

Coronaviruses and their Host Range: Implications for Zoonotic Transmission**21**Waqar Saleem^{1*}, Waqar Zaib², Ateeqa Aslam¹ and Qurratulain Amin³**ABSTRACT**

Coronaviruses cause infections in various species, including mammals, birds, and humans. Their zoonotic potential has surfaced with the occurrences of severe acute respiratory syndrome (SARS), Middle Eastern respiratory syndrome (MERS), and Coronavirus disease 2019 (COVID-19). Additionally, the natural and intermediate hosts for other known coronaviruses to infect humans also originate from the animals. The ability of coronaviruses to infect a wide range of hosts can be attributed to factors such as genetic variability, utilization of different receptors, host immune response, and environmental conditions. Consequently, these viruses can undergo spillover events by adapting to new hosts through amplification hosts. Several factors contribute to the facilitation of spillover events. Pro-zoonotic elements such as interaction with infected animals, the existence of live animal markets, uncontrolled deforestation, and the impact of climate change all play a role in promoting these events. In the absence of proper surveillance, regulation of animal trade, misconceptions surrounding the "one health" approach, and inadequate public health interventions, the likelihood of future spillover events is heightened. This chapter focuses on the critical association between the host range of coronaviruses and their ability to be transferred from animals to humans. It also reviews the current knowledge on the epidemiology of zoonotic coronaviruses and the factors associated with their spread, thus highlighting the gaps and challenges that need to be addressed for better preparedness and response. By understanding this relationship, this chapter stresses the risks associated with zoonotic transmission of coronaviruses, which is crucial to devise prevention and mitigation strategies against them.

Keywords: Coronaviruses; zoonosis; host range; spillover event; one health**CITATION**

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CHAPTER HISTORY

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1. INTRODUCTION

Coronaviruses (family: Coronaviridae; order: Nidovirales) are common pathogens for vertebrates, including humans (Zhou et al. 2021). Nidoviruses are divided into four subfamilies based on the structure of genome and phylogenetic relationships: *Alphacoronaviruses*, *Betacoronaviruses*, *Gammacoronaviruses* and *Deltacoronaviruses*. The *Alpha*- and *Betacoronaviruses* produce infections in mammals only. The *Gamma*- and *Deltacoronaviruses* infect mainly birds, but a few can also produce infection in mammals (Woo et al. 2012). *Alphacoronaviruses* and *Betacoronaviruses* are correlated with respiratory ailments in humans. However, in animals, they predominately cause gastroenteritis (Su et al. 2016).

Recently, the reputation of coronaviruses in terms of zoonosis peaked, especially after the COVID-19 pandemic (Smith et al. 2022). The current phylogenetic analysis shows that all human coronaviruses have originated from animal-origin coronaviruses. Domestic animals usually act as intermediate hosts between natural hosts of coronaviruses (usually bats) and humans (Woo et al. 2012; Zhou et al. 2018). Due to evolution, genetic recombination and a variety of host range in the Coronaviridae family, these viruses can modify host range and tissue tropism, making their adaptation to new environments effective (Rohaim et al. 2020). Coronavirus replication in different host cells depends upon the presence of specific receptors with varying expression among species (Tai et al. 2020). This chapter outlines the host range of existent coronaviruses, emphasizing its importance in the zoonotic implications of these viruses. The factors affecting the zoonotic spillover are also discussed.

1.1. STRUCTURE OF CORONAVIRUS

Coronavirus genome is made up of a large, positive sense, non-segmented single-stranded RNA, 26-31 kbps in size (Mousavizadeh and Ghasemi 2021). The organization of the genome is 5'-Untranslated Region (UTR)-leader followed by two ORFs (open reading frames; ORF1a, ORF1b, highly variable among strains) that produce replicase/transcriptase further followed by Spike (S), Envelope (E), Membrane (M), Nucleocapsid (N) and ends with 3' UTR- poly A tail (Yang and Leibowitz 2015). The virus exhibits pleomorphism in its size (80-120nm) (Bárcena et al. 2009). Structurally, S protein is highly variable among coronaviruses that harbors a receptor-binding domain (S1; RBD) and membrane-fusion domain (S2; MFD), helping the virus in adsorption and entry into the host cell. This protein also contributes to the host specificity of the virus (Nao et al. 2017). SARS-like viruses have polybasic cleavage sites, which enhance the cell-cell fusion without viral entry being affected (Follis et al. 2006), ultimately helping in the spillover from bats to humans (Menachery et al. 2020). Some coronaviruses also express hemagglutinin protein that exhibits acetyl-esterase activity, which aids in viral entry and progression of the viral pathogenesis (Ashour et al. 2020).

1.2. HISTORICAL BACKGROUND OF CORONAVIRUSES

Coronaviruses first surfaced in the 1930s, when the first coronavirus was reported in chickens with upper respiratory tract infection symptoms in the United States (US). This virus was initially called as infectious bronchitis virus (IBV), later called the Avian coronavirus (Lalchandama 2020). In mammals, it was first reported in 1946, also in the US, when gastroenteritis in pigs with high mortality led to the discovery of porcine transmissible gastroenteritis virus (TGEV) (Chen et al. 2023). Between 1947 and 1950, 2 murine coronaviruses were discovered: JHM and mouse hepatitis virus (Grabherr et al. 2021). In cats, a new inflammatory intestinal disease reported in 1966 was linked to feline infectious peritonitis virus (FIPV) (Decaro et al. 2021). Later, canine coronavirus was reported in US military dogs in 1974 (Pratelli et al. 2022).

In humans, two coronaviruses were reported in the 1960s with common cold symptoms in England and Chicago and designated as B814 and 299E, respectively (Poutanen 2018). Later, viruses like Human Coronavirus-229E, HCoV-HKU1 and HCoV-NL63 were discovered, causing self-limiting respiratory and digestive tract symptoms (van der Hoek et al. 2004). Human coronaviruses were considered of less importance amid mild infection till the outbreak of SARS caused by SARS-CoV in 2003 (Zhong et al. 2003). The gradual genetic evolution in coronaviruses demonstrated the unstable nature of the coronavirus genome and its adaptability to become more virulent, even fatal, to humans. In 2012, a more lethal form of SARS originated in Saudi Arabia, caused by MERS coronavirus (MERS-CoV) through dromedary camels as intermediate hosts (Zaki et al. 2012). In 2019, coronaviruses' evolutionary and zoonotic potential was etched in history with the pandemic caused by SARS-CoV2. These coronavirus cases were reported worldwide, making SARS-CoV2 a natural catastrophe (Zhou et al. 2021).

2. HOST RANGE OF CORONAVIRUSES

Due to the large single-stranded RNA genome, Coronaviruses undergo rapid genetic recombination and mutations, resulting in several new strains for each virus and the ability to cross host species barriers (Millet et al. 2020). Many human coronaviruses like HCoV-229E, HCoV-NL63, MERS-CoV, SARS-CoV, and SARS-CoV-2 can eventually originate back to bat viruses (Cui et al. 2019). It is interesting to see the host range of known coronaviruses in domestic, wild and companion animals (Table 1-4, adapted from Zhou et al. 2021).

2.1. FACTORS AFFECTING HOST RANGE

Coronaviruses have this broad host range due to the following factors:

2.1.1. GENETIC VARIABILITY

A two-pronged genetic variability from coronaviruses and their hosts is a critical factor in the broad host range for these viruses. Studies have shown that genes involved in the immunity of hosts, including humans, exhibit a strong selection pattern, exerting a selection pressure for genes and pathways key to the host defense, leading to inter-species heterogeneity. Similarly, due to the extremely high mutation rate in the coronavirus genome, new phenotypes can pertain ability to infect new hosts (Quintana-Murci 2019).

2.1.2. RECEPTOR USAGE

A correlation between the host range and these hosts' phylogenetic conservation of coronavirus receptors is critical. The RBD and MFD in the spike protein of different coronaviruses are highly diverse and lead to variability in receptor specificity. Sequence length in the S1 subunit has a low conservation threshold, resulting in variability in sequence length ranging from 544 (IBV) to 944 (229-related bat coronaviruses) (Hulswit et al. 2016). Expression and location of proteinaceous ectopeptidase receptors (APN, ACE2, and DPP4) in different species offer room to cross the host species barrier (Bosch et al. 2014).

2.1.3. INNATE IMMUNE RESPONSE

Most viral infections in mammals are mediated by Toll-like receptors (TLRs) and retinoic acid-inducible gene I (RIG-I)-like receptors (RLRs). Variation in these mediators in terms of expression, recognition, and activation, coupled with immune evasion strategies of coronaviruses like protein translation blocking by coronaviral non-structural protein 1 (nsp1), can also affect the host range (Kasuga et al. 2021).

Table 1: Host range of known *Alphacoronaviruses* in domestic, wild and companion animals

Host	Virus	Year
Human	HcoV-229	1967
	EHCoV-NL63	2004
Bat	BtCoV/512	2006
	Bat-CoV HKU2	
	HKU10	2012
	HuB-2013	
	Sax-2011	
	SC-2013	2016
	3398	
CDPHE15	2017	
Tr-BatCoV HKU33	2019	
Pig	TGEV	1946
	PEDV	1978
	PRCV	1986
	SeACoV	2018
Cat	FcoV/FIPV	1963
Mink	McoV	1990
Dog	CcoV	2003
Ferret	FRSCV	2006
	FRECV	2010
Rat	RatCoV LRNV	2015
Camel	DcCoV-229E	2016
Shrew	Shrew-CoV/Tibet2014	2017
Rabbit	WESV	2018
	L232	2019

Table 2: Host range of known *Betacoronaviruses* in domestic, wild and companion animals

Host	Virus	Year
Human	HcoV-OC43	1966
	SARS-CoV	2003
	HcoV-HKU1	2005
	MERS-CoV	2012
	SARS-CoV2	2020
Bat	HKU4	2006
	HKU5	
	HKU9	2007
	BtHp-BetaCoV/ZJ2013	2016
	Ro-BatCoV GCCDC1	2016
	CMR704	2018
Pig	PHEV	1962
Mouse	MHV	1964
Bovine	BcoV	1973
Equine	EcoV	2000
Dog	CRCoV	2003
Alpaca	BcoV	2007
Giraffe	GiCoV	2007
Sable antelope	SACoV	2008
Camel	DcCoV-HKU23	2014
Hedgehog	Hedgehog coronavirus 1	2014
Rat	HKU24	2015
	RtMruf-CoV-2/JL2014	2018

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Table 3: Host range of known *Gammacoronaviruses* in domestic and wild animals

Host	Virus	Year
Poultry	IBV	1931
	Avian coronavirus 9203	2022
Turkey	TcoV	1951
Beluga Whale	BWCoV SW1	2008
Duck	Duck coronavirus 2714	2013
Bottleneck Dolphin	BdCoV HKU22	2014
Goose	Goose coronavirus CB17	2019

Table 4: Host range of known *Deltacoronaviruses* in domestic, wild and companion animals

Host	Virus	Year
Asian Leopard Cat	ALC/GX/F230/06	2007
Chinese ferret badger	CFB/GX/F247/06	
Bulbul	CFB/GX/F250/06	2009
	BuDCoV HKU11	
Thrush	ThDCoV HKU12	2012
Munia	MunDCoV HKU13	
Pig	PDCoV HKU15	2018
White-eye	WEDCoV HKU16	
Sparrow	SpDCoV HKU17	2022
Magpie robin	MRDCoV HKU18	
Night heron	NHDCoV HKU19	2022
Wigeon	WiDCoV HKU20	
Common moorhen	CMDCoV HKU21	2018
Falcon	FaIDCoV UAE-HKU27	
Houbara bustard	HouDCoV UAE-HKU28	2022
Pigeon	PiDCoV UAE-HKU29	
Quail	QuaDCoV UAE-HKU30	2022
Common magpie	HNU1-1, HNU1-2, HNU2 and HNU3	

2.1.4. ENVIRONMENTAL FACTORS

Deforestation is directly linked to the emergence of Ebola, SARS and other bat-borne viruses due to the human-related selectivity of environments suitable for wild animals like bats, leading to increased chances of transmission of viruses (Afelt et al. 2018). Population growth and globalization are other essential factors linked to the spread of zoonotic viruses like SARS-CoV and SARS-CoV2 (Colson et al. 2022). Climate changes can also cause a revival of viral replication under stress, resulting in more spillover events (Bhattacharya et al. 2020a).

2.2. CROSS-SPECIES SPREAD OF CORONAVIRUSES

Coronaviruses jump between species courtesy of their reservoir hosts; bats in the case of most *Alpha-* and *Betacoronaviruses*, while wild birds for *Gamma-* and *Deltacoronaviruses* (Woo et al. 2012). The following points highlight the potential for cross-species transmission of coronaviruses:

2.2.1. SPILLOVER EVENTS

Throughout history, coronaviruses have crossed the species barrier on multiple occasions. Molecular epidemiological studies on SARS-CoV show that the primary human cases of the disease likely contracted

the virus through masked palm civets as intermediate hosts (Wang et al. 2018), while horseshoe bats were identified as reservoir hosts for the virus (Li et al. 2005). SARS-CoV also shows infection in many lab and companion animals under experimental conditions (Ruiz-Aravena et al. 2022). For MERS, bats are established as putative reservoirs, while dromedary camels are intermediate hosts. Although rare, direct transmission from camels to humans is also documented (Azhar et al. 2014). SARS-CoV2 is probably the most important in this aspect as it caused a pandemic. Although its primary reservoir host has not been established yet, horseshoe bats, pangolins, and minks are probable candidates based on molecular docking studies (Ruiz-Aravena et al. 2022). Apart from coronaviruses of public health importance, many viruses infecting domestic animals also spilled over from wild animals. Bovine coronaviruses (BCoVs) emerged from rodents over 600 years ago (Lau et al. 2015). Canine coronaviruses like Canine Respiratory CoV (CRCoV) originated from BCoVs due to a host species shift (Erles et al. 2007). Feline Coronavirus-I (FCoV-I) has a genetic resemblance to CCoV-I, and FCoV-II is a product of recombination between FCoV-I and CCoV-II (Pratelli et al. 2003). Porcine coronaviruses like TGEV, Porcine Hemagglutinating and Encephalomyelitis Virus (PHEV) and Porcine Deltacoronavirus (PDCoV) originated from canines, bovines and wild birds, respectively (Decaro and Lorusso 2020). These events suggest that coronaviruses show high diversity among host species and are not shy to cross the host barrier, hinting towards more zoonotic spillover events in the future.

2.2.2. AMPLIFICATION HOSTS

Domestic animals are in direct contact with human populations and are indirectly linked to wild animals, thus facilitating the virus amplification in these populations (Johnson et al. 2015). Animals like civets (Guan et al. 2003), horseshoe bats (Li et al. 2005), camels (Reusken et al. 2013), and pigs (McLean and Graham 2022) have all been established as amplifying hosts for a variety of coronaviruses of zoonotic importance.

2.2.3. ADAPTATION TO NEW HOSTS

Coronaviruses owe their adaptation to novel hosts and environmental niches to their high recombination and mutation rates (Latif and Mukaratirwa 2020). For example, the process of adaptation of SARS-CoV-2 to humans likely started years ago, when its antecedent strayed from the bat coronavirus (Burki 2020). Coronaviruses use strategies like overcoming the host defense barriers, replicating, and shedding out of the host cells. These are coupled with virus-induced modification of physiological responses like weakening of interferon production, cuffing immunogenic motifs, evading viral RNA detection, exploiting cell autophagy, activating host cell apoptosis, bringing lymphocyte enervation and diminution, and finally, mutation and evasion from immunity (Kasuga et al. 2021). These strategies help coronaviruses evade existing hosts and adapt to new hosts, causing more spillover events.

3. ZOONOTIC TRANSMISSION OF CORONAVIRUSES

The term "spillover" or "evolutionary jump" describes the event in which a virus spreads from a natural host to a new host, infecting the latter. This could happen by accident, through a first-time exposure, repeatedly, or by a crucial genetic mutation that allows the pathogenic infection of the new host (Plowright et al. 2017). This infection can lead to a dead end or spread to conspecifics by resultant epidemiological cycling or even zoonothonotic transmission, evident from COVID-19 (Zhu et al. 2020). Spillover is a chance occurrence instead of a typical organism's infection cycle component. In common parlance, cross-species spillover is described as a pathogen jump from animals to humans, where it gets established (Plowright et al. 2017).

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3.1. DEFINITION AND TYPES OF ZOOTIC TRANSMISSION

The World Health Organization describes zoonosis as "any infection that is naturally transmissible from vertebrate animals to humans" (WHO 2022). This is strengthened by the fact that the virus is kept alive in a population of animals (a reservoir), making it a constant source of infection for people (WHO 2020). There are many different types of viruses in the coronavirus family, and some of them have the capacity to infect humans from other species. The most egregious instance is the zoonotic spread of SARS-CoV-2, which caused the COVID-19 epidemic (Andersen et al. 2020; Lam et al. 2020; Xiao et al. 2020).

3.1.1. DIRECT ZOOTIC TRANSMISSION

When a virus spreads from an infected animal to a human, it is said to have a direct zoonotic transmission. Close contact with infected animals, such as handling or eating them or exposure to their body fluids, can cause this. For instance, the SARS-CoV-2 virus is thought to have originated in a seafood market in Wuhan, China, where live animals, including wildlife species, were offered for sale (Zhou et al. 2020).

3.1.2. INDIRECT ZOOTIC TRANSMISSION

Indirect transmission is the process by which a virus is transferred from an animal to a human. The virus first spreads from animals to an intermediate host, and then human contact with the intermediate host results in human exposure. The intermediate host acts as a link between the animal reservoir and the people. Regarding SARS-CoV-2, it is believed that an intermediate animal host, such as a wild animal possibly a pangolin, might have played a role in the transmission to humans (Zhang et al. 2020).

3.1.3. ENVIRONMENTAL ZOOTIC TRANSMISSION

Environmental transmission occurs when humans encounter a contaminated environment that contains the virus. Humans may contract the virus from infected animals when they touch certain surfaces or objects. While less common, environmental transmission has been reported for certain coronaviruses, although the specific mechanisms and risks can vary (Wang et al. 2018).

Fig. 1 schematically shows the common types of zoonoses. Note that all the zoonotic coronaviruses described so far involve an intermediate host. Rabies is a classic example of direct viral zoonosis, while animal trade markets played a crucial role in the spread of COVID-19, making it a substantiated example of environmental zoonosis.

3.2. TRANSMISSION OF CORONAVIRUSES

A basic summary of coronaviruses and their transmission, including zoonotic transmission, is provided by the WHO, which explains how several coronaviruses, including SARS-CoV (from civet cats) and MERS-CoV (from dromedary camels), have been transmitted from animals to people (WHO 2020). SARS-CoV2 was the reason for the most recent COVID-19 outbreak in 2019, which significantly impacted people's health, standard of living, and economy. Given the recent outbreak, there are numerous knowledge gaps regarding this novel virus's comparative and zoonotic features. A correlation between the known natural and intermediate hosts of human coronaviruses and the factors contributing to this zoonotic

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relationship is important. Fig. 2 represents the natural and intermediate hosts of seven known human coronaviruses. Bats are the natural hosts for 5 out of 7 known human coronaviruses; as discussed, they all involve intermediate mammalian hosts. Farm animals like cows and camels are prone to coronaviruses and spread infections to humans. Hence, this figure highlights the need for active surveillance of coronaviruses circulating in these animals and the pursuit of uncovering other unknown intermediated hosts.

3.3. FACTORS CONTRIBUTING TO ZOOTIC TRANSMISSION

Zoonotic transmission is a multipronged phenomenon and can involve a variety of factors, some of which are discussed below:

3.3.1. CONTACT WITH INFECTED AND DISEASED ANIMALS

The zoonotic transmission of coronaviruses is significantly influenced by contact with infected animals. However, they spread more easily through direct contact with diseased animals or bodily fluids. Activities like handling, butchering, or eating diseased animals might cause this. For instance, in the case of SARS-CoV, it is thought that people contracted the disease by touching infected civets (Guan et al. 2003).

3.3.2. OCCUPATIONAL EXPOSURE TO ANIMALS

Some activities, like those involving animal farming, veterinary care, and wildlife research, increase the risk of zoonotic transmission. Animal-related jobs can expose people to coronaviruses through direct contact, bites, scratches, or inhaling contaminated particles, especially in settings with high viral loads (Johnson et al. 2020).

3.3.3. VETERINARY AND ANIMAL CARE PRACTICES

Zoonotic disease transmission can occur due to inadequate infection control procedures and poor handling of affected animals in veterinary offices, animal shelters, or wildlife rehabilitation facilities. These environments present chances for the spread of coronaviruses to veterinary staff, caregivers, and visitors (Smith et al. 2022).

3.3.4. EXPOSURE TO ANIMAL WASTE

In areas with infected animals, contact with animal waste, polluted surfaces, or contaminated soil can increase the risk of zoonotic transmission. Animal excrement or respiratory secretions can carry viruses that might linger in the environment and potentially infect people who encounter contaminated objects (Decaro et al. 2021).

3.3.5. CONSUMPTION OF INFECTED ANIMALS

The consumption of diseased animals has the potential to spread coronaviruses to people. Consumption of civets in China during the SARS-CoV pandemic in 2002–2003 has been connected to the disease (Guan et al. 2003). Consuming raw camel meat or milk has been linked to MERS-CoV (Azhar et al. 2014). Eating exotic animals in Wuhan's live animal markets is linked to SARS-CoV2 (Wu et al. 2020).

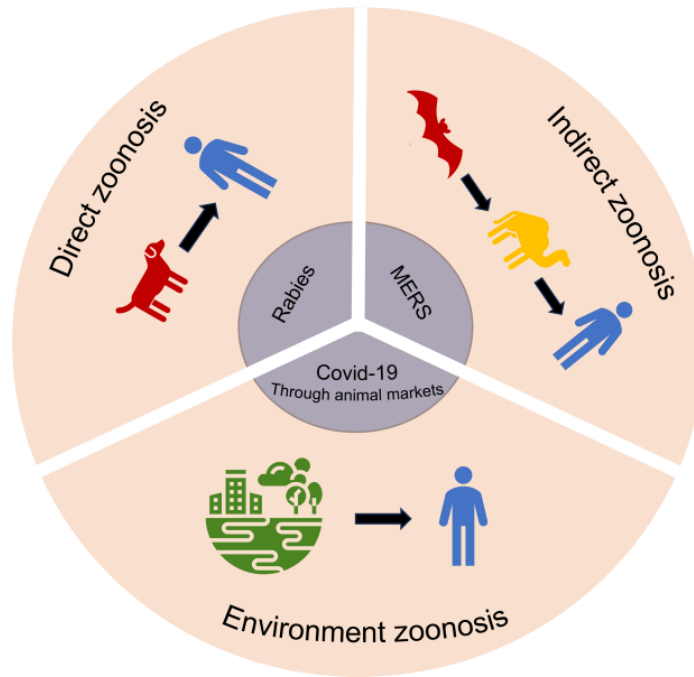


Fig. 1: Common types of zoonotic transmission. Red represents natural hosts, yellow represents intermediate hosts, and blue represents humans.

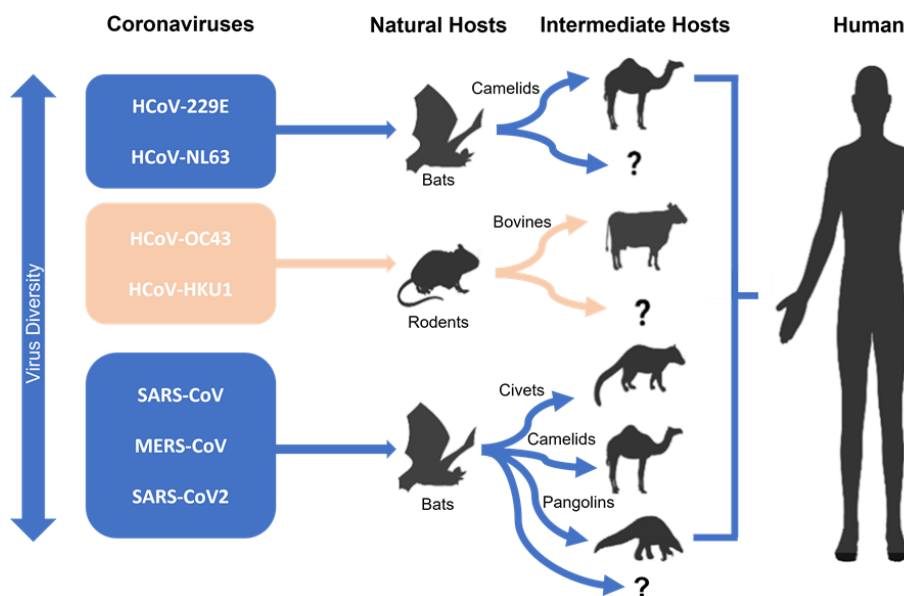


Fig. 2: Schematic representation of natural and intermediate hosts of seven known human coronaviruses. Possible unknown intermediate hosts (represented by ?) provide major knowledge gaps in studying these viruses.

3.3.6. ENVIRONMENTAL FACTORS

Environmental factors such as deforestation and ecological disruption may force bats and other species to seek new habitats close to human habitations (Daszak et al. 2013). Global warming and climate change also affect the ability of the virus to survive and spread, potentially changing the probability of zoonotic spread to humans. Human encroaching in wildlife habitats increases the interactions with animal species that are coronavirus carriers, making it easier for infections to spread to people (Olival et al. 2017). Globalization and cross-border travel also have the potential to spread the virus quickly. Traveling infected people can spread the virus to new locations and populations, causing small-scale outbreaks and even sparking larger-scale epidemics or pandemics (Bogoch et al. 2015).

4. IMPLICATIONS AND CHALLENGES FOR PREVENTING ZONOTIC TRANSMISSION OF CORONAVIRUSES

Control and preventive measures for coronavirus-related zoonosis depend on the type and strain of the virus, the seeming or known risk of transmitting a particular virus to humans, and the country/place of the disease spread. Monetary resources available for control programs and the structure and capacity of one health further impact control and preventive measures (Gebreyes et al. 2014). The following points can explain the challenges involved in preventing coronavirus zoonosis:

4.1. SURVEILLANCE AND EARLY DETECTION

Resources and training for thorough surveillance and early virus detection are significant limitations, particularly in the developing world. Problems like under-detection and, inadequate reporting, untimed and incomplete surveillance data further delay the prevention measures (Ibrahim 2020).

4.2. REGULATION OF ANIMAL MARKETS AND TRADE

Even in the 21st century, effective lawmaking on regulating animal markets, particularly the wildlife trade, is not well established in developing countries. Policies on the protection of habitats for animals like Bats have caused them to adapt to the same environment inhabited by humans, increasing the probability of interaction and disease spread. Wildlife trade also increases the chances of direct contact between people and animal species (Bhattacharya et al. 2020b).

4.3. ONE HEALTH APPROACH

One Health approach depends on the smooth interplay between sectoral power relations and the priorities of public health institutes. Competing interests between livestock and human authorities, lack of understanding of a combined One Health surveillance system, and poor coordination and active collaboration between responsible authorities are key hurdles that must be conquered to enforce the One Health policies effectively (Ruckert et al. 2020).

4.4. PUBLIC HEALTH INTERVENTIONS

Due to the highly variable genome structure for most coronaviruses, the vaccine and therapeutic cover are usually inept. To cover this, public health policymakers must primarily rely on non-therapeutic interventions to minimize the disease burden (Peak et al. 2017). Implementing them is not always easy and depends on the role of the government, media, healthcare providers, and eventually, the people, which makes the zoonotic risk even more challenging to face.

5. FUTURE PERSPECTIVES

This chapter has outlined the importance of understanding the host range of coronaviruses concerning their zoonotic potential on multiple fronts. Without urgently addressing these factors at the local and international level, coronavirus epidemics will emerge and persist for the foreseeable future. The following points highlight some of these nuisances:

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5.1. INCREASED RISK OF FUTURE SPILLOVER EVENTS

As discussed earlier, without progressed surveillance and regulation of animal trade, the hazard of zoonotic spillover events from animals to humans remains high (Bhattacharya et al. 2020b). A recent example is the replication of Simian Hemorrhagic Fever Virus (SHFV) in human monocytes and its similarity with the Human Immunodeficiency Virus (HIV) in evading host immune response, calling for human serological surveillance (Warren et al. 2022). This further accentuates the continuous surveillance of these red flags to avoid future spillover events and the emergence of new infectious diseases.

5.2. GLOBAL HEALTH VULNERABILITY

Without proper preparedness, implementation of public health policies and international collaboration, countries become vulnerable to swift disease spread. Apart from developing countries, where millions live in high-density communities, the developed world is also at risk of harboring vulnerable groups and health inequalities (Sam 2020). Lack of capital in healthcare framework and research can pressure healthcare systems during such outbreaks.

5.3. ECOLOGICAL IMBALANCE

Wildlife obliteration and habitat destruction can unsettle ecosystems and force species like bats to adapt to habitats closer to human settlements, increasing the likelihood of disease transmission. A comprehensive 25-year study on bat population dynamics concerning changing ecology has shown the change in land use by bats and their persistence in agricultural areas previously uninhabited by them (Eby et al. 2023). Ignoring the environmental impact of climate change can further exacerbate these issues.

5.4. SOCIOECONOMIC COSTS

Epidemics and pandemics can have overwhelming socioeconomic consequences, including loss of life, economic downturns, and social upheaval. Even in a developed country like the United States, huge socioeconomic disparities emerged at the beginning of the spread of COVID-19 (Banerjee 2022). Failure to learn from previous outbreaks can lead to repetitive economic and societal commotions.

6. CONCLUSIONS

This chapter underscores the grave importance of comprehending the host range of coronaviruses and their zoonotic potential. The evidence presented strongly highlights that most human coronaviruses originate from animals, thus accentuating the need for keen vigilance and regulation of animal trade. A complex interplay of genetic variability, receptor usage, host immune response, and environmental influences also causes the coronaviruses to infect diverse hosts, contributing to spillover events and viral adaptation in new host species. As human populations continue to intrude into wildlife habitats, our interactions with potential intermediate hosts of coronaviruses become more frequent. Due to these epidemics and pandemics, the straining healthcare systems demand an urgent and collective response. Wildlife habitat destruction and climate change intensify the probability of future spillover events, demanding swift conservation and environmental restoration efforts. Furthermore, the socioeconomic status of particularly marginalized communities is national and international cooperation. Understanding this intricate relationship between coronavirus host range and zoonotic potential is imperious to craft effective strategies to prevent and mitigate future outbreaks.

REFERENCES

- Afelt A et al., 2018. Distribution of bat-borne viruses and environment patterns. *Infection, Genetics and Evolution* 58: 181-191.
- Andersen KG et al., 2020. The proximal origin of SARS-CoV-2. *Nature Medicine* 26: 450-452.
- Ashour HM et al., 2020. Insights into the recent 2019 novel coronavirus (SARS-CoV-2) in light of past human coronavirus outbreaks. *Pathogens* 9: 186.
- Azhar El et al., 2014. Evidence for Camel-to-Human Transmission of MERS Coronavirus. *New England Journal of Medicine* 370: 2499-2505.
- Banerjee T, 2022. Causal connections between socioeconomic disparities and COVID-19 in the USA. *Scientific Reports* 12(1): 15827.
- Bárcena M et al., 2009. Cryo-electron tomography of mouse hepatitis virus: Insights into the structure of the coronavirus. *Proceedings of the National Academy of Sciences* 106: 582-587.
- Bhattacharya S et al., 2020a. Emergence of a zoonotic pathogen-novel coronavirus (SARS-CoV-2) in the context of changing environment. *Journal of Communicable Diseases* 52: 18-24.
- Bhattacharya S et al., 2020b. The relationship between bats and human coronavirus: An exploratory review. *Journal of Health and Social Science* 5: 219-230.
- Bogoch II et al., 2015. Assessment of the potential for international dissemination of Ebola virus via commercial air travel during the 2014 west African outbreak. *The Lancet* 385: 29-35.
- Bosch BJ et al., 2014. Membrane ectopeptidases targeted by human coronaviruses. *Current Opinion in Virology* 6: 55-60.
- Burki T, 2020. The origin of SARS-CoV-2. *The Lancet Infectious Diseases* 20: 1018-1019.
- Chen Y et al., 2023. Transmissible Gastroenteritis Virus: An Update Review and Perspective. *Viruses* 15(2): 359.
- Colson P et al., 2022. Analysis of SARS-CoV-2 variants from 24,181 patients exemplifies the role of globalization and zoonosis in pandemics. *Frontiers in Microbiology* 12: 4202.
- Cui J et al., 2019. Origin and evolution of pathogenic coronaviruses. *Nature Reviews Microbiology* 17: 181-192.
- Daszak P et al., 2013. Interdisciplinary approaches to understanding disease emergence: the past, present, and future drivers of Nipah virus emergence. *Proceedings of the National Academy of Sciences* 110: 3681-3688.
- Decaro N and Lorusso A, 2020. Novel human coronavirus (SARS-CoV-2): A lesson from animal coronaviruses. *Veterinary Microbiology* 244: 108693.
- Decaro N et al., 2021. Possible Human-to-Dog Transmission of SARS-CoV-2, Italy, 2020. *Emerging Infectious Diseases* 27: 1981-1984.
- Eby P et al., 2023. Pathogen spillover driven by rapid changes in bat ecology. *Nature* 613(7943): 340-344.
- Erles K et al., 2007. Isolation and sequence analysis of canine respiratory coronavirus. *Virus Research* 124: 78-87.
- Follis KE et al., 2006. Furin cleavage of the SARS coronavirus spike glycoprotein enhances cell-cell fusion but does not affect virion entry. *Virology* 350: 358-369.
- Gebreyes WA et al., 2014. The Global One Health Paradigm: Challenges and Opportunities for Tackling Infectious Diseases at the Human, Animal, and Environment Interface in Low-Resource Settings. *PLOS Neglected Tropical Diseases* 8: e3257.
- Grabherr S et al., 2021. Insights into coronavirus immunity taught by the murine coronavirus. *European Journal of Immunology* 51(5): 1062-1070.
- Guan Y et al., 2003. Isolation and Characterization of Viruses Related to the SARS Coronavirus from Animals in Southern China. *Science* 302: 276-278.
- Hulswit RJG et al., 2016. Advances in Virus Research. In: Hulswit RJG, editor. *Coronavirus Spike Protein and Tropism Changes*: Academic Press; pp: 29-57.
- Ibrahim NK, 2020. Epidemiologic surveillance for controlling Covid-19 pandemic: types, challenges and implications. *Journal of Infection and Public Health* 13: 1630-1638.
- Johnson CK et al., 2015. Spillover and pandemic properties of zoonotic viruses with high host plasticity. *Scientific Reports* 5: 1-8.
- Johnson CK et al., 2020. Global shifts in mammalian population trends reveal key predictors of virus spillover risk. *Proceedings of the Royal Society* 287: 20192736.

- Kasuga Y et al., 2021. Innate immune sensing of coronavirus and viral evasion strategies. *Experimental and Molecular Medicine* 53: 723-736.
- Lalchhandama K, 2020. The chronicles of coronaviruses: the bronchitis, the hepatitis and the common cold. *Science Vision* 20: 43-53.
- Lam TTY et al., 2020. Identifying SARS-CoV-2-related coronaviruses in Malayan pangolins. *Nature* 583: 282-285.
- Latif AA and Mukaratirwa S, 2020. Zoonotic origins and animal hosts of coronaviruses causing human disease pandemics: A review. *Onderstepoort Journal of Veterinary Research* 87: 1-9.
- Lau SKP et al., 2015. Discovery of a novel coronavirus, China Rattus coronavirus HKU24, from Norway rats supports the murine origin of Betacoronavirus 1 and has implications for the ancestor of Betacoronavirus lineage A. *Journal of Virology* 89: 3076-3092.
- Li W et al., 2005. Bats Are Natural Reservoirs of SARS-Like Coronaviruses. *Science* 310: 676-679.
- McLean RK and Graham SP, 2022. The pig as an amplifying host for new and emerging zoonotic viruses. *One Health* 14: 100384.
- Menachery VD et al., 2020. Trypsin treatment unlocks barrier for zoonotic bat coronavirus infection. *Journal of Virology* 94: 1774-1719.
- Millet JK et al., 2020. Molecular diversity of coronavirus host cell entry receptors. *FEMS Microbiology Reviews* 45.
- Mousavizadeh L and Ghasemi S, 2021. Genotype and phenotype of COVID-19: Their roles in pathogenesis. *Journal of Microbiology, Immunology and Infection* 54: 159-163.
- Nao N et al., 2017. Genetic predisposition to acquire a polybasic cleavage site for highly pathogenic avian influenza virus hemagglutinin. *MBio* 8: 2298-2216.
- Olival KJ et al., 2017. Host and viral traits predict zoonotic spillover from mammals. *Nature* 546: 646-650.
- Peak CM et al., 2017. Comparing nonpharmaceutical interventions for containing emerging epidemics. *Proceedings of the National Academy of Sciences* 114: 4023-4028.
- Plowright RK et al., 2017. Pathways to zoonotic spillover. *Nature Reviews Microbiology* 15: 502-510.
- Poutanen SM, 2018. Human coronaviruses. *Principles and practice of pediatric infectious diseases* 2018: 1148.
- Pratelli A et al., 2003. Genetic diversity of a canine coronavirus detected in pups with diarrhoea in Italy. *Journal of Virological Methods* 110: 9-17.
- Pratelli A et al., 2022. The knotty biology of canine coronavirus: A worrying model of coronaviruses' danger. *Research in Veterinary Science* 144: 190-195.
- Quintana-Murci L, 2019. Human Immunology through the Lens of Evolutionary Genetics. *Cell* 177: 184-199.
- Reusken CBEM et al., 2013. Middle East respiratory syndrome coronavirus neutralising serum antibodies in dromedary camels: a comparative serological study. *The Lancet Infectious Diseases* 13: 859-866.
- Rohaim MA et al., 2020. Evolutionary Analysis of Infectious Bronchitis Virus Reveals Marked Genetic Diversity and Recombination Events. *Genes* 11.
- Ruckert A et al., 2020. What role for One Health in the COVID-19 pandemic? *Canadian Journal of Public Health* 111: 641-644.
- Ruiz-Aravena M et al., 2022. Ecology, evolution and spillover of coronaviruses from bats. *Nature Reviews Microbiology* 20: 299-314.
- Sam P, 2020. Redefining vulnerability in the era of COVID-19. *Lancet* 395(10230): 1089.
- Smith SM et al., 2022. Opportunities for expanding access to veterinary care: Lessons from COVID-19. *Frontiers in Veterinary Science* 9: 804794.
- Su S et al., 2016. Epidemiology, Genetic Recombination, and Pathogenesis of Coronaviruses. *Trends in Microbiology* 24: 490-502.
- Tai W et al., 2020. Characterization of the receptor-binding domain (RBD) of 2019 novel coronavirus: implication for development of RBD protein as a viral attachment inhibitor and vaccine. *Cellular and molecular immunology* 17: 613-620.
- Van der Hoek L et al., 2004. Identification of a new human coronavirus. *Nature Medicine* 10: 368-373.
- Wang N et al., 2018. Serological evidence of bat SARS-related coronavirus infection in humans, China. *Virologica Sinica* 33: 104-107.

- Warren CJ et al., 2022. Primate hemorrhagic fever-causing arteriviruses are poised for spillover to humans. *Cell* 185(21): 3980-3991.
- WHO, 2020. Coronavirus disease (COVID-19) outbreak: rights, roles and responsibilities of health workers, including key considerations for occupational safety and health.
- WHO, 2022. Multisectoral coordination mechanisms operational tool: an operational tool of the Tripartite zoonoses guide. Food and Agriculture Organization 2022.
- Woo PC et al., 2012. Discovery of Seven Novel Mammalian and Avian Coronaviruses in the Genus Deltacoronavirus Supports Bat Coronaviruses as the Gene Source of Alphacoronavirus and Betacoronavirus and Avian Coronaviruses as the Gene Source of Gammacoronavirus and Deltacoronavirus. *Journal of Virology* 86: 3995-4008.
- Wu F et al., 2020. A new coronavirus associated with human respiratory disease in China. *Nature* 579: 265-269.
- Xiao K et al., 2020. Isolation and characterization of 2019-nCoV-like coronavirus from Malayan pangolins. *BioRxiv* 2020.2002.
- Yang D and Leibowitz JL, 2015. The structure and functions of coronavirus genomic 3' and 5' ends. *Virus Research* 206: 120-133.
- Zaki AM et al., 2012. Isolation of a Novel Coronavirus from a Man with Pneumonia in Saudi Arabia. *New England Journal of Medicine* 367: 1814-1820.
- Zhang T et al., 2020. Probable Pangolin Origin of SARS-CoV-2 Associated with the COVID-19 Outbreak. *Current Biology* 30: 1346-1351
- Zhong NS et al., 2003. Epidemiology and cause of severe acute respiratory syndrome (SARS) in Guangdong, People's Republic of China, in February, 2003. *Lancet* 362: 1353-1358.
- Zhou P et al., 2018. Fatal swine acute diarrhoea syndrome caused by an HKU2-related coronavirus of bat origin. *Nature* 556: 255-258.
- Zhou Z et al., 2021. The taxonomy, host range and pathogenicity of coronaviruses and other viruses in the Nidovirales order. *Animal Diseases* 1: 5.
- Zhu N et al., 2020. A Novel Coronavirus from Patients with Pneumonia in China, 2019. *New England Journal of Medicine* 382: 727-733.