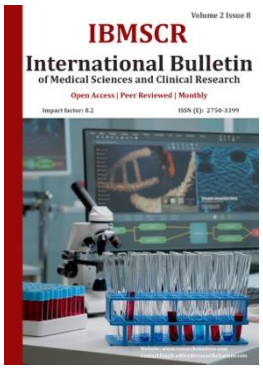

THE RISE AND REEMERGENCE OF VIRAL ZOONOTIC DISEASES: A CONFLUENCE OF HUMAN ACTIONS AND MISJUDGMENTS

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Abstract

Zoonotic diseases are illnesses transmitted from vertebrate animals to humans. Although a variety of microbial agents, such as bacteria and parasites, are associated with zoonotic events, viruses constitute a significant proportion of emerging zoonotic diseases. Alarmingly, the 21st century has witnessed a sharp rise in the emergence and re-emergence of viral zoonotic diseases. Despite the millennia-long coexistence of humans and animals, human-driven activities have significantly increased the frequency of interactions between the two, elevating the risk of disease spillover. Factors like climate change, land-use alteration, and wildlife trade directly contribute to the (re-)emergence of these diseases, while globalization, geopolitical influences, and social dynamics facilitate their spread. This opinion piece explores the "intelligent" behavior of viruses and how they exploit anthropogenic factors to drive the (re-)emergence and spread of zoonotic diseases in our modern, interconnected world.

Keywords: zoonotic viruses, emerging infectious diseases, land-use change, wildlife trade, livestock and domestic animals, climate change, globalization, geopolitics, social factors.

1. Introduction

More than 70% of the thousands of pathogens known to infect humans are zoonotic, with many of these being viral in nature [1]. Zoonoses are diseases transmitted from vertebrate animals—such as reptiles, mammals, and birds—to humans [2]. These animals, acting as reservoir or amplifier hosts, facilitate the initial cross-species transmission to humans through direct or indirect interactions [3]. Although viral zoonoses are recurring, humans often serve as dead-end hosts for these pathogens [4]. However, in some cases, viruses acquire genetic mutations that enable sustained human-to-human transmission. In rare instances, animal viruses may adapt so effectively to human hosts that they establish new, exclusive human-to-human transmission cycles [5]. Most viruses, however, are unable to coexist long-term with humans; as a result, they fail to sustain replication and are typically eliminated from the body through routes such as the blood, gastrointestinal, urogenital, and respiratory tracts without causing significant harm. In fact, many acute viral zoonoses require repeated introductions from non-human hosts to initiate human-to-human spread [6].

Despite the rarity of successful adaptation, the emergence and re-emergence of viral zoonoses has been on the rise in recent decades. While viruses are capable of rapid mutation, the primary drivers of their zoonotic potential are largely linked to human activities, such as deforestation, farming, and shifting population dynamics [7]. Additionally, human disturbances of complex biodiversity within natural ecosystems further contribute to this trend [8]. Given the significant role of human actions in the (re-)emergence of viral zoonoses, are our behaviors, beliefs, and pursuit of modernization ultimately contributing to our own

vulnerability? This article explores the adaptability of viruses and the consequences of human activities in the (re-)emergence and spread of viral zoonotic diseases.

2. Are Viruses "Smarter" Than We Think?

Viral infections have plagued humanity since the beginning of time [9]. While the earliest recorded pandemic linked to a viral infection dates back to 165 CE [10,11], recent evidence suggests that an outbreak affecting around 300 villagers in China over 5,000 years ago may have been caused by an unknown virus. Throughout history, numerous pandemics, epidemics, and outbreaks have been associated with viruses such as coronaviruses, Marburg virus, Ebola virus, variola virus (smallpox), human immunodeficiency virus (HIV), Zika virus, measles virus, and various influenza strains (Figure 1) [9,12,13]. Viral zoonoses are notorious for their sporadic and unpredictable emergence. Could it be that viruses are evolving specifically for sustained infection and transmission?

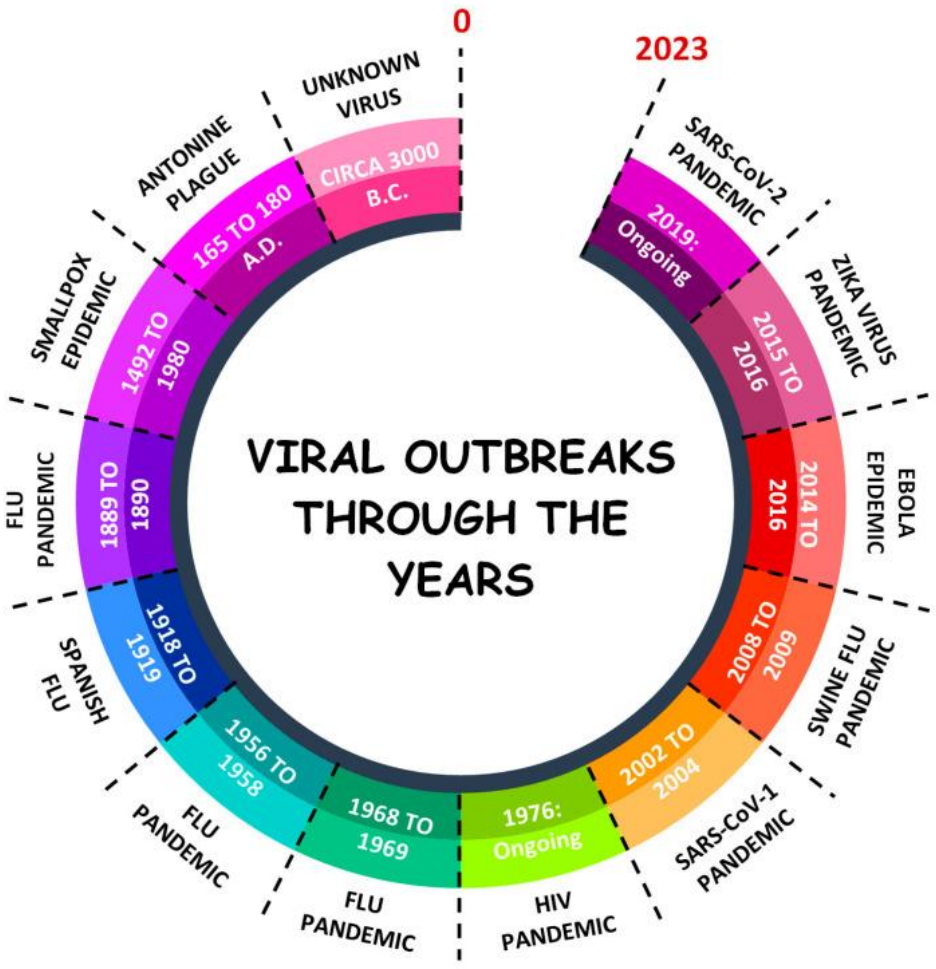

Figure 1

Timeline of history's most notable viral pandemics and epidemics. Most major pandemics were attributed to mutated influenza viruses (H1N1, H2N2, H3N2) that were thought to have originated in animal reservoirs and which subsequently spread to humans. The 2003 SARS-CoV-1 pandemic is regarded as the first pandemic of the 21st century and, similar to SARS-CoV-2, likely emerged from bats. Note 1: Although the agent responsible for the outbreak 5000 years ago is not known, scientists hypothesise that due to the rapid mortality and transmission rate, the disease was likely caused by the measles virus. Note 2: Based on descriptions by Greek physician Galen, the Antonine plague may be attributed to smallpox.

For instance, while the incubation period for rabies lyssavirus varies, symptoms typically manifest 20 to 90 days after exposure. In advanced stages, the virus targets specific parts of the brain, inducing extreme paranoia. This paranoia often leads to aggressive behavior, which facilitates transmission, as infected animals are more likely to bite other animals or humans. Additionally, rabies causes throat spasms when liquids are consumed, resulting in hydrophobia. This aversion to water likely increases the viral load in the animal's saliva, further enhancing transmission potential [14,15]. These adaptive transmission strategies have evidently evolved to help rabies lyssavirus avoid extinction [16].

Another example is the Ebola virus. During the 2013-2016 outbreak in West Africa, the largest recorded Ebola outbreak, sequencing revealed an amino acid substitution in the virus's surface glycoprotein, increasing its ability to bind to the human receptor NPC1. This adaptation may have contributed to increased virulence and transmission, thus worsening the outbreak [17].

A similar case occurred with SARS-CoV-2, the virus responsible for COVID-19. In 2020, Korber et al. [18] identified a recurring amino acid substitution at position 614 in the spike protein of SARS-CoV-2. This mutation, from D614 to G614, led to increased viral loads, suggesting a fitness advantage for infectivity, though not for disease severity [18]. The D614 wild-type variant has since disappeared from circulating SARS-CoV-2 strains [19].

Another interesting example is the poliovirus, which is transmitted through the fecal-oral route and causes poliomyelitis. Despite widespread vaccination that has brought the virus to the brink of eradication, live-attenuated vaccines, especially for polio type 2, can occasionally revert to a virulent form, resulting in vaccine-derived poliovirus outbreaks [20]. Most of these outbreaks occur in regions with low vaccination coverage [21], and the poliovirus vaccine's limited potential for immune escape restricts the evolution of vaccine-derived variants [22].

These examples illustrate how viruses make adaptive changes to persist in their hosts. Most viruses tend to attenuate over time, accumulating mutations that confer selective advantages, but these mutations may not always become fixed in future populations [23]. A historical example is the 1889 flu pandemic, which was linked to the human coronavirus OC43, a virus that diverged from bovine coronaviruses [24]. Since that pandemic, OC43 has attenuated, and now typically causes only the common cold in humans. While attenuation may involve negative effects, such as reduced replication ability, the long-term coexistence with the host is advantageous, as it allows the host to survive longer, facilitating continued viral transmission [25].

A more recent example is SARS-CoV-2, which evolved a preference for infecting the upper respiratory tract rather than lung tissue. The D614 mutation played a role in this shift in tropism, leading to milder symptoms, shorter incubation periods, and greater transmissibility between individuals [26]. This raises the question: are we witnessing a repeating pattern in pandemics? What is clear is that successful interaction between a virus and its newly acquired host is crucial. As the Red Queen famously says in Lewis Carroll's *Through the Looking-Glass*: "Now, here, you see, it takes all the running you can do, to keep in the same place" [27]. This phrase, often used to describe coevolutionary dynamics [28], suggests that the more things change, the more they stay the same. In this continuous cycle of infections and re-infections, are we keeping pace? Given that human influence on the environment and the risk of (re-

)emerging zoonotic viruses is at an all-time high, it is imperative for us to learn from these experiences and be better prepared for future pandemics.

3. Human Impactful Drivers in the (Re-)Emergence of Viral Zoonoses

3.1. Land-Use Change and Its Role in the Species–Pathogen Biodiversity Interface

Land-use change refers to all human-induced modifications of land and its ecosystems on a global scale [29]. It is one of the most significant factors driving the (re-)emergence of viral zoonoses [30]. Activities such as deforestation, urbanization, agriculture, and livestock farming have profound effects on the natural landscape, creating a domino effect on the abundance of pathogens and host species, exposure rates, and pathogen coevolution [31,32]. García-Peña et al. [33] conducted a study that found areas with high rodent species diversity where croplands expanded into pastures and forests had an increased risk of zoonotic disease emergence, involving a range of pathogens such as hantaviruses. Similarly, a longitudinal study by Plowright et al. [34] demonstrated that pregnant and lactating flying fox bats were at a higher risk of Hendra virus infection, highlighting the seasonal significance of Hendra virus outbreaks in bats and the potential zoonotic transmission to humans. Interestingly, the study also revealed that flying foxes experiencing nutritional stress during times of food scarcity showed higher seroprevalence of the virus, suggesting that habitat loss negatively impacts both Hendra virus infection and its transmission among host populations [34].

Historically, two conflicting models have been proposed regarding biodiversity and zoonotic diseases [35], as illustrated in Figure 2. The first model, known as the amplification effect, posits that diverse habitats are hotspots for new or emerging zoonotic pathogens due to high levels of both pathogen and host diversity [36,37]. In contrast, the second model, called the dilution effect, suggests that diverse habitats are negatively correlated with the transmission of existing or re-emerging zoonotic pathogens [38,39]. Unlike the amplification effect, the dilution effect has been a subject of considerable debate within the field of ecology. While some studies support the dilution effect [39,40,41], others challenge its validity, particularly in the context of zoonotic disease dynamics [42].

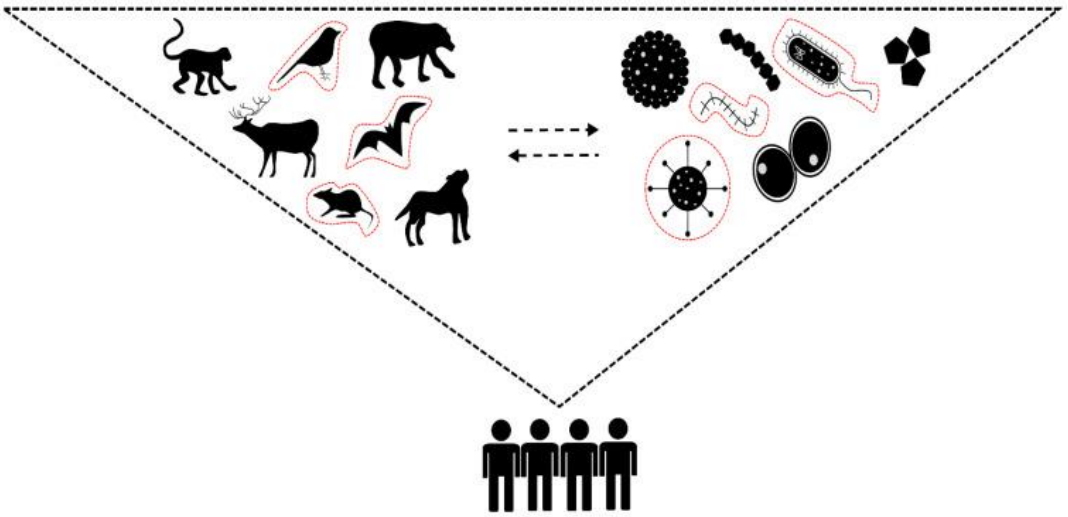

Figure 2

Alternative biodiversity models linking host and pathogen dynamics in the (re-)emergence of zoonotic disease. (1) In both the amplification and dilution models, total host diversity assumes a spectrum of circulating microbes that have the ability to jump the species barrier; (2) the zoonotic host species diversity model (animals circled in red) assumes that potential

host species are more likely to harbour zoonotic pathogens (microbes circled in red); (3) the zoonotic pathogen–host species diversity and abundance model assumes that both host species diversity and the prevalence of pathogens determine the potential for zoonotic disease emergence (adapted from [35]).

Understanding these models is challenging and often depends on limited, selectively characterized data available at the time of analysis. Most research models are based on either (i) host–pathogen diversity, (ii) zoonotic host–pathogen diversity, or (iii) zoonotic host–pathogen abundance and diversity (Figure 2), with data being collected and analyzed within these specific contexts. Despite their differences, all of these models share a common theme: opportunities for cross-species transmission and pathogenic establishment [35]. It is also important to consider multiple host species for the same zoonotic pathogen, as well as the capacity of each host to effectively transmit the pathogen, when evaluating biodiversity-related zoonoses [5].

Human-induced disruptions of natural biodiversity are significant drivers of viral zoonoses emergence. For instance, Tapia-Ramírez et al. conducted a systematic review that identified novel mammarenaviruses (associated with viral hemorrhagic fever) in 27 of 47 rodent species across the Americas. While no virions were detected in the remaining 20 rodent species, antibodies to mammarenaviruses were found, suggesting exposure. In another study, Dacheux et al. used viral metagenomics to analyze insectivorous bats in France that had interactions with humans. They identified several new mammalian viruses, including gammaretroviruses and bornaviruses, as well as known mammalian viral families. They also identified the first bat nairovirus, named Ahun nairovirus, which significantly differed from previously known nairoviruse. These examples illustrate the diversity of host species in the former case and pathogen diversity in the latter, both of which contribute to the risk of viral zoonotic diseases.

Another example of species diversity impacting zoonotic potential is provided by French et al., who used meta-transcriptomic sequencing to investigate viral diversity in water samples from various anthropogenically affected sites along a river in New Zealand. Their findings revealed that 94% of the identified viral species were novel, with 63 of these viruses having the potential to infect birds and fish. Furthermore, viral species found in urban and farming areas were absent in native forest sites, indicating the impact of human activities on viral diversity. The study suggests a potential transmission pathway from animals to humans via direct animal contact or through indirect contact with contaminated water, emphasizing how human-modified environments can facilitate viral spread.

A further example of how human encroachment contributes to zoonotic disease is the Ebola virus. Rulli et al. demonstrated that Ebola virus spillover events in West and Central Africa were linked to areas of habitat fragmentation. These fragmented habitats likely increased interactions between humans and wildlife, contributing to disease transmission by bringing humans into contact with reservoir species.

The complexity of land-use change and its ecological impacts is evident. To reduce the (re-)emergence of zoonotic diseases, it is crucial to balance these activities strategically to conserve natural ecosystems and limit human–wildlife interactions.

3.2. Wildlife Trade

The fragile relationship between humans and nature is often overlooked, particularly when it comes to the wildlife trade. The practice of trading wild or domesticated animals, whether legally or illegally, poses a significant risk for the global spread of zoonotic diseases [51]. It is estimated that over one billion direct or indirect contacts between animals and humans occur annually. In an effort to quantify the risk associated with global wildlife trade, Shivaprakash et al. found that approximately 26.5% of mammals are natural carriers of about 75% of the known zoonotic viruses examined in their study. They also indicated that, aside from rodents and bats, carnivores, primates, and hoofed animals such as deer pose a substantial zoonotic risk, as 58% of the 228 known zoonotic viruses were found within this group of traded animals.

The illegal wildlife trade is a lucrative business, generating between USD 7 billion and USD 20 billion in annual revenue. Its ties to crime syndicates make it challenging to regulate. Additionally, legal but poorly regulated activities, such as those in wet markets, increase the risk of exposure and close proximity between diverse species, thus elevating the likelihood of multiple zoonotic pathogens circulating in one location.

While much of the attention has been focused on the role of bushmeat in the (re-)emergence of zoonotic diseases [55], other activities—such as relocating exotic animals for repopulation efforts, zoological institutions, domestication, or ecotourism—should not be underestimated. These scenarios provide effective transmission routes for introducing novel and re-emerging zoonotic pathogens to human hosts.

In 2003, a multistate outbreak of the Mpox virus led to 71 human cases following the importation of infected rodents by an exotic animal distributor in Texas. Investigations revealed that the proximity of the infected rodents to prairie dogs facilitated animal-to-animal transmission, which subsequently enabled prairie dogs purchased by the public or other distributors to serve as a secondary host for further transmission to humans. More recently, a 53-year-old veterinary surgeon working at a research facility in Beijing specializing in non-human primates contracted monkey B virus, also known as herpes B virus. After dissecting two monkeys, the individual developed symptoms including fever, nausea, vomiting, and neurological issues, eventually succumbing to the infection. Although monkey B virus has a mortality rate of 70–80% in humans, its zoonotic transmission is sporadic, with minimal risk of secondary spread. However, repeated introductions might provide the virus with the opportunity it needs to gain a fitness advantage over humans.

Certainly, one of the most intriguing examples of a human-related zoonotic event involved a bacterial–viral coinfection observed in birds. Researchers discovered that a novel adenovirus (psittacine adenovirus HKU1) and the bacterium *Chlamydophila psittaci* (C. psittaci) jointly infected mealy parrots, which led to a psittacosis outbreak among humans at an animal detention center in Hong Kong. They also found that higher concentrations of *C. psittaci* coincided with higher viral loads of adenovirus HKU1. It was suggested that immune suppression caused by adenovirus HKU1 facilitated more severe *C. psittaci* infections, creating conditions favorable for zoonotic transmission. This highlights the significant role that bacterial and viral coinfections in animals can play in the (re-)emergence of zoonotic diseases.

Moreover, with adventure travel at an all-time high, the role of ecotourism in zoonotic disease emergence must not be overlooked. Activities such as safaris, extreme travel, and adventure sports present a high risk of exposure to unknown pathogens. An illustrative example is the Balinese Hindu temple in Indonesia, where macaques that have been shown to

carry antibodies for the herpes B virus freely roam. Since the temple is a popular tourist destination, the potential for zoonotic transmission exists due to close interactions between tourists and the macaques [61].

These examples underscore the significant risk associated with working with, housing, or interacting with exotic animals. On a broader scale, any interaction with wildlife or involvement in wildlife trade poses a considerable risk to human health. Since it is unrealistic to expect these activities to be entirely eliminated, it is essential to establish effective institutional frameworks that can be implemented and managed on an international level, without compromising funding and policies related to biodiversity conservation efforts.

3.3. Livestock and Domesticated Animals

Beyond wildlife trade and exotic animals, a significant number of zoonotic events are linked to human interactions with domesticated animals. A situation analysis by the International Union for the Conservation of Nature found that 99% of ongoing zoonotic diseases are associated with domesticated animals. One often overlooked example of a zoonotic spillover from domestic animals to humans is the measles virus (MeV). MeV is believed to have emerged from cattle, given its close relation to rinderpest morbillivirus, a pathogen that affected cattle but is now eradicated. A study by Dux et al. suggests that MeV likely originated around 600 BCE, coinciding with the rise of large human settlements. Alarmingly, other paramyxoviruses still have the potential to emerge from livestock and cause zoonotic events. For instance, Abdullah et al. found that the peste des petits ruminants virus (PPRV) is prevented from entering human cells due to insufficient interaction with the human cell receptor SLAMFI. Through structural analysis, the researchers demonstrated that a single amino acid substitution in the PPRV haemagglutinin protein could enhance SLAMFI interactions, potentially allowing it to evade cross-protection and anti-MeV antibodies.

Another well-known example involves zoonotic influenza viruses, which frequently emerge from domesticated animals, especially poultry and swine. Mena et al. found that the 2009 H1N1 influenza pandemic likely originated from infected swine in central Mexico and was spread globally through swine trade. Additionally, Graham et al. reported that the risk of H5N1 outbreaks in humans is significantly higher in commercial poultry farms, suggesting a direct link between livestock production and zoonotic disease prevalence. Another notable case was the Nipah virus outbreak in Malaysia in 1998. Chau et al. found that deforestation led to a decline in flowering and fruit-bearing forest trees, forcing fruit bats to forage in cultivated orchards located near pig farms. This proximity enabled the Nipah virus to spread from fruit bats to domesticated pigs, and subsequently to humans. Lastly, high-mortality viruses like the Crimean-Congo hemorrhagic fever (CCHF) virus can be transmitted to humans through tick bites or contact with animal secretions, particularly in livestock farming areas.

3.4. Climate Change

Geoclimatic factors, such as ocean and land temperatures, wind patterns, severe weather, and land characteristics, have become significant drivers of infectious disease transmission. As global temperatures continue to rise at an unprecedented rate, it is crucial to understand the effects of human-driven climate change on disease incidence. One of the most notable impacts of climate change is its effect on vector-borne zoonoses. Beyond altering natural ecosystems, climate change affects hosts, pathogens, and vectors, influencing the (re-)emergence, geographic distribution, and transmission dynamics of vector-borne diseases.

In a multiscenario modeling study, Colón-González et al. demonstrated that low greenhouse gas emissions were associated with shorter transmission seasons and lower population risk for vector-borne diseases, such as dengue and malaria. Shocket et al., using a trait-based modeling study, found that human cases of West Nile virus peaked at 24°C in the United States. Their findings suggest that global warming may shift disease dynamics, increasing the transmission of mosquito-borne viruses in cooler areas rather than warmer regions, a result supported by other research. Ryan et al. also observed that while mosquito-borne diseases are likely to spread poleward, some lower-latitude areas may become too hot to support transmission, potentially reducing transmission seasons and preventing an overall net increase in spread. Another example involves the impact of drought and the El Niño–Southern Oscillation on the transmission of Rift Valley fever virus (RVFV); unusual rainfall patterns can lead to an increase in vectors, boosting infection rates in both animals and humans. A five-year study conducted in South Africa's Free State province showed that high surface temperatures, severe drought, and reduced vegetation in 2015–2016 created unfavorable conditions for the breeding of RVFV mosquito vectors. However, higher-than-normal rainfall during the 2017–2018 agricultural season led to a localized RVFV outbreak. Several studies have also linked the incidence of Crimean-Congo hemorrhagic fever virus (CCHFV) to climate variables like precipitation, temperature, and humidity. Since ticks thrive in warm, dry conditions, rising temperatures may increase CCHFV vector populations and their spread. Changes in climate may also allow migratory birds carrying CCHFV to infect naïve livestock populations, potentially increasing CCHFV cases in livestock within endemic regions and heightening the risk of spread to non-endemic areas through international trade.

Beyond vector-borne diseases, climate change can influence other mammalian spillover events. Beyer et al. found that regions in Central Africa, South and Central America, and a large cluster within Yunnan province in China (as well as neighboring Laos and Myanmar) experienced increased bat biodiversity due to greenhouse gas emissions, raising the risk of zoonotic spillover events. Additionally, Tian et al., using field surveillance data collected over a 54-year period in central China, identified temperature and rainfall as key factors in hantavirus transmission and rodent host reproduction. Recent studies by Ferro et al. and Douglas et al. supported these findings, highlighting direct correlations between temperature, rainfall, rodent host dynamics, and hantavirus emergence in Latin America and the Caribbean. Furthermore, statistical modeling of Ebola virus spillover events in sub-Saharan Africa over three decades showed that spillover intensity peaked during transitions between wet and dry periods and in areas with either very high ($1000/km^2$) or very low ($<100/km^2$) human population densities. Climate projections by Rupasinghe et al. suggested that the increasing intensity of water-borne, vector-borne, rodent-borne, air-borne, and food-borne zoonotic events is likely to accelerate, driven in part by expanding host habitats.

Although climate predictions are complex, these examples emphasize the role of climate factors in the (re-)emergence of viral zoonotic diseases. There are still significant gaps in our understanding, but to better plan for and prevent future pandemics, more research on the interplay between climate and host-virus ecology is urgently needed.

4. Human Impactful Drivers Related to the Spread of (Re-)Emerging Viral Zoonotic Disease

4.1. Globalization

Globalization refers to the interconnectedness of societies that transcends geographical and cultural boundaries. Integral to globalization is the concept of modernization, which involves societal or geographical advancement through modern practices. While globalization aims to foster a culture of interconnectedness for mutual benefit, it can also inadvertently promote disease transmission through tourism, transportation, migration, and international exchange of knowledge and trade. Although the link between globalization and disease spread is often underestimated, it is not a new phenomenon. One of the earliest recorded cross-border epidemics was the Athenian plague, which occurred in 430 BCE. This disease, attributed to smallpox or typhus, is believed to have originated in Ethiopia and spread to Greece via grain shipments.

From a viral zoonotic perspective, Giorgio et al. argued that the transmission of HIV in Africa was facilitated by globalization. The collapse of colonial rule, international trade efforts, socio-political reform, and cultural changes provided the conditions for HIV to evolve and adapt to human hosts. Another notable example is the 2014 Ebola virus epidemic, which initially emerged due to the consumption of bushmeat but later posed an international threat largely due to air travel between cities worldwide. More recently, the COVID-19 pandemic highlighted the role of globalization in disease spread. Although SARS-CoV-2 is believed to have originated in Wuhan, China, its rapid global spread was facilitated by intercontinental travel and trade, making containment efforts nearly impossible at the time.

Additionally, while the relocation of diseased vectors through air travel is unlikely, air travel itself facilitates contact between infected individuals and invasive or native vector populations, enabling local transmission. For instance, the origins and timing of the 2015–2016 Zika virus outbreak in Brazil have been a subject of debate. A phylogenetic study by Zanluca et al. found that viral sequences isolated from Brazil in March 2015 belonged to the Asian clade previously circulating in the Pacific Islands. Campos et al. supported these findings, showing a 99% sequence similarity between Brazilian isolates and those from French Polynesia. Moreover, a mathematical model by Massad et al. suggested that based on the viral replication rate, force of infection in French Polynesia, and volume of travel, the Zika virus responsible for the Brazilian outbreak was likely exported from French Polynesia. Influenza is another virus that spreads through air travel. Belderoc et al. found that travelers to subtropical regions frequently contracted influenza viruses, as these viruses continuously circulate in these areas. They further suggested that travelers, given the incubation period and volume of travel, could act as vectors, facilitating the global spread of influenza. Contact tracing by Kim et al. revealed that one of two individuals infected with influenza A who traveled on the same flight from Los Angeles to Seoul likely acquired the virus in-flight.

Transnational infectious disease spread is not a novel concept—historical instances still resonate today. However, what stands out is the ever-growing scale of globalization and the associated movement of microbes. In the past, cross-border transmission took months or even years; today, it takes only hours to days. It is crucial to strike a balance between the positive aspects of globalization and the factors contributing to the (re-)emergence and transmission of viral zoonotic diseases.

4.2. Geopolitics

Geopolitics represents a silent yet significant challenge in disease control. The term refers to the projection of power within a political and geographical context. Infectious diseases, as economic and social threats, have the potential to create negative geopolitical impacts. For

instance, during the rapid human-to-human spread of the H5N1 "bird flu" virus across Asia, which had a mortality rate of 40%, a vaccine research and development program was initiated to prepare for a potential global pandemic. Viral samples isolated from infected individuals were shared with laboratories worldwide. However, Indonesia, which had the highest number of H5N1 cases at the time, implemented a policy of "viral sovereignty," declaring these samples as state property and halting their distribution to other countries. This political stance was rooted in concerns over the fairness of access to future biomedical interventions and benefits. Despite condemnation at the time, the concept of viral sovereignty persists today.

Another example of geopolitics influencing disease control was the Ebola outbreak in the Democratic Republic of Congo (DRC) in 2018. Despite the availability of therapeutic interventions, the response to the outbreak was severely hindered by civil unrest and militant attacks targeting healthcare workers. Additionally, the delayed response of global leadership during previous Ebola epidemics in West Africa forced resource-poor countries to confront epidemics they were ill-equipped to manage.

Historical conflicts have also played a significant role in the spread of infectious diseases. During the Boer War (1900–1902) in South Africa, the British Army confined rural farming families of Dutch heritage to concentration camps. Originally established for military purposes, these camps became disaster sites where measles and other acute respiratory infections spread widely. Similarly, during World War I (1917–1918), US military recruits stationed in overcrowded camps experienced large-scale measles outbreaks, which spread further during transport to Europe. These outbreaks provided crucial insights that later informed the military's response to the 1918 influenza pandemic, which infected one-third of the world's population and resulted in an estimated 50–100 million deaths. Although the origin of the pandemic H1N1 virus remains unknown, it is clear that the war played a key role in its spread, providing an efficient mechanism for viral dissemination and mutation.

These examples represent just a fraction of the many geopolitical events that have influenced the spread of (re-)emerging pathogens throughout history.

4.3. Social Perceptions

Science is ever-evolving, and what is considered true today may change tomorrow. It is important to recognize that when a scientific concept or finding changes, it reflects the discovery of new knowledge rather than a previous falsehood. Science aims to uncover the unknown, and with each answer comes more questions. In many ways, science is an ongoing effort to answer questions that have not yet been asked.

Unfortunately, predictions regarding emerging or re-emerging viral zoonotic diseases and their epidemiology are never entirely accurate. Microbes, particularly viruses, are constantly evolving. Their ability to acquire adaptive genetic mutations in a short time is unmatched, which means predictions often rely on historical data that resemble the disease of interest. However, when a new viral disease emerges, historical patterns do not always provide reliable guidance. One of the greatest challenges lies in maintaining effective communication with the public and the media. While science communication by journalists can be incredibly valuable, a single ambiguous statement can lead to confusion and panic. Additionally, information is no longer disseminated solely through traditional journalism. Today, it spreads globally through social media, blogs, podcasts, and other internet-based platforms, often by unqualified individuals.

During the early stages of the COVID-19 pandemic, misinformation and conspiracy theories spread rapidly, despite open access to scientific research. This resulted in widespread public distrust. A retrospective study by Islam et al. found that, from January to April 2020, there were 2,311 cases of stigma, rumors, and conspiracy theories recorded across 87 countries in 25 languages. These incidents were related to disease causation, transmission, control, treatment, and mortality. Alarmingly, misinformation led to 5,876 hospitalizations, 60 cases of blindness, and 800 deaths in 2020. Furthermore, preventative measures such as social distancing and mask-wearing were challenged, ultimately harming those at higher risk. Al-Ramahi et al. used machine learning techniques to analyze the relationship between negative attitudes toward mask-wearing and new COVID-19 infections by examining 51,170 English tweets posted between January and October 2020. The study found that negative tweets were strongly correlated with an increase in new infections, with rising negativity preceding new infections by nine days.

Another example highlighting the impact of social perceptions and knowledge barriers was the Ebola virus outbreak in West Africa. In Ghana, Tenkorang found that misinformation and inadequate understanding of the Ebola virus led to unsafe burial practices, such as touching the bodies of the deceased. In Sierra Leone, Yamanis et al. discovered that many people distrusted the accuracy of Ebola tests, with some choosing to get tested only after an individual had died. Additionally, when experiencing fever, individuals often self-medicated, sought care at local clinics, or delayed medical attention entirely—either to confirm the fever's cause or due to fear of dying after treatment. Much of this behavior stemmed from distrust of the government and likely contributed to increased transmission of the virus, thereby extending the duration of the epidemic.

One of the most consequential misinformation events in recent history was the "Duesberg phenomenon." Berkeley virologist Peter Duesberg publicly denied that HIV was the cause of AIDS, challenging well-established scientific evidence. Despite widespread rejection of his claims by the scientific community, his views gained traction among HIV denialists. In South Africa—where HIV prevalence is the highest in the world—former President Thabo Mbeki questioned the role of HIV in the development of AIDS during the initial stages of the national rollout of antiretroviral treatment. This led to an international outcry from medical professionals and scientists, who petitioned for the reinstatement of antiretrovirals and reaffirmed that AIDS was caused by HIV. Although the ban was eventually lifted under international pressure, it is estimated that over 330,000 people died, and at least 35,000 infants were born with HIV due to the delay.

5. Conclusions

Humans lack acquired immunity to many emerging viral zoonotic diseases and have lost herd immunity to some re-emerging ones. Therefore, greater focus is needed on zoonotic disease detection, prevention, and response. Given that many anthropogenic factors contributing to the (re-)emergence or spread of viral zoonoses are interconnected, effective initiatives must operate at a multisectoral level. This makes partnerships like One Health crucial. Although One Health is not a new concept, it has gained renewed importance due to the rapidly evolving interactions between animals, humans, plants, and the environment. To ensure the success of One Health and future global governance, competitive interests between public and private sectors must be put aside.

Additionally, greater emphasis must be placed on addressing the relationship between negative social perceptions and scientific evidence, as social factors represent some of the most significant and unpredictable drivers of disease transmission. By bridging gaps between resource and land governance, conservation, sociology, disease ecology, and geopolitics, we may be able to prevent future pandemics. The examples presented in this paper underscore both the consequences of human actions and the impact of neglecting the microscopic world, which can lead to the (re-)emergence and spread of devastating diseases. If anything, COVID-19 has taught us a valuable lesson and may hopefully pave the way for positive change. As George Santayana once said, "Those who cannot remember the past are condemned to repeat it."

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