressed by the target cells of the respiratory system and other organs, while the receptor-binding domain (RBD) on the S protein's N-terminal is the key element for beta-coronavirus entering into host cells. SARS-CoV-2 not only uses ACE2 as a host receptor similarly to the SARS-CoV virus, but also shows 10 to 20 times higher binding capacity [25]. Indeed, the binding affinity for the ACE2 receptors is one of the key factors for the infectivity and the high efficiency of person-to-person transmission.

3. The zoonotic origin of COVID-19 pandemic

The majority (70%) of emerging diseases (eg. Ebola, Zika, Nipah encephalitis) and all known pandemics (eg. influenza, SARS, MERS, HIV/AIDS) are zoonoses, predominantly originating from wildlife [26]. Epidemiological investigations of the first cases of COVID-19, detected in late December 2019 in Wuhan, Hubei Province, China, found an association of the first and second-generation cases of SARS-CoV-2 infections with the Huanan seafood wholesale market [27]. This was also supported by the detection of genome sequences of environmental samples, such as doorknobs and floors from that market, very closely related to viruses sampled from the earliest Wuhan patients. However the lack of direct animal sampling made it difficult to accurately identify any animal reservoir at this location [28]. Moreover, 13 of the 41 confirmed cases of COVID-19 in the first wave had no connection to the market [29]. Since SARS-CoV-2 has an incubation time of approximately two weeks, the first zoonotic transfer most likely happened in November 2019 [30]. Though the origins of the pandemic remain unclear, phylogenetic analyses using a large subgenomic data set of bat coronaviruses from China indicate that SARS-CoV-2 likely originated in horseshoe bats, as its genome sequence has approximately 96% nucleotide identity with RaTG13, isolated from Chinese *Rhinolophus affinis* [31] [32]. In addition, there is 97.4% amino acid sequence similarity in the receptor-binding domain (RBD) to and 85.5%–92.4% nucleotide identity in the genome of Guangdong pangolin coronaviruses, and higher amino acid identity to SARS-CoV-2 in the E, M, N and S proteins of Malayan pangolins, suggesting that pangolins might be the intermediate host in which recombination to produce the SARS-CoV-2 precursor occurred [33] [34,35]. To investigate their possible role, samples were collected from 334 pangolins confiscated in Malaysia and Sabah in 2019, but none of these yielded a positive PCR result for coronavirus. The lack of coronavirus infection in wild pangolin entering the upstream portion of the wildlife trade in Malaysia supports the hypothesis that infection could reflect exposure to infected humans, wildlife or other animals within the wildlife trade network [36]. Another possible scenario is that the SARS-CoV-2 progenitor has jumped directly from bats to humans a relatively long time before the first human cases were identified [37]. Inside the human host, the SARS-CoV-2 progenitor could have undergone rapid evolutionary adaptation that enabled the efficient replication in human cells and produced the number of cases large enough to be detected by the surveillance system. This progenitor could even be the RaTG13 sarbecovirus that, interestingly, can infect cells expressing the human ACE2 receptor [38]. The 4% genetic differences between RaTG13 and SARS-CoV-2 represent 40–70 years of mutation, at the rate generally found in coronaviruses, suggesting that the common ancestor dates back to about 1948–1982 [39]. This indicates that the lineage giving rise to SARS-CoV-2 have been circulating in bat populations for

decades and also supports the belief that SARS-CoV-2 is not a laboratory construct or a purposefully manipulated virus [40]. The evidence of high affinity and binding capacity of RBD in the S protein of SARS-CoV-2 to ACE of different animal species, especially felids and mustelids, thereby increasing their susceptibility to infection, supports inter-species transmission [41].

4. Human-animal-human transmission of SARS-CoV-2

Although the COVID-19 pandemic is exclusively a human phenomenon, there are concerns about the possibility of adaptation of the original virus in an intermediate animal species, to produce a SARS-CoV-2 with a greater infection efficiency for humans and the capacity for the rapid and uncontrolled community spread that has been seen in the pandemic. These concerns have their basis in findings in several animal species that have been reported to be susceptible to SARS-CoV-2 infection either naturally (cats, dogs, minks, lions, tigers), with the transmission source coming from humans, or after experimental infection (mice, cats, ferrets, hamsters, primates, treeshrew. [42–44]. Some of them may be able to contribute to the continuation of the pandemic, by animal-human transmission following human-animal infection (reverse zoonosis). The risk of reverse zoonosis, where humans transmit coronaviruses to other animals in nature [45,46], could also include naïve wildlife and other animal populations. Free-ranging bats, immunologically naïve and susceptible to infection by SARS-CoV-2, are a key group of concern for spillover from humans back to wildlife [47]. Close contact between humans (pet-owners and zoo-workers) and their animals seems necessary for human-animal infection. So far, there is no evidence of further animal-human spread from infected pets or zoo felids and infections in the animals themselves appear to be self-limiting and not usually fatal. Notably, the sporadic cases of SARS-CoV-2 infection in dogs and cats revealed the detection of the RNA virus in respiratory and/ or fecal samples with or without clinical signs, as well as of specific antibodies in sera from pets in COVID-19-affected areas [48,49,109]. Despite cats showing a higher susceptibility than dogs, no cases of cat-human transmission have been documented to date. Experimental studies have shown that the most highly susceptible species to SARS-CoV-2 are felines (cats, tigers, lions), mustelids (ferrets, mink), Golden Syrian hamsters, Egyptian fruit bats and Macaques [41,50–52]. Indeed, the RBD in the S protein of SARS-CoV-2 shows a higher affinity and binding capacity to ACE2 of ferrets, cats, minks with high homology of receptors, which explains their susceptibility to infection [53]. In contrast, SARS-CoV-2 binding is unlikely with the ACE2 receptors of mice, rats, most birds, fishes, amphibians, and reptiles. Experimental studies have also shown susceptibility of the canid *Nyctereutes*, the raccoon dog, to intranasal infection [54] and cattle and sheep, but not pigs, using ex-vivo organ cultures, in this case lungs and trachea [55]. Additional studies of in vivo susceptibility of these domestic species are warranted to determine their potential role in the epidemiology of SARS-CoV-2. That human-animal-human transmission exists is shown by COVID-19 in mink and in-contact humans on mink-farms in the Netherlands, Denmark, Spain, Sweden, Italy and the United States of America [56]. Since June 2020, Denmark has experienced extensive SARS-CoV-2 outbreaks in mink farms with disease in farm-workers and via them into the human community [57] with early circulation of a unique mink-associated SARS-CoV-2 variant, referred to as the "cluster 5", presenting a combination of mutations in the S protein never observed before, [58] with potential implications for viral fitness (ability to infect humans and animals), transmissibility, and antigenicity [59]. ECDC has recently published a rapid risk assessment of the human health risk posed by COVID-19 outbreaks in mink [60]. There is also the potential for establishment of a non-human reservoir of SARS-CoV-2 in the wild, for example should the virus become established in wild mink after escape from farms [61], as has been reported in Utah, USA [62]. Therefore it is imperative to prevent or contain the jump from animals to human and vice versa, and the subsequent risk of an epidemic or pandemic, which, as demonstrated by the COVID-19, produces crippling and long-term effects on human health and the global economy. To reduce the risk of introduction of SARS-CoV-2 to susceptible farmed animal populations from humans, from animal to humans and between animals, the OIE has published a draft guidance for public health authorities and other partners and recommended risk reduction strategies based on the One Health approach [63]. In a previous paper, FAO assessed the likelihood of exposure of humans or animals to SARS-CoV-2 in COVID-19 affected areas at a global level, through contact with wild animals, livestock, companion animals, aquatic animals, and handling or consumption of animal carcasses, meat/organs, body fluids and excretions [64]. The FAO paper does not include the assessment of the likelihood of post-exposure human or animal infection. It is clear that adopting the One Health approach is essential to address the risks and related pathways associated with different farming systems, and for timely and effective measures to adopt in case of SARS-CoV-2 introduction to a farm, just as much as helping understand dynamics of infection in companion animals.

5. The environment and the COVID-19 pandemic

In addition to elucidating the pathway of SARS-CoV-2 from its animal origin to humans, and monitoring susceptible wildlife for infection, a new environment-orientated field that needs to be better explored in the fight against COVID-19 is Wastewater-Based Epidemiology (WBE). Several studies have reported the detection of SARS-CoV-2 RNA in wastewater in the early stages of local outbreaks, and a quantitative relationship can be seen between RNA densities in sewage and human infection prevalence. This means that adoption of WBE on a wider basis would efficiently generate useful and probably necessary data for the detection and management of infectious disease transmission in communities and predict spill-over into wildlife hosts or virus concentrators via water run-off [65]. This is especially important given that asymptomatic and pauci-symptomatic infections are unlikely to be detected during clinical surveillance [66] [67] and, in any case, viral RNA is undetectable within 5 or 6 days in such cases [68]. SARS-CoV-2 can survive for extended periods in the aqueous environment, so that infective virus can be still detected in the effluent from water-treatment plants [69]. It could certainly be possible that an infection cycle could be established, as for Hepatitis E virus, from human excreta, through municipal wastewater treatment plants [70] and introduction into the natural aquatic environment, contaminating drinking water. Another environmental source of SARS-CoV-2 for humans might be edible filter-feeders, such as bivalve seafoods (mussels, oysters), already well-known to filter out and concentrate viruses such as norovirus and hepatitis A and B from coastal waters contaminated with effluents [71]. Together with concerns about wildlife hosts such as European mink, these findings clearly signal the need to conduct wastewater and environmental surveillance of COVID-19 in the community in the framework of epidemiological monitoring of COVID-19 with the aim to reduce virus circulation in the environment and the potential SARS-CoV-2 spillback from infected humans to naive wildlife hosts that reside near the treatment plants, and can act as a novel viral reservoir [72]. What also makes this pressing is the continuous encroachment of human activities into wildlife habitats and the corresponding habituation of wildlife into human settings, leading to increased pressure for animal-human pathogen exchange [73] [26]. It goes without saying that if SARS-CoV-2 can be successfully transmitted to humans via infected food items such as shellfish, an enormous collaborative effort will be required between public health, food safety and aquaculture professionals to deal with the risks.

6. The one health approach to tame COVID-19

The One Health approach was born in 2004 during the symposium "Building Interdisciplinary Bridges to Health in a Globalized World" at

The Rockefeller University, Manhattan, hence the twelve 12 Manhattan Principles agreed at that symposium [74], reaffirmed and updated as the Berlin Principles in 2019 [75]. The Berlin Principles are much more comprehensive than the original Manhattan Principles and three of them, Nos. 2, 5 and 8, are especially relevant to management of COVID-19 and future pandemics. These are: that strong institutions be developed that integrate understanding of human and animal health with the health of the environment, with investment in the translation of robust science-based knowledge into policy and practice; that adaptive, holistic and forward-looking approaches need to be devised to manage emerging and resurging diseases, taking account of the complex interconnections among species, ecosystems, and human society; and that capacity for cross-sectoral and trans-disciplinary health surveillance needs enhancing, with clear, timely information-sharing to improve coordination of responses among governments and NGOs, health, academia and other institutions, industry and other stakeholders. If the knowledge of the environment and ecosystems is crucial to improve the control of neglected and emerging infectious diseases, many of which are zoonoses, a further cultural move suggests a methodological convergence between One Health, dominated by the veterinary and medical disciplines, and EcoHealth. Although both challenge the traditional reductionism of biomedical approaches by placing animal and human health in their wider ecological context and promoting transdisciplinary and interdisciplinary research, EcoHealth devotes greater attention to the broader relationships between health and ecosystems, focusing on the environment and related socio-economic systems [76]. Basically, by exploiting this convergence and with a holistic vision of multi-systemic relationships, the health authorities can place the health emergencies within a much wider system and ensure effective and sustainable prevention and control measures of health threats.

7. The veterinary contributions to the management of the COVID-19 pandemic

The COVID-19 pandemic, like SARS and MERS, indicates that health of humans, animals and the environment is inextricably linked and supports the need for a transdisciplinary collaboration according to the One Health approach. But how can public health veterinarians constructively and proactively interface with the human health sector to deal with COVID-19 or future pandemics and operate in the same epidemiological surveillance program? Given the animal-origin of COVID-19 and the predominance of zoonoses in merging infections, the veterinarians' key role is provided by their important work in animal and public health disease surveillance to prevent disease outbreaks, including of zoonotic diseases. They have long years of experience of and expertise in dealing on the one hand with the circulation of pathogenic viruses among wild animals (epidemiological surveillance) and on the other hand with epidemics caused by emerging or exotic pathogens introduced into fully sensitive animal populations. This will contribute strongly to both the study of SARS-CoV-2 animal reservoirs and the application of sampling strategies used for the surveillance of animal epidemics and adjustment to the COVID-19 epidemic. Indeed, the contribution of public health veterinarians from a One Health perspective can be envisaged and substantiated through different levels of expertise, such as viral surveillance of wildlife, management and control of past animal epidemics, laboratory services to diagnose and characterize pathogens including SARS-CoV-2, the processing of human and animal COVID-19 tests, animal research and developing vaccines for humans and for animals, and animal import risk assessment.

7.1. Viral surveillance of wildlife

It is recognised that about 75% of infectious pathogens in humans are zoonotic in origin. Environmental destruction, caused by intense agriculture, land clearing, deforestation, wildlife trade and climate change, is putting humans into closer contact with animals carrying microbes that can be transferred to people during these encounters. Given that an estimated 1.7 million currently undiscovered viruses are thought to exist in mammalian and avian hosts, up to 850,000 could have the ability to cause the next animal-man spill-over [26]. Among the targeted species, bats play a key role as reservoir, harbouring known dangerous viruses such as malaria, yellow fever, chikungunya, Zika, Ebola and Nipah virus. Bats have very limited immunological and inflammatory responses to many viruses, mediated via a highly unreactive form of NLRP3 protein, allowing them to tolerate, carry and spread viruses that can be highly pathogenic for other species [77]. This poses a serious threat to human and animal health, in particular when human activities disrupt their habitat and create conditions for constant and repeated jumps of viruses from these natural hosts to humans. Coupled with human hunting, sale, and consumption of wild animals, this creates the conditions for the transmission of coronavirus either from bats to humans directly, as for Ebolavirus, or through proximity to intermediate hosts, as for SARS and MERS or Nipah virus. To predict and prevent future pandemics caused by further emerging viruses, it is therefore necessary to understand their origin, evolutionary diversity and geographical distribution in reservoir species and to define hotspots that could help target them for proactive zoonotic disease surveillance. The role of veterinary virologists, with their study of virus evolution, notably the circulation and pathogenesis of viruses in domestic and wild animals, is essential for coordinating integrated surveillance studies on the aetiology of viral zoonoses and their impact on the health of animals, humans, and the ecosystem. The related studies will provide essential data to explain their role as emerging and zoonotic pathogens, streamline the viral surveillance in reservoir populations, address the drivers of disease emergence and fine-tune pandemic preparedness. Bats do appear to be strong candidates for the source of other viruses. 7 of the 15 known alfa and beta-coronavirus genera, which primarily affect mammals, have only been isolated in bats and coronaviruses that are genetically related to HCoV 229E and NL63 have also been detected in bats [78]. A three-year veterinary monitoring study in Northwest Italy focused on coronavirus and paramyxoviruses (PMV) due to their proven ability to switch hosts and their zoonotic potential, and helped to characterize viral diversity in the bat population [79]. 20 new coronaviruses and 3 PMV strains were identified and phylogenetically characterised using PCR. The study enabled the identification of alfa and beta-coronavirus in new species of bats and in Italian regions that have never previously been monitored. More recently, a SARS-like β-coronavirus was detected in three bat species in Sardinia [80]. The SarBatCoV1 virus, identified using phylogenetic analysis based on RNA-dependent RNA polymerase (RdRp) sequences, belonged to clade 2b, which includes most of the SARS-like CoVs found in bats, as well as human SARS-CoV. These studies demonstrate how veterinary surveillance activities carried out within specific geographical areas can contribute to knowledge of the extent of viral circulation in bats that live in close proximity to other animal hosts with direct implications for the prevention of diseases in humans. Phylogenetic analyses also have the advantage of identifying viruses with genetic prerequisites for human infection, especially at hot-spots with ecological conditions facilitating spillover and informing the most appropriate prevention and control strategies for the management of potential threats to public health. Unfortunately, as we previously noted, a stronger integration of veterinary (eg. virologists and epidemiologists) and human medicine, regrettably struggles to be centrally structured within the public health system. However, under the One Health umbrella, there are good examples of collaboration, supported by informatic pipelines for sharing integrated data on the animal, human and environmental health, and providing evidence-based resources for policymakers and risk assessment studies. One of these is the Italian West Nile virus (WNV) national preparedness and response plan. WNV is an infection of birds, transmissible by vector mosquitoes (*Culex spp.*) to horses and humans, and endemic in some Italian regions, mainly in the northern provinces located in the Po river basin. Since 2018, over 247 autochthonous human cases of WNV neuro-invasive infections have

been notified in Italy. The implementation of the surveillance plan allowed veterinarians to detect viral circulation in the vectors nine days before symptoms-onset of the first confirmed human case, and to prevent the transmission of human infection by means of vector control and the adoption of blood and transplant safety measures [81].

In recent years many global collaborative projects have thrived with the contribution of veterinarians, such as the PREEMPT [82], PREDICT [83] and PREDICT 2 projects in the U.S. Agency for International Development USAID's Emerging Pandemic Threats (EPT) and EPT-2 programs [84]. Using the One Health approach and collaboration across disciplines, the projects aim to build viral surveillance platforms that will identify and monitor zoonotic pathogens such as influenza viruses, coronaviruses, paramyxoviruses, filoviruses, and flaviviruses, before they can spill-over from animal hosts to people, and allow investigation of the behaviours, practices, and ecological and biological factors driving disease emergence, transmission, and spread. Notably, PREDICT fed data from field and lab studies into computer models that predict virus spill-over potential. The main aims are to develop recommendations and countermeasures to minimize the risk of pandemics and to identify optimal timing for application of vaccines targeting virus elimination.

7.2. Opening the livestock epidemic toolbox for public health

Veterinarians have gained extensive field experience in the control of past epidemics of infectious and contagious diseases (e.g. bluetongue, foot and mouth disease, contagious bovine pleuro-pneumonia) and zoonoses (e.g. avian and swine flu, brucellosis and tuberculosis, BSE). From the lessons learned in the management of so many animal health emergencies, they have developed a special aptitude to 'get ready in the field' and to perform in a timely manner an array of activities, such as diagnosis, epidemiological investigations, molecular/antigenic characterization, planning of surveillance programs. Notably they have successfully applied a variety of surveillance methods to understand the ways in which viral agents spread, and to support evidence-based, effective, sustainable and timely measures for the reduction of the level of prevalence or the elimination of infectious diseases in animal populations [85].

To overcome the fragmented management response to COVID-19 across the EU [86], the EU Commission and the Council, at the request of the European Council Members, has developed a new Joint European Roadmap towards lifting COVID-19 containment measures to define an exit strategy as much as possible coordinated with the member states [87]. Comparison of this fragmented approach and related surveillance strategies adopted by EU member states at the outset of the COVID-19 emergency to control the infection, with ones applied by veterinarians for the control of animal infectious disease outbreaks shows that, although both sets of control strategies share the same goal, i.e. to limit the transmission of infection to humans and animals, the way they are achieved differs substantially. Traditionally, the human health system focuses on treatment of the individual patient, whilst rarely are measures directed to the whole population. On the contrary, in veterinary medicine, the health control strategy is directed to the whole animal population at risk, since epizootic diseases cause high cost for livestock and the general agricultural sector or companion animals and their owners, albeit with limited risks to public health. More practically, controlling an infectious outbreak requires understanding the nature, scale and dynamics of the epidemic, with the aim of reducing disease prevalence (i.e., the proportion of cases present in a particular animal population at any given time) and to provide swift evidence to decision-makers for implementing measures able to mitigate the economic and animal health burden. This is usually achieved by carrying out random investigations (e.g. serological tests) on samples of animals representative of the whole population. By using specific sampling procedures, all animals in the selected groups are systematically tested, including animals that are asymptomatic, to understand the likely exposure and to

estimate the real prevalence of the infection, the extent of the spread, as well as to monitor the situation over time and to suggest, predict or model what will happen in the future. Progress in the program is measured by the reduction of the incidence of the infection, i.e., the proportion of new infections in a given animal population at any given time. In essence, a control program has to be continued indefinitely. Depending on the prevalence level, the overall and long-term objective of the surveillance can be the eradication of the disease, meaning that the infectious agent has to be eliminated from a given animal population when the prevalence has been reduced to a level close to 2% of production units. When eradication is achieved, a country is deemed "free from the disease", the post-eradication measures consist mainly of surveillance and live animals are free to be traded internationally if originating from a recognised disease-free country. With this collection of information, disease characteristics are obtained such as the percentage of mild and asymptomatic infections and the lethality rate. The systematic data collected from a large population provides continuous and reliable estimates of the transmission parameter R_0 (basic reproduction ratio). These epidemiological indicators, along with the use of the Susceptible – Infectious – Resistant (SIR) models, are then used to provide evidence-based feedback to streamline the control policies and to make necessary adjustments. There are several applications and software as well as links from the web that are employed by veterinarians to calculate the appropriate sample sizes and to estimate the real prevalence or to reach the level of 'freedom' of a population. Based on the prevalence of infection and in order to limit the animal outbreak, veterinarians adopt specific containment measures (eg. prohibition on movement of animals of susceptible species, tracing of contacts, the identification of animals or herds affected to prevent further spread). The overall goal is to contain the epidemic at an early stage and to minimize economic losses. The strategy of prevention and control of transmissible animal diseases including zoonoses is a core task of the Veterinary Services of each OIE Member Country and is well harmonized at the international level. The animal health standards at EU level (e.g. animal registration and identification, definition of infected, protection and surveillance zones) are supported by a harmonized legal framework and are uniformly implemented by each EU member state. The overall goal is to stop the spread of infection and to facilitate trade. It goes without saying that all these standards facilitate the epidemiological investigations, enable the prediction of animal infections, and inform the international early warning system. In sharp contrast with the EU harmonized surveillance and control of animal infection epidemics, the management of COVID-19 by some European countries showed very poorly harmonized responses, most likely stemming from diverse cultures and health systems, phase of the epidemic curve, and the lack of efficient surveillance mechanisms able to provide timely evidence for informing control approaches in advance. Moreover, the surveillance strategies and protocols for carrying out the tests were divergent and not harmonized at a central level through the exchange of expert advice and data, leading to different containment measures depending on the country, with variability in requiring quarantine, social distancing, wearing of masks at all times in public, numbers of different household able to meet in public or within houses, or sizes and nature of large public gatherings such as sports events [88]. To overcome these intrinsic limitations of the European Union, the Commission and the Council of the EU, at the request of the members of the European Council, develop the Joint European Roadmap, for the phasing out of containment measures and definition of an exit strategy coordinated as much as possible with the Member States. Moreover with the aim of achieving agreement on a coherent approach to COVID-19 testing across Europe, the EU Commission has provided recommendations on different aspects of the testing activity [89]. This was accomplished in parallel with the ECDC's guidance encompassing five different testing approaches for symptomatic and asymptomatic cases to achieve specific public health objectives under different epidemiological situations existing in the EU member states [90]. However in this context, and

considering the experience gained by veterinarians in the epidemiology of diseases within populations, using active and passive surveillance systems and risk analysis, veterinary medicine might provide a valuable contribution of knowledge to public health for the control of infection in human populations. A basic veterinary protocol that will set up real-time active random surveillance has been proposed for COVID-19, with the aim of assessing COVID-19 outbreaks consistently and objectively and have a positive impact on the management of long-term epidemics [91]. The benefits of carrying out repeated random surveys for the control of epidemics are well documented in animal health veterinary surveillance, and public health bodies and decision-makers should recognize their usefulness when duly adapted to the human COVID-19 epidemic. Indeed, once the infection is widespread (high prevalence) as is the case of COVID-19, and it is no longer possible to trace individual clusters, the syndromic and risk-based surveillance are ineffective for guiding decisions on control at the community level, since identified cases are not representative of infected individuals in the population. In these circumstances the use of repeated representative random samplings of the human population (with the ad hoc calculation of sample size) at the local or regional level, with utility for other areas sharing similar characteristics, allows the estimation of the "real prevalence" of infected people (symptomatic and non-symptomatic) corrected for the test's error (i.e. for sensitivity and specificity <100%), or even the "real" prevalence of antibody positives. The proposed protocol would: allow representative "snapshots" of disease presence in the population, including the newly infected, not yet symptomatic; facilitate evidence-based control strategies at a higher level (i.e. regional-national level); generate parameters to "predict" the trend of the epidemic curve; facilitate selection of the best control options; prevent overwhelming the health care system; and inform decisions on when community control measures can be lifted. Furthermore, the protocol is fit-for-purpose and can be adapted to different circumstances and levels of responsiveness, provided that resource constraints are overcome (notably a wide and sufficient availability of tests) and collaboration between veterinary epidemiologists and public health representatives is duly strengthened. A rational combination of an individual patient-based approach and measures aimed at population health is therefore essential [92].

7.3. The veterinary contribution on vaccines

The EU veterinary strategy for animal health, inspired by the principle "prevention is better than cure", is linked to the availability and best use on farms of vaccines, drugs, and bio-safety measures, to limit episodes of viral transmission inter-species (animals wild-domestic), and prevent farms from becoming a source of global health problems. International cooperation, the harmonized standards governing animal husbandry, markets, and transport, and the advances in veterinary medicine, seek to ensure that infections on farms, including zoonosis, do not spread globally in the same way and at the same speed as COVID-19. A strong acceleration in the action against COVID-19 comes from the progress of the genome sequencing technique (Next-generation sequencing) and related global sharing of sequences and bioinformatics analysis. Moreover, in the case of COVID-19 the animal research and the use of animal models, notably the species susceptible to SARS-CoV-2, such as ferrets, non-human primates, pigs and rodents, along with the availability of artificial intelligence programs and algorithms, clearly support the development of human treatments and vaccines in relation to many different disorders [93]. Indeed animal research has contributed to the successful development of vaccines against human infections such as polio, measles, tuberculosis, meningitis and human papillomavirus that saved millions of lives [94] [95], and more recently to the development of animal vaccines against zoonoses such as Ebola, which is consistent with the One Health approach. The Jenner Institute at the University of Oxford developed a new vaccine against Rift Valley Fever (RVF), called ChAdOx1 [96], whose protective efficacy has been confirmed by researchers from the Pirbright Institute (UK). RVF

primarily affects ruminants (sheep, goats, cattle, camels) but is transmissible to humans through contact with infected animals and related contaminated tissues, as well as by the bite of infected mosquitoes. In severe cases, human infection leads to blindness, encephalitis, and hemorrhagic fever, and to date there are no human vaccines. ChAdOx1 is a new vector vaccine technology which uses a non-replicating monkey adenovirus integrated with the genes encoding some glycoproteins of the viral envelope responsible for the immune response. This is now making a direct contribution to the control of human diseases: in addition to RVF, ChAdOx1 is being used for the development of vaccines against MERS [97], Chikungunya [98], and Nipah viral infections [99]. These new vaccines, a result of an integrated research area and interdisciplinary collaboration, offer an excellent example of a One Health approach, that permits delivery of solutions that benefit animals, people, and ecosystems simultaneously. In the current global race to develop human COVID-19 vaccines, the University of Oxford in collaboration with the Anglo-Swedish pharmaceutical company AstraZeneca has used the ChAdOx1 technology for the production of the vector viral vaccine ChAdOx1 nCov-19 containing the genetic material of the SARS-CoV-2 virus peak protein [100]. With respect to One Health, it is worth mentioning the ZAPI (Zoonoses Anticipation and Preparedness Initiative) project, a platform for the rapid characterization, design, and large-scale production of vaccines to prevent the spread of viruses responsible for animal and human infections, such as RVF, Schmallenberg, and MERS [101]. ZAPI, which pulls together veterinary research and medical institutions, NGOs, regulatory agencies and vaccines and biotechnologies manufacturers, is financed with 9.5 million euros (2015–2021) under the "Preparation and Response" action, and focuses on the study of the defence against animal coronaviruses in order to seek effective human treatments.

7.4. The diagnosis and molecular characterization of SARS-CoV-2

The COVID-19 pandemic has severely stressed the actual capacity of health care systems globally, particularly in countries ill-prepared to slow down the spread of the virus and "flatten the curve" of new cases. Besides the overloading of hospitals, urgent issues came to the fore such as the lack of equipment and materials, disposable personal protective gear, and the massive workload of COVID-19 tests. The veterinary sector played an important One Health role during the crisis. To support the heavy workload of public health laboratories, veterinary laboratories in many EU countries carried out SARS-CoV-2 testing of human samples and jointly developed common diagnostic and data exchange protocols, and provided masks and other protective materials to hospitals and key equipment such as respirators.

7.5. Animal import risk assessment knowledge to tackle COVID-19

International travel poses substantial risks for continued introduction of SARS-CoV-2. The veterinary experience in animal import risk assessment can support government in defining a COVID-19 risk strategy for international air travel. Animal import risk methodology can be quickly updated and adapted to COVID-19 prevalence estimate for countries to assess the impact of any further changes to international travel policy or disease occurrence. Such methodology was developed by the UK Public Health England modelling team, composed of veterinary epidemiologists, risk assessor and animal infectious disease modellers, and responsible for providing scientific advice to inform Government's COVID-19 policy on travel controls [102].

8. The challenges ahead to fully implement the One Health approach

The One Health approach requires overcoming a series of gaps related to communication, training, and financial resources. If not enough has been done to prevent the COVID-19 pandemic, it is bluntly

evident that for the next global health emergency, well-equipped and effective national emergency plans will require adequate human and material resources, synergies and inter-professional collaborations, and the availability of advanced artificial intelligence forecasting tools. To cope with the COVID-19 and similar threats with high socio-economic and health impacts, communication is a key element to ensure swift information flows within the surveillance systems, with data shared among veterinarians, physicians, and other professionals, between them and government functions, and externally with interested parties and the general public, with the overall aim to develop evidence-based containment and mitigation policies. Since viruses don't know borders and lack of adequate response by one country makes global control and prevention less effective, the success of communication relies on the cooperation between countries, and at the national level on the coordination of relevant institutions, policymakers, and experts. Communication difficulties may be exacerbated by the lack of a coordination strategy between countries, and at the national level between agencies and involved institutions. A useful lesson on how to better manage the COVID-19 crisis and the future health threats can be borrowed from the military model: to be well prepared and to minimize the impact of COVID- 9 or similar pandemic ("win the war"), is necessary to deploy simulation and scenario analysis tools ("weapons") within a strategic plan, where the roles of policymakers, experts, and business subjects ("forces") are well defined. This exercise requires, on the national scale, the government's commitment to greater funding and careful and efficient spending of such funding and, under the guidance of health institutions, the scheduling of annual epidemic simulations, to know when and how to answer. Education and training play a fundamental role in building a One Health mindset, and promoting cultural action to change the societal perception of a lesser role of animals (reservoirs or intermediate hosts of pathogens) in the epidemiology of human infections. If, on the one hand, it is necessary to increase the awareness of policymakers of the importance of veterinary wildlife surveillance programs to prevent future pandemics or panzootic, on the other hand, One Health knowledge must be included in education programs starting from early school years (eg. primary and secondary education) and maintained throughout training courses in colleges and universities and postgraduate education [103]. Indeed, early school years are an important period for building a strong foundation for children who might become future politicians, teachers, parents, or other influential people, on the linkages between the environment, animals, plants, and human health, as well on the positive behavioural changes [104].

It is evident that both communication and training gaps stem from the general lack of political commitment to deploy adequate financial resources to implement One Health projects at all levels (local, national, and global) and to develop interdisciplinary networks. When looking at recent EU initiatives, the principles of One Health are grievously absent, whether from the broader vision of the European Commission in the strategic document 'From producer to consumer: for a fair, healthy and environmentally friendly food system (From Farm to Fork-F2F)' [105] [106], or from specific COVID-19 initiatives, notably the ten priority and coordinated short-term research and innovation actions of the first 'ERAvsCorona' action plan [107]. To deal with the COVID-19 emergency, the EU has mobilized €72 million for therapies and diagnostics projects from Horizon 2020, the EU's research and innovation programme, €45 million will be provided by the pharmaceutical industry, Innovative Medicines Initiative (IMI) associated partners and other organisations involved with the projects, bringing the total investment to €117 million [108]. The actions will concern epidemiology, epidemic preparedness and response programs, diagnostic tools, treatments, vaccines, and infrastructure, exactly the areas where veterinary knowledge and practical experiences can make a huge impact. Unfortunately, compared to the availability of such huge grants for human health, the funds appear inadequate in the same sectors in veterinary medicines. This incompleteness is confirmed by the absence of veterinary research projects and One Health within the 'European Research Area corona platform', in spite of existing foundations, in the earlier EU-supported ERA-NET STAR-IDAZ, ERA-NET ICRAD and DISCONTOOLS.

9. Final remarks

SARS-CoV-2 is rapidly transmitting across the globe and causing unprecedented disruption of human health and political, social, humanitarian and economic situations. More and better science is needed to address the many sources of uncertainties around COVID-19, notably its original animal reservoir, the intermediate host, the route of virus transmission to humans, the role of pets and wildlife in spreading or maintaining the disease in human communities. The COVID-19 pandemic, likewise past pandemics (SARS, MERS), tells us that the One Health perspective, which considers human and animal health to be interdependent and closely linked to the health of ecosystems, must be strongly promoted among the medical and veterinary professions, by overcoming the dichotomy between public health and animal health. If the COVID-19 pandemic is imposing new challenges to all participants in the public health systems, to better operationalize the One Health approach, there is the need to consider several lines of contributions the veterinary profession might provide to manage the COVID-19 pandemic. Veterinarians have always been a core influential group of health professionals on a global scale by virtue of their experience, know-how, and responsibility to promote the health and welfare of animals, people, and the environment. They have always been in the frontline of monitoring and zoonosis surveillance of viruses (some of them lethal for humans) among animal reservoirs, and successfully applied different types of surveillance methods and sampling strategies in the context of animal infectious epidemics. The related experience and data shared with dedicated platforms between both professions (veterinary and physicians) can be extremely informative of early warning signs for the rapid detection and early control of transmissible diseases and potential human epidemic or pandemic. New scientific evidence proves that pigs, cats, ferrets, and minks, have similar or identical SARS cellular receptors found in humans, and support viral replication. This highlights the possibility that SARS-CoV-2 makes a further jump into new animal hosts, without the need for significant genetic modifications. Moreover, the random genetic mutations incurred by the virus during replication, could increase the potential for endemic development in some animal species, including domestic species, and the subsequent panzootic potential. To be able to predict and prevent future pandemics, it is therefore necessary to work collaboratively across borders and disciplines and to bolster regional and global wildlife surveillance in hotspots that have ecological conditions conducive to an inter-species viral transmission. For these reasons, the new SARS-CoV-2 surveillance guidelines should also include livestock and pets. The task of curbing the spread of SARS-CoV-2 requires a nationwide coordinated approach, as does the task of ensuring optimal medical care, to increase the knowledge base, and an effective and centralised multidisciplinary task-force. Considering the limited funds allocated to manage the health threats, the hope is that both at the EU and global level government and decision makers commit to greater funding and careful and efficient spending for pandemic early warning systems and epidemic intelligence gathering inside the One Health approach. In order to fully operationalize the One Health concept it is of the utmost importance to ensure that veterinarians, notably veterinary epidemiologists and virologists, have a prominent place within the national and international management and monitoring structures of the COVID-19 epidemic. For the future, it is hoped that both the EU and the international community will assign funding priorities for the development of epidemic intelligence systems and surveillance platforms aimed at the identification and monitoring of emerging zoonotic pathogens and knowledge of the factors that contribute to their spread pandemic, bringing the animal and human public health specialisms together with risk analysers and epidemiologists to manage future pandemics more effectively.

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References

[1] United Nations Industrial Developments Organizations (UNIDO), Coronavirus: The Economic Impact 10. https://www.unido.org/stories/coronavirus-economic-impact, July 2020.

[2] Europen Centre for Disease Prevention and Control (ECDC), COVID-19 Situation Update for the EU/EEA and the UK, As of Week 53, 31 December, https://www.ecdc.europa.eu/en/cases-2019-ncov-eueea, 2020.

[3] P. Zhou, X.L. Yang, X.G. Wang, et al., A pneumonia outbreak associated with a new coronavirus of probable bat origin, Nature 579 (2020) 270–273, https://doi.org/10.1038/s41586-020-2012-7.

[4] T. Zhang, Q. Wu, Z. Zang, Probable Pangolin Origin of 2019-nCoV Associated with Outbreak of COVID-19, Current-biology-D-20-00299, https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3542586, 2020.

[5] American Society for Microbiology (ASM), COVID-19 Transmission Dynamics, April 20, https://www.asm.org/Articles/2020/April/COVID-19-Transmission-Dynamic, 2020.

[6] J.M. Santini, S.J.L. Edwards, Host range of SARS-CoV-2 and implications for public health, The Lancet Microb. (August 2020) 1. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7302768/.

[7] Y. Hangping, L. Xiangyun, C. Qiong, X. Kaijin, C. Yu, C. Linfang, L. Lanjuan, Patient-derived mutations impact pathogenicity of SARS-CoV-2, preprint, medRxiv (2020), https://doi.org/10.1101/2020.04.14.20060160.

[8] B. Ju, Q. Zhang, X. Ge, R. Wang, J. Yu, S. Shan, L. Zhang, Potent Human Neutralizing Antibodies Elicited by SARS-CoV-2 Infection, 2020, https://doi.org/10.1101/2020.03.21.990770v2.

[9] M. Tobaiqy, M. Qashqary, S. Al-Dahery, A. Mujallad, A.A. Hershan, M.A. Kamal, N. Helmi, Therapeutic management of COVID-19 patients: a systematic review, Infect. Prevent. Pract. 2 (3) (September 2020), https://doi.org/10.1016/j.infpip.2020.100061.

[10] Europen Centre for Disease Prevention and Control (ECDC), COVID-19 Vaccination and Prioritisation Strategies in the EU/EEA, Technical report, https://www.ecdc.europa.eu/en/publications-data/covid-19-vaccination-and-prioritisation-strategies-eueea, 22 Dec 2020.

[11] J.H. Amuasi, C. Walzer, D. Heymann, H. Carabin, L.T. Huong, A. Haines, A.S. Winkler, Calling for a COVID-19 One Health Research Coalition, The Lancet Correspondence 395 (10236) (May 16, 2020) 1543–1544, https://doi.org/10.1016/S0140-6736(20)31028-X.

[12] K. Gruetzmacher, W.B. Karesh, J.H. Amuasi, et al., The Berlin principles on one health – Bridging global health and conservation, Sci. Total Environ. (2021), https://doi.org/10.1016/j.scitotenv.2020.142919.

[13] Dept of Health National Public Health Emergency Team (NPHET) for COVID-19: Governance Structures. https://www.gov.ie/en/publication/de1c30-national-public-health-emergency-team-nphet-for-covid-19-governance, 2020.

[14] Royal College of Veterinary Surgeons (RCVS). https://www.rcvs.org.uk/setting-standards/advice-and-guidance/coronavirus-covid-19/covid-19-taskforce/, 2020.

[15] A.E. Gorbalenya, S.C. Baker, Coronaviridae Study Group of the International Committee on Taxonomy of Viruses, et al., The species severe acute respiratory syndrome-related coronavirus: classifying 2019-nCoV and naming it SARS-CoV-2, Nat. Microbiol. 5 (2020) 536–544, https://doi.org/10.1038/s41564-020-0695-z.

[16] V.M. Corman, D. Muth, D. Niemeyer, C. Drosten, Hosts and sources of endemic human coronaviruses, Adv. Virus Res. 100 (2018) 163–188. https://pubmed.ncbi.nlm.nih.gov/29551135/.

[17] F. Pene, A. Merlat, A. Vabret, F. Rozenberg, A. Buzyn, F. Dreyfus, A. Cariou, F. Freymuth, P. Lebon, Coronavirus 229E-related pneumonia in immunocompromised patients, Clin. Infect. Dis. 37 (7) (2003 Oct 1) 929–932. https://www.ncbi.nlm.nih.gov/pubmed/13130404.

[18] G.J. Gorse, T.Z. O'Connor, S.L. Hall, J.N.. Vitale, K.L. Nichol, human coronavirus and acute respiratory illness in older adults with chronic obstructive pulmonary disease, J. Infect. Dis. 199 (6) (2009 Mar 15) 847–857. https://www.ncbi.nlm.nih.gov/pubmed/19239338.

[19] P. Zhou, et al., Fatal swine acute diarrhoea syndrome caused by an HKU2-related coronavirus of bat origin, Nature 556 (2018) 255–258, https://doi.org/10.1038/s41586-018-0010-9.

[20] E.E. Caitlin, L.Y. Boyd, R.L. Grahama, S.R. Leista, Y.J. Houa, K.H. Dinnon, A.C. IIIb, J. Simsc, K. Swanstrom, T.D. Gullyd, M.R. Scobeya, C.G. Cooleya, S.H. Randelle Curriea, R.S. Baric, Swine acute diarrhea syndrome coronavirus replication in primary human cells reveals potential susceptibility to infection, PNAS 117 (43) (October 27, 2020), https://doi.org/10.1073/pnas.2001046117.

[21] A. Lorusso, P. Calistri, A. Petrini, G. Savini, N. Decaro, Novel coronavirus (SARS CoV 2) epidemic: a veterinary perspective, Vet. Ital. 56 (1) (2020) 5–10, https://doi.org/10.12834/VetIt.2173.11599.1. http://www.izs.it/vet_italiana/pdf_4/VetIt_2173_11599_1.pdf.

[22] J.W. Rausch, A.A. Capoferri, M.G. Katusiime, S.C. Patro, M.F. Kearne, Low genetic diversity may be an Achilles heel of SARS-CoV-2, Proc. Natl. Acad. Sci. U. S. A. 117 (40) (2020) 24614–24616, https://doi.org/10.1073/pnas.2017726117.

[23] F. Robson, K.S. Khan, T.K. Le, C. Paris, S. Demirbag, P. Barfuss, P. Rocchi, W.-L. Ng, Coronavirus RNA proofreading: molecular basis and therapeutic targeting. Review, Mol. Cell. Rev. 79 (5) (September 03, 2020) 710–727, https://doi.org/10.1016/j.molcel.2020.07.027.

[24] https://nextstrain.org/.

[25] D. Wrapp, N. Wang, K.S. Corbett, J.A. Goldsmith, C.-L. Hsieh, et al., Cryo-EM structure of the 2019-nCoV spike in the prefusion conformation, Science 367 (6483) (13 Mar 2020) 1260–1263. https://science.sciencemag.org/content/367/6483/1260.

[26] P. Daszak, J. Amuasi, J. das Neves, D. Hayman, T. Kuiken, B. Roche, C. Zambrana-Torrelio, P. Buss, H. Dundarova, Y. Feferholtz, G. Földvári, E. Igbinosa, S. Junglen, Q. Liu, G. Suzan, M. Uhart, C. Wannous, K. Woolaston, P. Mosig Reidl, K. O'Brien, U. Pascual, P. Stoett, H. Li, H.T. Ngo, PBES, Workshop Report on Biodiversity and Pandemics of the Intergovernmental Platform on Biodiversity and Ecosystem Services, 2020, https://doi.org/10.5281/zenodo.4147318.

[27] N. Zhu, D. Zhang, W. Wang, X. Li, B. Yang, J. Song, X. Zhao, B. Huang, W. Shi, R. Lu, P. Niu, F. Zhan, et al., A novel coronavirus from patients with pneumonia in China 2019, N. Engl. J. Med. 382 (2020) 727–733, https://doi.org/10.1056/NEJMoa2001017.

[28] Y.Z. Zhang, E.C. Holmes, A genomic perspective on the origin and emergence of SARS-CoV-2, Cell 181 (2) (2020) 223–227, https://doi.org/10.1016/j.cell.2020.03.035.

[29] Q. Li, X. Guan, P. Wu, X. Wang, L. Zhou, Y. Tong, et al., Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia, New Engl. J. Med. 382 (13) (2020) 1199–1207, https://doi.org/10.1056/NEJMoa2001316.

[30] J. Coen, Wuhan seafood market may not be source of novel virus spreading globally, Science (January 26, 2020), https://doi.org/10.1126/science.abb0611. https://www.sciencemag.org/news/2020/01/wuhan-seafood-market-may-not-be-source-novel-virus-spreading-globally.

[31] P. Zhou, X.L. Yang, X.G. Wang, A.L. ET, A pneumonia outbreak associated with a new coronavirus of probable bat origin, Nature 579 (2020) 270–273, https://doi.org/10.1038/s41586-020-2012-7.

[32] A. Latinne, B. Hu, K.J. Olival, et al., Origin and cross-species transmission of bat coronaviruses in China, Nat. Commun. 11 (2020) 4235, https://doi.org/10.1038/s41467-020-17687-3.

[33] T.T.Y. Lam, N. Jia, Y.W. Zhang, et al., Identifying SARS-CoV-2-related coronaviruses in Malayan pangolins, Nature 583 (2020) 282–285, https://doi.org/10.1038/s41586-020-2169-0.

[34] K. Xiao, J. Zhai, Y. Feng, N. Zhou, X. Zhang, J.J. Zou, N. Li, Y. Guo, X. Li, X. Shen, Z. Zhang, F. Shu, W. Huang, Y. Li, Z. Zhang, R.A. Chen, Y.J. Wu, S.M. Peng, M. Huang, W.J. Xie, Q.H. Cai, F.H. Hou, W. Chen, L. Xiao, Y. Shen, Isolation of SARS-CoV-2-related coronavirus from Malayan pangolins, Nature 583 (7815) (2020 Jul) 286–289, https://doi.org/10.1038/s41586-020-2313-x.

[35] X. Li, E.E. Giorgi, M.H. Marichann, et al., Emergence of SARS-CoV-2 through Recombination and Strong Purifying Selection, Preprint, bioRxiv, 2020; 2020.03.20.000885, Mar 22 2020, https://doi.org/10.1101/2020.03.20.000885.

[36] J. Lee, T. Hughes, M.-H. Lee, H. Field, J.J. Rovie-Ryan, F.T. Sitam, S. Sipangkui, N. Symphorosa, S.K.S.S. Nathan, D. Ramirez, S.V. Kumar, H. Lasimbang, J.H. Epstein, P. Daszak, No evidence of coronaviruses or other potentially zoonotic viruses in Sunda pangolins (*Manis javanica*) entering the wildlife trade via Malaysia, BioRxiv, preprint (2020), https://doi.org/10.1101/2020.06.19.158717.

[37] F. Wu, S. Zhao, B. Yu, et al., A new coronavirus associated with human respiratory disease in China, Nature 579 (2020) 265–269, https://doi.org/10.1038/s41586-020-2008-3.

[38] J. Shang, G. Ye, K. Shi, et al., Structural basis of receptor recognition by SARS-CoV-2, Nature 581 (2020) 221–224, https://doi.org/10.1038/s41586-020-2179-y.

[39] M.F. Boni, P. Lemey, X. Jiang, et al., Evolutionary origins of the SARS-CoV-2 sarbecovirus lineage responsible for the COVID-19 pandemic, Nat. Microbiol. 5 (2020) 1408–1417, https://doi.org/10.1038/s41564-020-0771-4.

[40] K.G. Andersen, A. Rambaut, W.I. Lipkin, et al., The proximal origin of SARS-CoV-2, Nat. Med. 26 (2020) 450–452, https://doi.org/10.1038/s41591-020-0820-9.

[41] J. Shi, Z. Wen, G. Zong, H. Yang, C. Wang, R. Liu, X. He, L. Shuai, Z. Sun, Y. Zhao, L. Liang, P. Cui, J. Wang, X. Zhang, Y. Guan, H. Chen, Z. Bu, Susceptibility of ferrets, cats, dogs, and different domestic animals to SARS-coronavirus-2, Science (2020), https://doi.org/10.1126/science.abb7015.

[42] E.M. Leroy, M. Ar Gouilh, J. Brugère-Picoux, The risk of SARS-CoV-2 transmission to pets and other wild and domestic animals strongly mandates a one-health strategy to control the COVID-19 pandemic, One Health (2020) 100133, https://doi.org/10.1016/j.onehlt.2020.100133. Dec;10, https://pubmed.ncbi.nlm.nih.gov/32363229/.

[43] W.K. Jo, E.F. de Oliveira-Filho, A. Rasche, A.D. Greenwood, K. Osterrieder, J.F. Drexler, Potential zoonotic sources of SARS-CoV-2 infections, Transbound. Emerg. Dis. (2020 Oct 9), https://doi.org/10.1111/tbed.13872. Epub ahead of print. PMID: 33034151; PMCID: PMC7675418.

[44] OIE Covid-19 Portal. https://www.oie.int/en/scientific-expertise/specific-inf ormation-and-recommendations/questions-and-answers-on-2019novel-coronavi rus/events-in-animals/, 2021.

[45] A.M. Messenger, A.N. Barnes, G.C. Gray, Reverse zoonotic disease transmission (zooanthroponosis): a systematic review of seldom-documented human biological threats to animals, PLoS One 9 (2) (2014), e89055, https://doi.org/10.1371/ journal.pone.0089055.

[46] K. Munir, S. Ashraf, I. Munir, H. Khalid, M.A. Muneer, S. Amin, S. Ashraf, M.A. Imran, U. Chaudhry, M.U. Zaheer, M. Arshad, R. Munir, A. Ahmad, X. Zhao, Zoonotic and reverse zoonotic viruses of SARS-CoV-2 and their impact on global health, Emerg. Microb. Infect. 9 (1) (2020) 2222–2235, https://doi.org/10.1080/22221751.2020.1827984.

[47] K.J. Olival, P.M. Cryan, B.R. Amman, R.S. Barik, D.S. Blehert, C.E. Brook, et al., Possibility for reverse zoonotic transmission of SARS-CoV-2 to free-ranging wildlife: a case study of bats, PLoS Pathog. 16 (9) (2020), e1008758, https://doi. org/10.1371/journal.ppat.1008758.

[48] T.H.C. Sit, et al., Infection of dogs with SARS-CoV-2, Nature 586 (2020) 776–778, https://doi.org/10.1038/s41586-020-2334-5.

[49] C. Schulz, R. Schoierer, L. Grundl, A. Juric-Neubauer, G. Sutter, K. Hartmann, M. von Kockritz-Blickwede, A. Beer, A. Volz, SARS-CoV-2 Infection, Cat, Germany, Retrieved from, https://promedmail.org/promed-post/?id=7332909.

[50] Y. Wan, J. Shang, R. Graham, R.S. Baric, F. Li, Receptor recognition by the novel coronavirus from Wuhan: an analysis based on decade-long structural studies of SARS coronavirus, J. Virol. 94 (2020), e00127-20, https://doi.org/10.1128/ JVI.00127-20.

[51] N. Oreshkova, R.J. Molenaar, S. Vreman, F. Harders, B.B.O. Munnink, R. W. Hakze-van der Honing, N. Gerhards, P. Tolsma, R. Bouwstra, R.S. Sikkema, M. G.J. Tacken, M.M.T. de Rooij, E. Weesendorp, M.Y. Engelsma, C.J.M. Bruschke, L. A.M. Smit, M. Koopmans, W.H.M. van der Poel, A. Stegeman, SARS-CoV-2 infection in farmed minks, the Netherlands, April and May 2020, Euro Surveill 25 (23) (2020), https://doi.org/10.2807/1560-7917.ES.2020.25.23.2001005 pii=2001005.

[52] K. Schlottau, M. Rissmann, A. Graaf, J. SchöN, J. Sehl, C. Wylezich, D. Höper, T. C. Mettenleiter, A. Balkema-Buschmann, T. Harder, C. Grund, D. Hoffmann, A. Breithaupt, M. Beer, SARS-CoV-2 in fruit bats, ferrets, pigs, and chickens: an experimental transmission study, Lancet Microbe (2020), https://doi.org/ 10.1016/S2666-5247(20)30089-6.

[53] C. Conceicao, N. Thakur, J.T. Kelly, L. Logan, D. Bialy, et al., The SARS-CoV-2 Spike protein has a broad tropism for mammalian ACE2 proteins, PLoS Biol. 18 (12) (2020), e3001016, https://doi.org/10.1371/journal.pbio.3001016.

[54] M.F. Conrad, A. Breithaupt, T. Müller, J. Sehl, A.B. Buschmann, M. Rissmann, T. C. Mettenleiter, Susceptibility of raccoon dogs for SARS-CoV-2, bioRxiv preprint (2020), https://doi.org/10.1101/2020.08.19.256800.

[55] G. Di Teodoro, F. Valleriani, I. Puglia, F. Monaco, C. Di Pancrazio, M. Luciani, I. Krasteva, A. Petrini, M. Marcacci, N. D'Alterio, V. Curini, M. Iorio, G. Migliorati, M. Di Domenico, D. Morelli, P. Calistri, G. Savini, N. Decaro, E. C. Holmes, A. Lorusso, SARS-CoV-2 replicates in respiratory ex vivo organ cultures of domestic ruminant species, Vet. Microbiol. 252 (January 2021), 108933, https://doi.org/10.1016/j.vetmic.2020.108933.

[56] WHO, SARS-CoV-2 mink-associated variant strain- Denmark. https://www.who. int/csr/don/06-november-2020-mink-associated-sars-cov2-denmark/en/, 2020.

[57] Ministry of Environment and Food of Denmark, Update 6 on the COVID-19 Situation in Denmark. https://www.oie.int/fileadmin/Home/MM/Update_6_ Letter_to_the_OIE_on_Sars-CoV-2_in_Denmark_5_november2020.pdf, 2021.

[58] B.B.O. Munnink, R.S. Sikkema, D.F. Nieuwenhuijse, R.J. Molenaar, E. Munger, Richard Molenkamp, Arco van der Spek, Paulien Tolsma, Ariene Rietveld, Miranda Brouwer, Noortje Bouwmeester-Vincken, Frank Harders, Renate Hakze-van der Honing, Marjolein C.A. Wegdam-Blans, Ruth J. Bouwstra, Corine GeurtsvanKessel, Annemiek A. van der Eijk, Francisca C. Velkers, Lidwien A.M. Smit, Arjan Stegeman, Wim H.M. van der Poel, Marion P.G. Koopmans, Transmission of SARS-CoV-2 on mink farms between humans and mink and back to humans, Science 371 (2021) 172–177. https://science.sciencemag.org/content /sci/371/6525/172.full.pdf.

[59] R. Lassaunière, J. Fonager, M. Rasmussen, A. Frische, A. Bøtner, A. Fomsgaard, Working Paper on SARS-CoV-2 Spike Mutations Arising in Danish Mink, Their Spread to Humans and Neutralization Data. https://files.ssi.dk/Mink-cluster-5-sh ort-report_AFO2, 2020.

[60] European Centre for Disease Control (ECDC), Detection of New SARS-CoV-2 Variants Related to Mink 12, Rapid risk assessment, https://www.ecdc.europa.eu /sites/default/files/documents/RRA-SARS-CoV-2-in-mink-12-nov-2020.pdf, November 2020.

[61] M. Koopmans, SARS-CoV-2 and the human-animal interface: outbreaks on mink farms, Lancet (2020), https://doi.org/10.1016/S1473-3099(20)30912.

[62] PROMED, International Society for Infectious Diseases, COVID 19 Update (536), Animal, USA (UT) Wild Mink, 1st Case. https://promedmail.org/promed-post/?id =8015608, 2020.

[63] OIE, Guidance on Working with Farmed Animals of Species Susceptible to Infection with SARS-CoV-2, Draft published 05/11/2020, https://www.oie.int /fileadmin/Home/MM/Draft_OIE_Guidance_farmed_animals_cleanMS05.11.pdf, 2021.

[64] FAO, Exposure of Humans or Animals to SARS-COV-2 From Wild, Livestock, Companion and Aquatic Animals, Qualitative Exposure Assessment, FAO Animal Production and Health/paper 181, 2021. http://www.fao.org/3/ca9959en/CA99 59EN.pdf.

[65] B. Bivins, N. Devin, A. Ahmad, et al., Wastewater-based epidemiology: global collaborative to maximize contributions in the fight against COVID-19, Environ. Sci. Technol. 54 (2020) 7754–7757, https://doi.org/10.1021/acs.est.0c02388.

[66] J. Peccia, A. Zulli, D.E. Brackney, N.D. Grubaugh, E.H. Kaplan, A. Casanovas-Massana, A.I. Ko, A.A. Malik, D. Wang, M. Wang, J.L. Warren, D.M. Weinberger, S.B. Omer, SARS-CoV-2 RNA concentrations in municipal sewage sludge leading indicator of COVID-19 outbreak dynamics, medRxiv preprint (June 12, 2020), https://doi.org/10.1101/2020.05.19.20105999.

[67] G. Medema, L. Heijnen, G. Elsinga, R. Italiaander, A. Brouwer, Presence of SARS-Coronavirus-2 RNA in sewage and correlation with Reported COVID-19 prevalence in the early stage of the epidemic in The Netherlands, Environ. Sci. Technol. Lett. (2020 May 20), https://doi.org/10.1021/acs.estlett.0c00357.

[68] A. Samaddar, R. Gadepalli, V. Lakshmi Nag, S. Misra, P. Bhardwaj, P. Singh, M. Meena, P.P. Sharma, M. Grover, M.K. Garg, N. Chauhan, N. Dutt, R. Niwas, D. Kumar, P. Sharma, A.D. Goel, M.K. Gupta, S. Saurabh, S. Rai, C. Lawdiya, J. Saini, D. Singh, Viral RNA shedding and transmission potential of asymptomatic and Pauci-symptomatic COVID-19 patients, Open Forum Infect Dis (2020), https://doi.org/10.1093/ofid.ofaa599.

[69] K.R. Wigginton, Y. Yea, R.M. Ellenberg, Emerging investigators series: the source and fate of pandemic viruses in the urban water cycle, Environ. Sci.: Water Res. Technol. 6 (2015). https://doi.org/10.1039/C5EW00125K.

[70] C. Geller, M. Varbanov, R.E. Duval, Human coronaviruses: insights into environmental resistance and its influence on the development of new antiseptic strategies, Viruses 4 (2012) 3044–3068. https://www.mdpi.com/1999-4915/4/ 11/3044.

[71] G. La Bella, M. Martella, M.G. Basanisi, G. Nobili, V. Terio, G. La Salandra, Food-borne viruses in shellfish: investigation on norovirus and HAV presence in Apulia (SE Italy), Food Environ. Virol. 9 (2017) 179–186, https://doi.org/10.1007/ s12560-016-9273-1.

[72] A.B. Franklin, S.N. Bevins, Spillover of SARS-CoV-2 into novel wild hosts in North America: a conceptual model for perpetuation of the pathogen, Sci. Total Environ. 733 (2020), 139358, https://doi.org/10.1016/j.scitotenv.2020.139358.

[73] S.O. Petrovan, D.C. Aldridge, H. Bartlett, A.J. Bladon, H. Booth, S. Broad, D. M. Broom, N.D. Burgess, S. Cleaveland, A.A. Cunningham, M. Ferri, et al., Post COVID-19: A Solution Scan of Options for Preventing Future Zoonotic Epidemics. https://osf.io/4t3en/.

[74] http://www.wcs-ahead.org/manhattan_principles.html.

[75] https://oneworldonehealth.wcs.org/About-Us/Mission/The-2019-Berlin-Principles-on-One-Health.aspx.

[76] S. Harrison, I. Kivuti-Bitok, A. Macmillan, P. Priest, EcoHealth and one health: a theory-focused review in response to calls for convergence, review article, Environ. Int. 132 (2019) 105058, https://doi.org/10.1016/j. envint.2019.105058.

[77] M. Han, D.E. Anderson, Q. Zhang, et al., Dampened NLRP3-mediated inflammation in bats and implications for a special viral reservoir host, Nat. Microbiol. 4 (2019) 789–799, https://doi.org/10.1038/s41564-019-0371-3.

[78] B. Hu, L.F. Wang, Z. Shi, Bat origin of human coronaviruses, Virol. J. 12 (2015) 221, https://doi.org/10.1186/s12985-015-0422-11.

[79] F. Rizzo, K.M. Edenborough, R. Toffoli, P. Culasso, S. Zoppi, A. Dondo, S. Robetto, S. Rosati, A. Lander, A. Kurth, R. Orusa, L. Bertolotti, M.L. Mandola, Coronavirus and paramyxovirus in bats from Northwest Italy, BMC Vet. Res. 13 (1) (2017 Dec 22) 396, https://doi.org/10.1186/s12917-017-1307-x. PMID: 29273042; PMCID: PMC5741894.

[80] R. Lecis, M. Mucedda, E. Pidinchedda, M. Pittau, A. Alberti, Molecular identification of Betacoronavirus in bats from Sardinia (Italy): first detection and phylogeny, Virus Genes 55 (2019) 60–67. https://www.ncbi.nlm.nih.gov/pub med/30426315.

[81] F. Riccardo, F. Monaco, A. Bella, G. Savini, F. Russo, R. Cagarelli, M. Dottori, C. Rizzo, G. Venturi, M. Di Luca, S. Pupella, L. Lombardini, P. Pezzotti, P. Patrizia, F. Maraglino, A.N. Costa, G.M. Liumbruno, G. Rezza, The working group, An early start of West Nile virus seasonal transmission: the added value of One Heath surveillance in detecting early circulation and triggering timely response in Italy, June to July 2018, Euro Surveill. 23 (32) (2018) pii=1800427.

[82] https://preempt.ucdavis.edu/.

[83] https://www.ecohealthalliance.org/program/predict.

[84] https://www.usaid.gov/global-health/health-areas/emerging-pandemic-threats/ programs-.

[85] L.J. Hoinville, L. Alban, J.A. Drewe, J.C. Gibbens, L. Gustafson, B. Häsler, C. Saegerman, M. Salman, K.D.C. Stärk, Proposed terms and concepts for describing and evaluating animal health surveillance systems, Prev. Vet. Med. 112 (1–2) (2013 Oct 1) 1–12, https://doi.org/10.1016/j.prevetmed.2013.06.006. Epub 2013 Jul 30. PMID: 23906392.

[86] J. Jordana, J.C. Triviño-Salazar, Where are the ECDC and the EU-wide responses in the COVID-19 pandemic? Lancet Correspond. 395 (2020) https://doi.org/ 10.1016/S0140-6736(20)31132-6.

[87] European Union, Joint European Roadmap Towards Lifting COVID-19 Containment Measures. https://ec.europa.eu/info/sites/info/files/communicati on_-_a_european_roadmap_to_lifting_coronavirus_containment_measures_0.pdf, 2020.

[88] A. Alemanno, The European response to COVID-19: from regulatory emulation to regulatory coordination? Eur. J. Risk Regul. 11 (2) (2020) 307–316, https://doi. org/10.1017/err.2020.44.

[89] EU Commission, DG for Health and Food Safety, EU Health Preparedness: Recommendations for a common EU Testing Approach for COVID-19. https://ec. europa.eu/health/sites/health/files/preparedness_response/docs/common_testi ngapproach_covid-19_en.pdf, 2020.

[90] Europen Centre for Disease Prevention and Control (ECDC), COVID-19 Testing Strategies and Objectives. https://www.ecdc.europa.eu/sites/default/files/documents/TestingStrategy_Objective-Sept-2020.pdf, 15 September 2020.

[91] A. Foddai, J. Lubroth, J. Ellis-Iversen, Base protocol for real time active random surveillance of coronavirus disease (COVID-19) - Adapting veterinary methodology to public health, One Health 9 (2020 Mar 28), 100129, https://doi.org/10.1016/j.onehlt.2020.100129. PMID: 32292815; PMCID: PMC7102574.

[92] A. Foddai, A. Lindberg, J. Lubroth, J. Elly-Iversen, Surveillance to improve evidence for community control decisions during the COVID-19 pandemic - opening the animal epidemic toolbox for Public Health, One Health 9 (2020), https://doi.org/10.1016/j.onehlt.2020.100130.

[93] L. Genzel, R. Adan, A. Berns, J. van den Beucken, A. Blokland, E.H.W.G. M. Boddeke, R. WM Bogers, R. Bontrop, T. Bulthuis, H. Bousema, T.C.J.J. Clevers, A.M. van Dam Coenen, P.M.T. Deen, K.W. van Dijk, B.J.L. Eggen, Y. Elgersma, I. Erdogan, J.R. Homberg, How the COVID-19 pandemic highlights the necessity of animal research, Curr. Biol. 30 (18) (21 September 2020) R1014–R1018, https://doi.org/10.1016/j.cub.2020.08.030.

[94] V. Gerdts, S. Littel-van den Hurk, P.J. Griebel, L.A. Babiuk, Use of animal models in the development of human vaccines, Future Microbiol. 2 (6) (2007 Dec) 667–675, https://doi.org/10.2217/17460913.2.6.667. PMID: 18041907.

[95] D.A. Stanley, A.N. Honko, C. Asiedu, J.C. Trefry, A.W. Lau-Kilby, J.C. Johnson, L. Hensley, V. Ammendola, A. Abbate, F. Grazioli, K.E. Foulds, C. Cheng, L. Wang, M.M. Donaldson, A. Colloca, M. Folgori, G.J. Roederer, J. Nabel, A. Mascola, R. Nicosia, R.A. Cortese, N.J. Sullivan Koup, Chimpanzee adenovirus vaccine generates acute and durable protective immunity against ebolavirus challenge, Nat. Med. 20 (10) (2014 Oct) 1126–1129, https://doi.org/10.1038/nm.3702. Epub 2014 Sep 7. PMID: 25194571.

[96] A. Stedman, D. Wright, P.J. Wichgers Schreuret, et al., Safety and efficacy of ChAdOx1 RVF vaccine against Rift Valley fever in pregnant sheep and goats, npj Vaccines 4 (2019) 44, https://doi.org/10.1038/s41541-019-0138-0.

[97] N. van Doremalen, E. Haddock, F. Feldmann, K. Meade-White, T. Bushmaker, R. J. Fischer, A. Okumura, P.W. Hanley, G. Saturday, N.J. Edwards, M.H.A. Clark, T. Lambe, S.C. Gilbert, V.J. Munster, A single dose of ChAdOx1 MERS provides broad protective immunity against a variety of MERS-CoV strains, Sci. Adv. 6 (2020), eaba8399, 10 June 2020, https://advances.sciencemag.org/content/advances/6/24/eaba8399.full.pdf.

[98] C. López-Camacho, Y.C. Kim, J. Blight, M.L. Moreli, E. Montoya-Diaz, J. T. Huiskonen, B.M. Kümmerer, A.R. Sandoval, Assessment of immunogenicity and neutralisation efficacy of viral vectored vaccines against Chikungunya virus, Viruses. 11 (4) (2019) 322, https://doi.org/10.3390/v11040322.

[99] N. van Doremalen, T. Lambe, S. Sebastian, T. Bushmaker, R. Fischer, F. Feldmann, E. Haddock, M. Letko, V.A. Avanzato, I. Rissanen, R. LaCasse, D. Scott, T. A. Bowden, S. Gilbert, V. Munster, A single-dose ChAdOx1-vectored vaccine provides complete protection against Nipah Bangladesh and Malaysia in Syrian golden hamsters, PLoS Negl. Trop. Dis. 13 (6) (2019 Jun 6), e0007462, https://doi.org/10.1371/journal.pntd.0007462. PMID: 31170144; PMCID: PMC6581282.

[100] P.M. Folegatti, K.J. Ewer, P.K. Aley, B. Angus, S. Becker, S. Belij-Rammerstorfer, D. Bellamy, S. Bibi, M. Bittaye, E.A. Clutterbuck, et al., Immunogenicity of the ChAdOx1 nCoV-19 vaccine against SARS-CoV-2: a preliminary report of a phase 1/2, single-blind, randomized controlled trial, Lancet (July 20, 2020), https://doi.org/10.1016/S0140-6736(20)31604-41.

[101] http://zapi-imi.eu/.

[102] R. Taylor, C.A. McCarthy, V. Patel, R. Moir, L. Kelly, E. Snary, The risk of introducing SARS-CoV-2 to the UK via international travel in August 2020, medRxiv preprint (2020), https://doi.org/10.1101/2020.09.09.20190454.

[103] K.J. Wabnitz, V. Guzman, V. Haldane, P.A. Ante-Testard, Y. Shan, I.M. Blom, Planetary health: young academics ask universities to act, The Lancet Planet Health 4 (7) (July 01, 2020) e257–e258. https://www.thelancet.com/action/showPdf?pii=S2542-5196%2820%2930142-X.

[104] R.von Borries, R. Guinto, D.J. Thomson, W.A. Abia, R. Lowe, Planting sustainable seeds in young minds: the need to teach planetary health to children, The Lancet Planet. Health 4 (November 2020), https://doi.org/10.1016/S2542-5196(20)30241-2.

[105] https://ec.europa.eu/food/sites/food/files/safety/docs/f2f_action-plan_2020_strategy-info_en.pdf.

[106] Federation of Veterinarians of Europe (FVE), Press release, EU Farm to Fork Strategy: An ambitious strategy which would gain from comprehensively embracing, One Health (2021). https://www.fve.org/cms/wp-content/uploads/051-FVE-press-release-F2F-200702.pdf.

[107] The ERAvsCorona's Action Plan is Agreed between the Commission and the Health Ministers of the EU Member Countries. https://ec.europa.eu/info/sites/info/files/covid-firsteravscorona_actions.pdf, 2021.

[108] EU Commission, Coronavirus: €117 Million Granted for Treatments and Diagnostics Through the Innovative Medicines Initiative. https://ec.europa.eu/commission/presscorner/detail/en/ip_20_837, 2021.

[109] Q. Zhang, H. Zhang, J. Gao, K. Huang, Y. Yang, X. Hui, X. He, C. Li, W. Gong, Y. Zhang, Y. Zhao, C. Peng, X. Gao, H. Chen, Z. Zou, Z.-L. Shi, M. Jin, A serological survey of SARS-CoV-2 in cat in Wuhan, Emerg. Microb. Infect. 9 (1) (2020) 2013–2019, https://doi.org/10.1080/22221751.2020.1817796.