



Analytical Encounters and Medical Features of Coronavirus (COVID-19) in New Millennium

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Abstract

Coronaviruses infect many species of animals, together with humans, and have described for more than 50 years. Severe Acute Respiratory Syndrome (SARS) is a strain of coronavirus in humans known for causing super-spreader events. Since late 2019 an outbreak of Coronavirus Disease 2019 (COVID-19), an infectious disease caused by a newly discovered coronavirus, has rapidly spread across the world, devastating lives, and livelihoods. Coronaviruses are a massive family of viruses reported first in Wuhan, China, on December 31st, 2019. This new virus presents dangers: There is no known pre-immunity, no vaccine, and no specific treatment, and the infection is contagious, and everyone is presumed to be susceptible. This new coronavirus appears to target cells in the lungs and possibly other cells in the respiratory system too. Cells infected by the virus generate more virus particles, which can then spread to other people, for instance, by coughing. The novel coronavirus is now known as SARS-CoV-2, because of its similarities to the virus that causes Severe Acute Respiratory Syndrome (SARS). COVID-19 induced pandemic involves the whole food method.

Keywords: SARS; Coronavirus; Spike Protein; COVID-19; Lockdown; Pandemic

Introduction

The word "Coronavirus" refers to a large group of viruses known to affect birds and mammals, including humans. COVID-19, which first appeared in China in December 2019, is a type of coronavirus. These resemble the points on a crown. Corona means "Crown" in Latin. There are hundreds of coronaviruses, but only seven trusted sources are known to affect people. Four human coronaviruses only cause mild cold or flu-like symptoms. Three other coronaviruses pose more severe risks [1]. Coronaviruses first develop in animals before being transmitted to humans are considered zoonotic. Once the virus grows in people, coronaviruses can be transmitted from person to person through respiratory droplets. The viral material hangs out in these droplets and can breathe into the respiratory tract (your windpipe and lungs), where the virus can then lead to an infection. You could acquire SARS-CoV-2 if you touch your mouth, nose, or eyes after touching a surface or object that has the virus on it. During the coronavirus COVID-19 pandemic, the term lockdown for actions related to mass quarantines or stay-at-home orders [2]. By early April 2020, 3.9 billion people worldwide were under lockdown, more than half the world's population. By late April, around 300 million people were under lockdown in nations of Europe, while approximately 200 million people were under lockdown in Latin America. Nearly 300 million people, or about 90 percent of the population, were under lockdown in the United States, and there were 1.3 billion people under lockdown in India [3].

Background Story

The 2019 coronavirus has not definitively linked to a specific animal. Researchers believe that the virus may have passed from bats to another animal, either snakes or pangolins, and then transmitted to humans. This transmission likely occurred in the open food market in Wuhan, China. From 2002 to 2003, Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV) infected 8,000 people, with a fatality rate of ~10%. Since 2012, Middle East Respiratory Syndrome Coronavirus (MERS-CoV) has infected more than 1,700 people, with a fatality rate of ~36%, and till June 14th, 2020 there have been 7,690,708 confirmed cases of COVID-19, including 427,630 deaths, reported to World Health Organization (WHO). As the death toll mounts and millions of us are confined to our homes by COVID-19, it's hard to ignore how connected we are to one another. But this tragedy also highlights how tied we are to wildlife, the likely source of the pandemic [4]. Some experts suggest the spread of the virus from wildlife to humans came from a "wet market" in China where live animals are purchased and slaughtered. It may have originated from a bat or an illegally trafficked

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scaly mammal called a pangolin or both. It has noted that a direct link has not been established [5]. But this proximity between people and wildlife (or sometimes domestic animals) has been shown to lead to 70 percent of zoonotic diseases. Indeed, scientists in China repeatedly warned the world about the coronavirus risks of wildlife markets. The solution could not be more precise: One crucial way to reduce disease risk is to curb wildlife exploitation [6]. To its credit, China slapped a moratorium on live markets and a temporary trade ban earlier this year. But much more durable, broader action is needed around the planet. Wildlife trade is not the only cause of this dangerous problem. Human destruction of and infringement into animal habitat also increase disease risk. Together, these practices have helped spread truly terrifying zoonotic diseases [7]. Ebola, for example, infected people as they entered pristine primate habitat and sought gorillas or chimpanzees for trade, food, or both [8]. With the occurrence of the SARS epidemic, coronaviruses may now "emerging pathogens." Since the SARS epidemic, two new human respiratory coronaviruses have been described. In this review, we discuss the pathogenesis of the previously known coronaviruses. We then discuss the newly isolated SARS-CoV. It has become evident that the body of information gathered over the last 30 years regarding coronavirus replication and pathogenesis has helped to begin an understanding of the origin and the biology of SARS-CoV [9].

Brief History of COVID-19

In early December 2019, Li Wenliang, a doctor from Wuhan, in China's Hubei province, reported in a group chat that he noticed a series of patients showing signs of a severe acute respiratory syndrome or SARS-like illness which subsequently reported to the WHO Country Office in China on December 31st, 2019. On January 12th, Chinese scientists published the genome of the virus, and the World Health Organization (WHO) asked a team in Berlin to use that information to develop a diagnostic test to identify active infection, which was developed and shared four days later. On January 30th, 2020 the outbreak basic knowledge by the WHO, a Public Health Emergency of International Concern (PHEIC). The first case of the disease was due to local person to person spread in the United States, which was confirmed in mid-February 2020. On March 11, WHO declared COVID-19 a pandemic. People worldwide have been affected by Coronavirus Disease 2019 (COVID-19), which is the fifth pandemic after the 1918 flu pandemic [10]. COVID-19 epidemic was not the first coronavirus outbreak of this century and indicated one of the increasing numbers of zoonoses from wildlife to impact global health. SARS-CoV-2, the virus causing the COVID-19 epidemic is distinct from, but closely resembles SARS-CoV-1, which was responsible for the Severe Acute Respiratory Syndrome (SARS) outbreak in 2002. SARS-CoV-1 and 2 share almost 80% of genetic sequences and use the same host cell receptor to initiate viral infection. However, SARS predominantly affected individuals in close contact with infected animals and health care workers. In contrast, CoV-2 exhibits robust person to person spread, most likely utilizing asymptomatic carriers, which have resulted in a greater spread of disease, overall morbidity, and mortality, despite its lesser virulence [11]. The first coronavirus has been discovered in chickens in the 1930s. It was a few decades until the first human coronaviruses were identified in the 1960s. To date, seven coronaviruses can cause disease in humans. Four are endemic (regularly found among particular people or in a specific area) and usually cause mild fever, but three can cause much more severe and even fatal disease. The novel human coronavirus disease COVID-19 has become the fifth documented pandemic since the 1918 flu

pandemic [12]. COVID-19 has spread rapidly to other provinces of China and now internationally. On January 30th, 2020, the World Health Organization (WHO) declared COVID-19 a public health emergency of international concern (PHEIC). At the beginning of the outbreak, COVID-19 was considered a zoonotic disease with limited human-to-human transmission. Still, as of June 04th, 2020, more than 6.57 million cases have been described across 188 countries and territories, resulting in more than 387,000 deaths, and more than 2.83 million people have recovered. The common symptoms include fever, cough, fatigue, shortness of breath, and loss of smell and taste. The time from exposure to onset of indicators is typically around five days but may range from two to fourteen days [13].

Taxonomy and Nomenclature of COVID-19

World Health Organization (WHO) naming the Coronavirus Disease (COVID-19) and the Official names have been announced for the virus responsible for COVID-19 (previously known as "2019 novel coronavirus"). The official name of the virus is Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), and the name of the disease is Coronavirus Disease (COVID-19) [8]. The name "coronavirus" coined in 1968 is derived from the "corona"- which means crown-like morphology observed for these viruses in the electron microscope [3]. In 1975, the *Coronaviridae* family established by the International Committee on the Taxonomy of Viruses. Recently, at the 10th International *Nidovirus* Symposium in Colorado Springs, Colo., in June 2005, it was proposed that the *Coronaviridae* family divided into two subfamilies, the coronaviruses, and the *toroviruses*, the latter of which causes enteric diseases in cattle and possibly in humans [2]. The *Coronaviridae* family, along with the *Arteviridae* and *Roniviridae* families, forms the *Nidovirales* order. The *Arteviridae* family includes swine and equine pathogens, and the *Roniviridae* family is composed of invertebrate viruses [7]. The present outbreak of a coronavirus-associated acute respiratory disease called Coronavirus Disease 19 (COVID-19) is the third documented spillover of an animal coronavirus to humans in only two decades that has resulted in a significant epidemic [5]. The *Coronaviridae* Study Group (CSG) of the International Committee on Taxonomy of Viruses, which is responsible for developing the classification of viruses and taxon nomenclature of the family *Coronaviridae*, has assessed the placement of the human pathogen, tentatively named 2019-nCoV, within the *Coronaviridae* [9]. Based on phylogeny, taxonomy, and established practice, the CSG recognizes this virus as forming a sister clade to the prototype human and bat Severe Acute Respiratory Syndrome Coronaviruses (SARS-CoVs) of the species severe acute respiratory syndrome-related coronavirus and designates it as SARS-CoV-2 [1]. Researchers studying coronaviruses - a family of enveloped positive-strand RNA viruses infecting vertebrates have been confronted with the need to define whether a newly emerged virus causing severe or even life-threatening disease in humans belongs to an existing or a new species [10]. Each time, the virus was placed in the taxonomy using information derived from a sequence-based family classification [11]. The current classification of coronaviruses recognizes 39 species in 27 subgenera, five genera, and two subfamilies that belong to the family *Coronaviridae*, suborder *Cornidovirineae*, order *Nidovirales*, and realm *Riboviria*. The family classification and taxonomy has been developed by the *Coronaviridae* Study Group (CSG), a working group of the ICTV20. The CSG is responsible for assessing the place of new viruses through their relation to known viruses in established taxa, including placements relating to the species' severe acute respiratory syndrome-related coronavirus [12].

In the classification of *Nidoviruses*, species are considered biological entities demarcated by a genetics-based method, while generally, virus species are perceived as human-made constructs. Although these viruses are isolated at different times and locations from various human and animal hosts, they all belong to the species severe acute respiratory syndrome-related coronavirus. Their relationship parallels that between human individuals and the species *Homo sapiens*. Concerning novelty, SARS-CoV-2 differs from the two other zoonotic coronaviruses, SARS-CoV, and MERS-CoV, introduced to humans earlier in the twenty-first century [14]. Finally, coronaviruses have divided into three genera (Group I to Group III), usually referred to as groups, and more recent genome sequence analysis has confirmed this grouping. Group I coronaviruses include animal pathogens, such as TGEV of the pig, Porcine Epidemic Diarrhea Virus (PEDV), and Feline Infectious Peritonitis Virus (FIPV) as the Human Coronaviruses HCoV-229E and HKU1, which cause respiratory infections. Group II includes pathogens of veterinary relevance, such as BCoV, porcine hemagglutinating encephalomyelitis virus, equine coronavirus, and human coronaviruses viruses OC43 and NL63, which, like HCoV-229E, also cause respiratory infections [15]. This group also includes viruses that infect both mice and rats. MHV often studied as a prototype coronavirus; MHV is a group of highly related strains causing a variety of diseases, such as enteric disease, hepatitis, and respiratory disease, as well as encephalitis and chronic demyelination. Group III includes only avian coronaviruses, such as IBV, turkey coronavirus, and pheasant coronavirus. Recently, using Reverse Transcription-PCR (RT-PCR), coronavirus sequences were detected in the graylag goose (*Anser anser*), feral pigeon (*Columba livia*), and mallard (*Anas platyrhynchos*); phylogenetic analyses of the replicase and Nucleocapsid (N) sequences suggest that these viruses are members of group III, but as yet they have not been isolated or characterized [16].

Structure and Life Cycle of Coronavirus

Coronaviruses belong to the family *Coronaviridae* in the order *Nidovirales* can be classified into four genera: α -coronavirus, β -coronavirus, γ -coronavirus, and δ -coronavirus. Among them, α - and β -coronaviruses infect mammals, γ -coronaviruses infect avian species, and δ -coronaviruses infect mammalian and avian species. α -coronaviruses represent human coronavirus (HCoV-NL63), porcine Transmissible Gastroenteritis Coronavirus (TGEV), and Porcine Respiratory Coronavirus (PRCV). β -coronaviruses represent SARS-CoV, human coronavirus (SCoV), bat coronavirus (HKU4), Mouse Hepatitis Coronavirus (MHV), Bovine Coronavirus (BCoV), and coronavirus (OC43) [17]. Similarly, γ - and δ -coronaviruses include avian Infectious Bronchitis Coronavirus (IBV) and Porcine δ -Coronavirus (PdCV). Coronaviruses (CoVs) are a significant group of viruses that are responsible for a broad spectrum of diseases in multiple species. Coronaviruses (CoVs) are spherical and approximately 125 nm in diameter, with club-shaped spikes projecting from the surface of the virus, giving the appearance of a solar corona, prompting the name, coronaviruses. Within the envelope are the helically symmetrical nucleocapsids, which is uncommon among positive-sense RNA viruses [15]. The coronavirus is large, enveloped, positive-stranded RNA viruses and has the largest genome among all RNA viruses, typically ranging from 27 kb to 32 kb. The genome is packed inside a helical capsid formed by the Nucleocapsid protein (N) and further surrounded by an envelope. Associated with the viral envelope are at least three structural proteins: The Membrane protein (M) and the Envelope protein (E) are involved in virus

assembly, whereas the Spike protein (S) mediates virus entry into host cells. The coronavirus spike contains three segments: A large ectodomain, a single-pass transmembrane anchor, and a short intracellular tail. The ectodomain consists of a receptor-binding subunit S1 and a membrane-fusion subunit S2. Electron microscopy studies revealed that the spike is a clove-shaped trimer with three S1 heads and a trimer S2 stalk. During virus entry, S1 binds to a receptor on the host cell surface for viral attachment, and S2 fuses the host and viral membranes, allowing viral genomes to enter host cells. Receptor binding and membrane fusion are the initial and critical steps in the coronavirus infection cycle; they also serve as primary targets for human inventions [16]. The life cycle of coronavirus is briefly summarized. It is not designed to be a comprehensive review, but rather to provide a context for discussion of the functions of various viral proteins. Coronaviruses attach to specific cellular receptors *via* the spike protein and trigger a conformational change in a spike, which then mediates fusion between the viral and cell membranes, which results in the release of the Nucleocapsid into the cell [17]. During infection with coronaviruses, as with all other RNA viruses, replication of genome and transcription of mRNAs must occur. Replication of the genome involves the synthesis of a full-length negative-strand RNA that is present at a low concentration and serves as a template for full-length genomic RNA. Multiple overlapping 3'-coterminal sub genomic RNAs serve as mRNAs, as does full-length genomic RNA. Each mRNA has a standard (75 to 78 nucleotide) leader sequence at its 5' end; this leader is derived from the 5' end of genome RNA. Besides, negative-strand RNAs corresponding in length to each of the mRNAs and the full genomic range are present at low concentrations. The mechanism by which the group of positive- and negative-strand RNAs is synthesized involves a unique discontinuous transcription mechanism that is not entirely understood. However, sub genomic mRNA synthesis is believed to be regulated by transcription-regulating sequences, present in the genome RNA, at the transcriptional start sites for each mRNA [18].

Mechanism and Pathogenesis of Coronavirus

Coronaviruses cause a large variety of diseases in animals, and their ability to cause severe illness in livestock and companion animals such as pigs, cows, chickens, dogs, and cats led to significant research on these viruses in the last half of the twentieth century. For instance, Transmissible Gastroenteritis Virus (TGEV) and Porcine Epidemic Diarrhea Virus (PEDV) cause severe gastroenteritis in young piglets, leading to significant morbidity, mortality, and ultimately economic losses [14]. PEDV recently emerged in North America for the first time, causing substantial injuries of young piglets. Porcine Hemagglutinating Encephalomyelitis Virus (PHEV) mostly leads to enteric infection that could infect the nervous system, causing encephalitis, vomiting, and wasting in pigs. Feline enteric Coronavirus (FCoV) causes a mild or asymptomatic disease in domestic cats [16]. FCoV, Feline Infectious Peritonitis Virus (FIPV), leads to the development of a lethal disease called Feline Infectious Peritonitis (FIP) has wet and dry forms, with similarities to the human condition, sarcoidosis. Bovine CoV, Rat CoV, and Infectious Bronchitis Virus (IBV) cause mild to severe respiratory tract infections in cattle, rats, and chickens [17]. More recently, a novel coronavirus named SW1 has been identified in a deceased Beluga whale. Large numbers of virus particles were identified in the liver of the dead whale with respiratory disease and acute liver failure. Although electron microscopic images were not sufficient to identify the virus as a coronavirus, the liver tissue's sequencing identified

the virus as a coronavirus. It was subsequently determined to be a γ -coronavirus based on phylogenetic analysis. Still, it has not yet verified experimentally that this virus is a causative agent of disease in whales. Besides, there has been intense interest in identifying novel bat CoVs, since these are the likely ancestors for SARS-CoV and MERS-CoV, and hundreds of novel bat coronaviruses have been identified over the past decade [18].

Animal Coronavirus

The most heavily studied animal coronavirus is *Murine* Hepatitis Virus (MHV), which causes a variety of outcomes in mice, including respiratory, enteric, hepatic, and neurologic infections. These infections often serve as incredibly useful models of disease. For instance, MHV-1 causes severe respiratory illness in susceptible A/J mice, A59 [19]. Attenuated versions of JHMV cause a chronic demyelinating disease that bears similarities to multiple sclerosis (M.S.), making MHV infection and one of the best models for this debilitating human disease. Early studies suggested that demyelination was dependent on viral replication in oligodendrocytes in the brain and spinal cord, and more recent reports demonstrate that the condition is immune-mediated. Irradiated mice or immunodeficient (lacking T and B cells) mice do not develop demyelination, but virus-specific T cells restore the development of demyelination [20]. Additionally, demyelination is accompanied by a massive influx of macrophages and microglia that can phagocytose infected myelin. However, it is unknown what the signals are that direct immune cells to destroy myelin. Finally, MHV can be studied under BSL2 laboratory conditions, unlike SARS-CoV or MERS-CoV, which require a BSL3 laboratory and provides a large number of suitable animal models. These factors make MHV an ideal model for studying the basics of viral replication in tissue culture cells and studying the pathogenesis and immune response to coronaviruses [21].

Human Coronaviruses

SARS-CoV coronaviruses only thought to cause mild, self-limiting respiratory infections in humans, and two of these are α -coronaviruses, HCoV-229E, and HCoV-NL63, while the other two are β -coronaviruses, HCoV-OC43, and HCoV-HKU1. HCoV-229E and HCoV-OC43 were isolated nearly 50 years ago, while HCoV-NL63 and HCoV-HKU1 have only recently been identified following the SARS-CoV outbreak [22]. These viruses are endemic in the human population, causing 15% to 30% of respiratory tract infections each year. One exciting aspect of these viruses is their differences in tolerance to genetic variability. HCoV-229E isolates from around the world have only minimal sequence divergence, while HCoV-OC43 strains from the same location but isolated in different years show significant genetic variability. Based on the ability of MHV to cause demyelinating disease, it has suggested that human CoVs may be involved in the development of Multiple Sclerosis (M.S.). However, no evidence indicates that human CoVs play a significant role in MS [23].

Diagnosis, Treatment, and Prevention

Diagnosis is also essential in locations where a severe CoV outbreak is occurring, such as, at present, in the Middle East, where MERS-CoV continues to circulate. It is also important to diagnose cases of severe veterinary CoV-induced diseases, such as PEDV and IBV, to control these pathogens and protect food supplies [24]. RT-PCR has become the method of choice for diagnosis of human CoV, as multiplex real-time RT-PCR assays have developed, can detect

all four respiratory HCoVs, and could be further adapted to novel CoVs. Serologic tests are essential in cases where RNA is difficult to isolate or is no longer present, and for epidemiological studies [25]. To date, there is no antiviral therapeutics that specifically target human coronaviruses, so treatments are only supportive. *In vitro*, Interferons (IFNs) are only partially effective against coronaviruses. IFNs in combination with ribavirin may have increased activity *in vitro* when compared to IFNs alone against some coronaviruses; however, the effectiveness of this combination *in vivo* requires further evaluation [26]. The SARS and MERS outbreaks have stimulated research on these viruses. This research has identified a large number of suitable antiviral targets, such as viral proteases, polymerases, and entry proteins. Significant work remains, however, to develop drugs that target these processes and can inhibit viral replication. Only limited options are available to prevent coronavirus infections [27]. Vaccines have only approved for IBV, TGEV, and Canine CoV, but these vaccines are not always used because they are either not very useful, or in some cases, have been reported to be involved in the selection of novel pathogenic CoVs *via* recombination of circulating strains [28]. Vaccines for veterinary pathogens, such as PEDV, may be useful in cases where the spread of the virus to a new location could lead to severe losses of veterinary animals. In the case of SARS-CoV, several potential vaccines have been developed, but none are approved for use. These vaccines include recombinant attenuated viruses, live virus vectors, or individual viral proteins expressed from DNA plasmids [29]. Therapeutic SARS-CoV neutralizing antibodies have been generated and could be retrieved and used again in the event of another SARS-CoV outbreak. Such antibodies would be most useful for protecting healthcare workers. Despite this success, vaccine development for coronaviruses faces many challenges. For mucosal infections, natural infection does not prevent subsequent infection. So vaccines must either induce better immunity than the original virus or must at least lessen the disease incurred during a secondary infection [30].

Pandemic and Vaccine Development

As the COVID-19 pandemic continues to spread globally, many countries are putting in place unprecedented lockdown measures designed to contain its impact on public health. However, such measures have significant implications for other domains of human activity, including food and nutrition security, jobs, livelihoods, gender equality, and potential social unrest [17]. The implications may be severe and particularly dire for the poor and vulnerable living in developing countries. It is estimated that the economic fallout of the COVID-19 pandemic could plunge more than half a billion people into poverty, with communities in Sub-Saharan Africa, North Africa, and the Middle East expected to suffer the most [19]. The impacts of this global health crisis and, ultimately, the economic crisis will disproportionately affect women and girls and reverse gender equality on many levels. Unless sound and decisive measures have taken fast to keep global food supply chains going and protect poor and vulnerable communities, a looming food crisis - with severe socio-economic consequences- becomes inevitable [14]. Coronavirus 'lockdowns' in developing countries are already triggering a mass exodus of the urban poor migrating to their rural homes. With no jobs, no incomes or savings, and limited means and space to practice good hygiene and social distancing, millions of women, men, children, and older people will face death, disease, or slow starvation [27]. Researchers worldwide are racing to develop potential vaccines and drugs to fight the new coronavirus, called SARS-Cov-2. A group

of researchers has figured out the molecular structure of a critical protein that the coronavirus uses to invade human cells, potentially opening the door to the development of a vaccine, according to new findings [24]. Previous research revealed that coronaviruses invade cells through so-called "spike" proteins, but those proteins take on different shapes in different coronaviruses. Figuring out the form of the spike protein in SARS-Cov-2 is the key to figuring out how to target the virus, said Jason McLellan, senior author of the study and an associate professor of molecular biosciences at the University of Texas at Austin [19]. Though the coronavirus uses many different proteins to replicate and invade cells, the spike protein is the major surface protein that it uses to bind to a receptor-another protein that acts as a doorway into a human cell. After the spike protein binds to the human cell receptor, the viral membrane fuses with the human cell membrane. It allows the genome of the virus to enter human cells and begin infection [29]. So "if you can prevent attachment and fusion, you may prevent entry," McLellan told Live Science. But to target this protein, you need to know what it looks like. Earlier this month, researchers published the genome of SARS-Cov-2. Using that genome, McLellan and his team collaborated with the National Institutes of Health (NIH) and identified the specific genes that code for the spike protein. They then sent that gene information to a company that created the genes and sent them back [30]. The group then injected those genes into mammalian cells in a lab dish, and those cells produced the spike proteins.

Social Tensions and Conflict due to Lockdown

COVID-19 could have adverse effects on social and political stability, creating the conditions for unrest, especially in the most vulnerable food crisis countries. Uncertainty of future impacts of the pandemic, combined with restricting movement, soaring unemployment, limited access to food, and the erosion of already fragile livelihoods may generate discontent among the population, fuelling violence and conflict [31]. Furthermore, the postponement of elections may jeopardize the democratic process and create tensions between ruling parties and oppositions, with possible consequences for political stability. Any COVID-19 response must consider that technical intervention may be understood through local conflict sensibilities and need to be conflict-sensitive to ensure the trust of local populations [32]. Crises can also be used as an opportunity for military and political gains in ongoing conflicts. Indeed, how crisis response is delivered and how it can enable other agendas can become independent conflict accelerants, as can perceptions of bias in terms of which communities' needs viewed as being prioritized [33]. Finally, the disease could hinder international mediation efforts for conflict resolution and peacekeeping operations, with consequent adverse effects on vulnerable and food insecure conflict-affected people [34]. All these impacts may further increase the numbers of IDPs and refugees, which are already of concern in food crisis countries. However, it is essential to note that moments of crisis can also provide turning points in the conflict, depending on how the parties behave and whether peace actors can seize opportunities for collaboration [35].

Conclusion

Over the past 50 years, the emergence of many different coronaviruses that cause a wide variety of human and veterinary diseases has occurred. These viruses may continue to emerge and evolve and cause both human and veterinary outbreaks due to their

ability to recombine, mutate, and infect multiple species and cell types. Coronaviruses have several non-structural and accessory proteins that have considered with no known function. If their mechanisms of action are identified, and their roles are defined in viral replication, this will increase the number of suitable therapeutic targets. Several appropriate antiviral targets, such as viral proteases, polymerases, and entry proteins, have been identified to inhibit viral replication. A few strategies have developed to produce a candidate vaccine that can reduce recombination by making large deletions in the E proteins, rearranging the 3' end of the genome, or using mutant viruses with abnormally high mutation rates that significantly attenuate the virus. Future research on coronaviruses will continue to investigate many aspects of viral replication and pathogenesis. First, understanding the propensity of these viruses to jump between species, establish infection in a new host, and identify significant reservoirs of coronaviruses dramatically aid in predicting when and where potential epidemics may occur. As bats seem to be a substantial reservoir for these viruses, it is interesting to determine how they seem to avoid clinically evident disease and become persistently infected. Second, many of the non-structural and accessory proteins encoded by these viruses remain uncharacterized with no known function. It is essential to identify mechanisms of action for these proteins as well as define their role in viral replication and pathogenesis. These studies should lead to a massive increase in the number of suitable therapeutic targets to combat infections.

Furthermore, many of the unique enzymes encoded by coronaviruses, such as ADP-ribose-1''-phosphatase, are also present in higher eukaryotes, making their study relevant to understanding general aspects of molecular biology and biochemistry. Third, gaining a complete picture of the intricacies of the RTC provide a framework for understanding the unique RNA replication process used by these viruses. Finally, defining the mechanism of how coronaviruses cause disease and understanding the host immunopathological response significantly improves our ability to design vaccines and reduce disease burden.

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