



COVID-19 and Emerging Zoonosis - The Clock is Counting Down: Time for Closer Collaboration between Veterinary and Human Medicine

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Review Article

Volume 6 Issue 1

Received Date: February 11, 2021

Published Date: April 07, 2021

DOI: 10.23880/oajvsr-16000209

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Abstract

The coronavirus disease 2019 (COVID-19) pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) quickly spread from China and crossed international borders. For the first time in this century, the world is facing a nightmare of 2 million deaths due to the respiratory pandemic by January 2021. Most of the emerging or re-emerging pathogens are likely to be zoonotic, and SARS-CoV-2 potentially has an animal origin, a circumstance that is a public health concern and a burden on any country's economy. Greater awareness and understanding of potential disease promoters and effective disease surveillance systems are crucial for detecting outbreaks of emerging zoonotic diseases as quickly as possible. In order to achieve this goal, there is an urgent need for a One Health approach between human and veterinary medicine. Indeed, the One Health approach, along with all the lessons learned from previous coronavirus threats (SARS- and MERS-CoVs), as well as the advance of science is essential for dealing with emerging zoonosis, including COVID-19. It is urgent to create task forces, networks and all types of collaborations between human and veterinary medicine to prevent future pandemic events.

Keywords: COVID-19; Emerging Zoonosis; One Health; Public Health; SARS-Cov-2

Abbreviations: COVID-19: Coronavirus Disease 2019; Covs: Coronaviruses; SARS-Cov-2: Severe Acute Respiratory Syndrome Coronavirus 2; SARS: Severe Acute Respiratory Syndrome; MERS: Middle East Respiratory Syndrome; MERS-Cov: Middle East Respiratory Syndrome Coronavirus; HIV: Human Immunodeficiency Virus; AIDS: Acquired Immune Deficiency Syndrome; IBV: Infectious Bronchitis Virus; FIPV: Feline Infectious Peritonitis Virus.

Introduction

The last two decades have shown a worrying situation

in the field of infectious diseases, since new pathogens emerged; old pathogens re-emerged after a long absence from a certain population; or have occurred in a previously non-recognized population or geographical area for the diseases they cause; and zoonotic agents, some of them neglected, are still present. In fact, since the beginning of the 21st century, numerous outbreaks of bacterial and viral zoonotic diseases have occurred worldwide [1]. However, the main outbreak to date has been COVID-19. Indeed, after its first outbreak in China, COVID-19 caused by SARS-CoV-2 has quickly spread and crossed international borders, reaching the pandemic status [2]. Coronaviruses (CoVs)

are positive-sense RNA viruses which belong to the family Coronaviridae. Taxonomically, SARS-CoV-2 is a member of the order Nidovirales, the genus *Betacoronavirus* and subgenus *Sarbecovirus* [3]. Coronaviruses have long been known in veterinary medicine. Primarily, they mainly caused enzootic infections in birds and mammals. However, in recent decades, they have crossed the barrier of host species and have also demonstrated to be capable of infecting humans, both in the upper and lower respiratory tracts, causing respiratory disease of varying degrees, such as bronchitis and pneumonia [4]. The outbreak of Severe Acute Respiratory Syndrome (SARS), in 2003, and of Middle East Respiratory Syndrome (MERS), in 2012, demonstrated pathogenicity and mortality of coronaviruses in humans and are examples of viruses that have crossed the species barrier [5]. This mini-review aims to emphasize the urgent need for collaboration between veterinary and human medicine through the One Health strategy for the prevention and control of COVID-19, as well as other emerging zoonosis.

Factors Associated to the Emergence of Zoonosis

The emergence and maintenance of zoonosis are multifactorial and affected by dynamic interactions among the host, aetiological agent and environment [6-8]. Regarding human activity and travel, globalization has been considered a factor in increasing the transfer of pathogens to pristine areas, such as tropical forests [9]. Tourism and travel to exotic places have steadily increased over recent years. Although they represent an important economic sector for any country, several health issues have been reported, as the outbreak of Middle East respiratory syndrome coronavirus (MERS-CoV) in South Korea caused by a returnee from the Middle East [10]. Moreover, the transmission of agents of airborne emerging diseases due to commercial airline networks has also been described Mangili A, et al. [11]. One example is the outbreak of SARS in 2003, whose pathogen was disseminated from China to at least 17 countries within a week [7].

History has shown that large-scale epidemics have followed large-scale human migratory movements. Some examples include the Black Death (caused by *Yersinia pestis*), cholera (*Vibrio cholerae*), SARS and malaria (*Plasmodium falciparum*) [12]. Millions of people and animals travel the world annually. The movement of people, animals and food (of animal and vegetable origin) may quickly disseminate pathogenic agents worldwide [13], since they can travel not only inside a sick host, but also by apparently healthy but infected carriers. Before COVID-19 outbreak, it was possible to travel to any part of the world within a few hours and thousands of air journeys were made daily. In addition, trip duration is shorter than the incubation periods of many diseases (especially viral ones) [14], a circumstance which

increase the odds of a rapid distribution of infectious agents into new areas. In fact, the last 10 years have shown that zoonotic diseases such as Chikungunya, Dengue, Ebola, MERS, and SARS may have the potential to spread across borders due to rapid human mobility via the global airline network [7]. Since last year, the world assists to the swiftly spread of COVID-19 across the globe, and travel restrictions and border control measures, like never seen before, have been enforced to limit the spread of the outbreak [15].

Pet ownership is another recognized factor. It is known that there are many health benefits, including physical, mental and emotional improvements, linked to pet ownership. New companion animals such as reptiles, birds or insects can also be responsible for zoonotic infections. Additionally, there is an increasing trend (particularly in high-income countries) to breed and maintain wild animals as pets, a situation which can lead to many infectious agents crossing the species barrier into humans [16]. SARS-CoV-2 has been detected in naturally infected dogs and cats in households, most of which lived in close contact with infected humans [17]. Understanding risk factors associated with this scenario and their potential to infect other species requires urgent investigation [18].

The global trade of animals (i.e. pets, livestock and wildlife) and products of animal origin has also been related to the dissemination of non-zoonotic diseases, such as foot and mouth disease, classical and African swine fevers, and zoonosis like brucellosis [19], human monkeypox in North America and H5N1 in the United Arab Emirates [12]. The global trade of illegally imported products of animal origin, and non-compliant or the absence of food and animal control allow vector insects, or other infected animals, to transmit pathogens that can be introduced into areas where there is no host resistance or native predators, and to reintroduce them into previous officially-free regions. Consequently, naïve populations can face large outbreaks and remarkable socioeconomic costs [19]. Several factors influence the ability of a new microorganism to become a public health threat. It is considered that viruses cause about 45% of emerging human diseases. RNA viruses, as SARS-CoV-2, are prone to emerge due to their high rates of replication and mutation, which may produce novel variants responsible for the emergence and re-emergence of infectious diseases [20]. As a consequence, new variants emerge as is the case of the emergent SARS-CoV-2 B.1.1.7 lineage in the United Kingdom defined by a novel set of spike mutations [21,22].

Anthropogenic practices associated with agricultural production or industrial processes have been identified and are linked to the spread of pathogens, creating new ecological niches and exposing human and animal populations to them [23]. Agricultural expansion contributes to encroachment into wildlife habitats, which causes changes in the ecosystem

and implies close proximity of humans and livestock to wildlife and vectors. Such circumstances are responsible for the potential spill over of wildlife pathogens in livestock and humans [24]. Deforestation has accelerated exponentially since the beginning of the 20th century, mainly due to human population growth, agricultural intensification and political and economic interests. This is inextricably linked to habitat destruction and a drastic reduction in biodiversity, since the population of natural predators is no longer sufficient to control rodents, insects and other potential transmitters of infectious agents. This may affect host and pathogen dynamics, forcing reservoirs of zoonotic diseases to become closer to potentially susceptible animal and human populations [25]. One example is the occurrence of the Nipah virus outbreak in Malaysia in the late 1990s, affecting pigs and humans [26].

Increased incidence of zoonosis and/or vector-borne diseases (as well as changes in their transmission pattern) is closely related to drastic changes in the environment and ecosystems caused by climate change associated with global warming [27]. The occurrence of extreme weather events such as heat waves, cold spells, droughts or floods may favour the increase of vectors and their movement from endemic areas, in addition to decreasing their natural predator population, and it have influenced the development, behaviour and survival of vectors as well as the dynamics of pathogen transmission [28].

Building the Bridge between Veterinary and Human Medicine

Global health challenges need an innovative and cooperative approach between human and animal health authorities. In the late 19th century and early 20th century, physicians as Rudolf Virchow and William Osler explained that animal and human health were inextricably linked [29]. Moreover, Virchow indicated the absence of boundaries between human and animal health, and emphasized their crossing lines [30]. Currently, the relationship among humans, animals and environment has gained importance associated with COVID-19 concerns [2]. One of the main problems of emerging and re-emerging diseases is their control, since they are sporadic and unpredictable, often appearing from unexpected reservoirs [26]. Since 60 to 80% of the new human infections likely originated in animals, research and control measures aimed at emerging/remerging zoonotic diseases should include appropriate veterinary support [31] (Table 1). Their impact is greater in developing countries because of risk factors, such as the lack of medical and human resources to tackle disease outbreaks and the high population growth and abundance of vectors and reservoirs of pathogens. Additionally, a high number of people with a compromised immune system due to the human immunodeficiency virus (HIV)/acquired immune deficiency syndrome (AIDS) or parasitic diseases, a dependence on animals as the main source of livelihood, low socio-economic status and hygienic deficits are considered important risk factors [7].

Disease	Etiology	Animal host	Mode of transmission
Bacterial Zoonosis			
Anthrax	<i>Bacillus anthracis</i>	Cattle, horses, sheep, pigs, dogs, bison, elks, white-tailed deer, goats, and mink	Cutaneous route; inhalation; infected animals or animal products; ingestion (undercooked or raw meat or dairy products)
Tuberculosis	<i>Mycobacterium bovis</i> , <i>Mycobacterium caprae</i> , <i>Mycobacterium microti</i>	Cattle, sheep, swine, deer, wild boars, camels, and bison	Inhalation of droplets
Brucellosis	<i>Brucella abortus</i> , <i>Brucella melitensis</i> , <i>Brucella suis</i> , <i>Brucella canis</i>	Cattle, goats, sheep, pigs and dogs	Contact with infected tissues or fluids; ingestion (raw milk or dairy products); contamination of a fresh wound with infected matter from animals (blood, urine, aborted fetuses and placenta); accidental needle-stick puncture with Brucella B19 vaccine while vaccinating animals

Leptospirosis	<i>Leptospira interrogans</i>	Wild and domestic animals including pet dogs	Cutaneous route (skin abrasions or exposed mucous membranes); contact with infected matter (urine or tissues) from animals (usually rodents); contact with surface water, soil or plants contaminated with the leptospirosis bacteria from the urine of infected animals
Lyme disease	<i>Borrelia burgdorferi</i>	Cats, dogs, and horses	Bite from an infected tick
Salmonellosis	<i>Salmonella enteritidis</i>	Poultry, domestic and wild animals	Ingestion (raw or improperly cooked food of animal origin, mainly meat, poultry, eggs and milk)
Ehrlichiosis	<i>Anaplasma phagocytophilum, Ehrlichia ewingii, Ehrlichia chaffeensis, Ehrlichia canis, Neorickettsia sennetsu</i>	Sheep, cattle, deer, dogs and cats	Bite from an infected tick
Viral Zoonosis			
Rabies	Rabies virus, Genus—Lyssavirus, Family—Rhabdoviridae	Cattle, horses, cats, dogs, bats, monkeys, wolves, skunks, rabbits, and coyotes	Bite or scratch from an infected animal; direct contact between infected saliva and human mucosa or fresh skin wounds
Avian influenza A(H5N1) and A(H7N9)	Influenza A virus, Genus—Alphainfluenzavirus, Family—Orthomyxoviridae	Ducks, chickens, turkeys, dogs, cats, pigs, whales, horses, seals, and wild, birds	Direct or indirect contact with sick or dead birds; contaminated products such as faecal material
Rift Valley fever	Rift Valley fever virus, fever virus, Genus—Phlebovirus, Family—Bunyaviridae	Buffaloes, camels, cattle, goats, and sheep	Bite of infected mosquitoes or other insects; contact with infected tissues or fluids; contact with the aborted material from infected animals; cutaneous route (through skin abrasions); inhalation of aerosols
Ebola virus disease (Ebola hemorrhagic fever)	Ebola virus, Genus—Ebolavirus, Family—Flaviviridae	Monkeys, gorillas, chimpanzees, apes, and wild antelopes	Introduced by contact with infected tissues or fluids; spread through human-to-human transmission (direct contact between broken skin or mucous membranes and infected fluids and tissues); burial ceremonies
Dengue fever	Dengue virus, Genus—Flavivirus, Family—Flaviviridae	Monkeys and dogs	Bite of infective female <i>Aedes mosquito</i> (<i>A. aegypti</i> ; <i>A. albopictus</i>)
Zika fever	Zika virus, Genus—Flavivirus, Family—Flaviviridae	Apes and monkeys	Bite of an infected <i>Aedes mosquito</i> (<i>A. aegypti</i> ; <i>A. albopictus</i>)
West Nile fever	West Nile virus, Genus—Flavivirus, Family—Flaviviridae	Horses, birds, and reptiles	Bite of an infected <i>Culex mosquito</i> . Mosquitoes become infected when they feed on infected birds
Severe acute respiratory syndrome (SARS)	SARS-CoV, Genus—Coronavirus	Bats, dogs, cats, ferrets, minks, tigers, and lions	Inhalation of droplets

Table 1: Bacterial and viral zoonotic diseases, their etiological agents, animal hosts and mode of transmission [6,8].

A One Health integrative approach for COVID-19 and new zoonosis must be implemented in order to develop epidemiological surveillance and to establish disease control mechanisms to limit zoonotic transmission [2]. Long-term veterinary experience with infections caused by CoVs, such as infectious bronchitis virus (IBV) in poultry, feline infectious peritonitis virus (FIPV) or swine CoVs, needs to be included for a better understanding of the origin and spread of SARS-CoV-2. The same is true regarding the use of animal models to study vaccines for humans [2,32]. Among the distinctive areas of action to anticipate ultimate threats caused by biological agents, four of them stand out and can be applied to SARS-CoV-2. The first one is related to the discovery of pathogenic agents through continuous longitudinal surveillance of wildlife and domestic animals, considering the animal origin of SARS-CoV-2 and its spill over into humans [2]. The second one refers to the quantifiable identification of the risk that a microorganism as SARS-CoV-2 may represent to humans as well as their transmission pathway to humans and other animals [33]. The third one is the ability to respond adequately to COVID-19 outbreaks by strengthening countries skills to detect them with effective rapid diagnostic tests [34] and vaccines [35]. Currently, many efforts have been directed towards the development of effective vaccines and therapies to prevent transmission person-to-person, between health professionals or the elderly [36]. The fourth is based on the reduction of human risk by minimizing human behaviors and practices that increase the probability of agent's transfer and amplification. In relation to COVID-19, the main measures are wearing a mask, frequent hand washing, promoting social distance and compliance with lockdowns [37].

Due to COVID-19, public awareness has reached an unprecedented scale. In the face of the current pandemic, the public is required to understand and trust the entities that are making recommendations to limit the exposure and spread of the disease. General public must trust on science and collaborate with public health services through practicing all measures and policies implemented to solve the pandemic problem. The battle against COVID-19 has not yet been won, and people's adherence to prevention and control measures are essential to ensure ultimate success, including collaboration between veterinary and human medicine through the One Health strategy for prevention and control of COVID-19, as well as other emerging zoonosis.

Conclusion

Emerging infections have been responsible for several dark days of widespread suffering and death in human and animal history and will certainly continue to pose a serious challenge into the future. The collaborative

efforts made worldwide in terms of diagnosis, quarantine, confinement, intensive care, vaccination and medicines with the collaboration of the population are fundamental and are beginning to bear fruit in the prevention and control of COVID-19. It is urgent to create task forces, networks and all types of collaborations between human and veterinary medicine, because the time is in countdown to the next zoonotic event. COVID-19 will not be the last pandemic and because of that the world needs to be prepared.

Funding: This study was supported by project UIDB/CVT/00772/2020 funded by Fundação para a Ciência e a Tecnologia (FCT).

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