zoonotic diseases

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Editorial

Drivers of Zoonotic Viral Spillover: Understanding Pathways to the Next Pandemic

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In the wake of the COVID-19 pandemic and amid growing concerns regarding viral threats such as avian influenza, Mpox, and HKU5 bat coronaviruses, the phenomenon of viral zoonotic spillover, when viruses leap from circulation in non-human animals to humans, has garnered unprecedented global attention. While such events may appear spontaneous, they are deeply intertwined with ecological, environmental, and social processes that are reshaping the boundaries between the domains of animal and human populations. As we move deeper into the Anthropocene, namely the current geological epoch defined by human dominance over Earth's ecosystems, the frequency and impact of viral zoonotic spillovers that lead to localized, regional, and global disease outbreaks are expected to rise. Understanding the current and future drivers of zoonotic viral spillover thus requires pro-active and integrated global One Health action. In this Editorial, I examine the key ecological, environmental, and socio-behavioral drivers of viral zoonotic spillover, highlight high-risk pathogens with pandemic potential, and provide a call-to-action by outlining several evidence-based strategies to reduce viral zoonotic spillover in the future.

1. Ecological and Environmental Drivers

Fundamentally, zoonotic spillovers are ecological events. As humans continue to alter natural environments, through deforestation, urban expansion, mining, agriculture, and infrastructure development, we are weakening the ecological barriers that once kept animal-borne viruses confined to their natural hosts. These disruptions increase the frequency and intensity of contact between wildlife, livestock, and people, creating new pathways for viruses to spill over across species [1–3]. This has resulted in the current reality, in which an increased risk of viral zoonotic transmission is observed; in this context, previously contained viruses gain the opportunity to infect human populations, sometimes with devastating consequences.

One of the most significant contributors to spillover is deforestation. Forests are being cleared for agriculture, mining, logging, and urban development, creating new interfaces at which wildlife, livestock, and humans come into contact. These ecotones, transitional zones between distinct ecological communities, become hotspots for interspecies viral exchange [4,5]. Studies have shown that tropical deforestation is linked to outbreaks of diseases such as Ebola, Nipah, and various bat-borne coronaviruses [6,7]. The loss of biodiversity accompanying deforestation also disrupts the ecological balances that once diluted the prevalence of pathogens in wildlife populations, creating opportunities for animal outbreaks and exposure to viral zoonoses by human communities [8].

Second, the conversion of forests and other natural habitats into farmland significantly increases the risk of zoonotic spillover by bringing humans and livestock into direct contact with wildlife and their disease vectors [9]. As agricultural frontiers expand, especially in tropical regions, people working or living near these newly developed lands are more

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likely to encounter wild animals, many of which serve as natural reservoirs for emerging viruses [10]. At the same time, farm animals, such as pigs, poultry, and cattle, frequently act as intermediate hosts, enabling pathogens to adapt and move between species. These domestic animals often have closer, more sustained interactions with both humans and wildlife, facilitating the genetic mixing and amplification of viruses in ways that enhance their ability to infect people [11]. When this process occurs in high-density, industrial farming settings, the risk is further exacerbated, creating ideal conditions for the emergence and spread of novel and reemerging zoonotic diseases.

A third and related phenomenon is urban sprawl, which is pushing cities into wild landscapes, while poorly planned peri-urban developments lack the sanitation and public health infrastructure required to prevent zoonoses. Rodents and bats, both known reservoirs for zoonotic viruses, thrive in these environments [12–14]. Informal settlements that emerge near forest edges or in recently deforested areas often become unintentional hotspots for zoonotic exposure and transmission [15]. In these transitional zones, humans live near fragmented wildlife habitats, increasing the frequency of direct and indirect encounters with wild animals [16]. Such interactions—through hunting, foraging, water use, or incidental contact—create repeated opportunities for exposure to animal-borne pathogens. Over time, this sustained contact can facilitate the spillover of viruses that, through genetic mutation or recombination or reassortment, acquire the capacity to infect human cells [9]. These ecotonal environments, shaped by poverty, rapid land-use change, and weak infrastructure, thus represent key interfaces at which emerging infectious diseases with pandemic potential are most likely to emerge [17].

2. Climatic Regime Alterations

Near- and long-term climate alterations have emerged as powerful indirect drivers of zoonotic spillovers in recent decades and will continue, in accordance with current planetary projections [18,19]. Warming temperatures and changing precipitation patterns are altering the geographical ranges of both host species and disease vectors [20,21]. Bats, in particular, are expanding their range in response to the changing climate, bringing these species into new areas and increasing the chance of human contact [22]. As ecosystems shift, new combinations of species interact, creating novel opportunities for viral recombination and transmission. For example, mosquitoes and ticks, which transmit a variety of viral pathogens, are moving into higher latitudes and altitudes due to the changing climatic conditions, increasing the risks posed to human communities in those regions [23,24].

Additionally, environmental stressors such as habitat degradation and food scarcity due to climatic alterations can increase viral shedding in wildlife [25,26]. Habitat loss and a reduction in the availability of food in eucalyptus forests have been linked to the increased shedding of Hendra virus by fruit bats, which are its natural reservoirs. Nutritional stress compromises bat immune defenses, leading to higher viral loads in the urine and saliva [27]. Under stress, bats have also been shown to release more viruses in their saliva, urine, and feces [28,29]. When these excretions contaminate food, water, or surfaces used by humans or livestock, the likelihood of transmission to human populations increases [30,31].

3. Anthropogenic and Socioeconomic Factors

Beyond environmental conditions, human behaviors and social structures profoundly shape spillover dynamics. The rapid movement of people and goods across the globe enables pathogens to spread far beyond their origin points [32–34]. A virus that spills over in one location can be transported to another within hours via air and other travel modalities, challenging containment efforts and turning local outbreaks into global emergencies [35,36]. There are socioeconomic inequality and governance gaps that also shape

the landscape of viral spillover. Communities with limited access to healthcare, education, and sanitation are more vulnerable to both initial spillover and widespread transmission, as evidenced by numerous outbreaks in which delayed detection, inadequate medical infrastructure, and insufficient public health awareness have exacerbated the spread of disease. For example, during the 2014–2016 West African Ebola epidemic, fragile health systems and poor sanitation contributed to the rapid transmission of the virus and hindered containment efforts [37,38]. Similarly, in regions with low health literacy and limited access to preventive information, behavioral interventions such as the safe handling of animals or use of personal protective equipment are less effectively implemented, increasing the risk of zoonotic spillover and human-to-human transmission [39]. Moreover, inadequate sanitation facilitates environmental contamination by viral excretions from wild and domesticated animals, further amplifying the risk of humans being exposed to viruses [40,41]. These systemic inequalities not only increase our vulnerability to emerging infectious diseases, but also perpetuate cycles of transmission, making comprehensive investment in healthcare access, education, and sanitation critical components of pandemic prevention and response. Political instability and weak governance can also hinder outbreak response, surveillance, and international cooperation. In conflict zones, public health systems are often degraded or nonexistent, leaving major gaps in our shared global toolkit for prevention, detection, and response.

Global food systems are also strained under population pressures, leading to intensified animal farming and an increased reliance on wild meat in some regions. Poor waste management and the overuse of antibiotics in animal agriculture also contribute to both zoonotic spillovers and the rise of antimicrobial resistance globally [42,43]. Both legal and illegal wildlife trade, in addition to widespread wild meat hunting, directly expose humans to a wide range of wild animals, many of which may serve as natural reservoirs for known and novel viruses [44,45]. These practices often involve the close and prolonged handling of live or freshly slaughtered animals, increasing the risk of cross-species viral transmission through blood, saliva, or the aerosolization of bodily fluids [44,46,47]. Live animal markets, especially those that bring together diverse wildlife species, often under poor sanitary conditions, create ideal conditions for viral amplification, recombination, and interspecies transmission.

These markets have been implicated in several major zoonotic outbreaks. For instance, the SARS outbreak in 2002–2003 was traced back to live animal markets in Guangdong, China, where civets and other species served as intermediate hosts for a bat-origin coronavirus. Similarly, although the precise origin of SARS-CoV-2 remains under investigation, early cases were epidemiologically linked to the Huanan Seafood Wholesale Market in Wuhan, which sold a range of wildlife species, reinforcing concerns regarding the role of such environments in pandemic emergence [48–50].

Despite heightened international awareness and calls for reform following these outbreaks, the enforcement of wildlife trade regulations remains patchy and inconsistent. Weak governance, insufficient resources, corruption, and high economic incentives continue to fuel both legal and black-market trade in wild animals. Additionally, cultural practices, food insecurity, and economic dependence on bushmeat in many regions complicate efforts to eliminate high-risk wildlife trade altogether [51,52]. Without stronger, more coordinated international frameworks, with community engagement in the development of alternative livelihoods, the risk of future spillovers from wildlife trade and markets will persist.

4. Microbial Evolution and Viral Adaptation

Viruses are dynamic and continuously evolving. Through processes such as genetic mutation, recombination, and reassortment, viral genomes can change in ways that enhance their ability to infect new hosts, including humans. Mutations in key viral proteins, particularly those involved in cell entry, such as the spike protein on coronaviruses or the hemagglutinin on avian influenza viruses, can increase a virus's affinity for human cellular receptors, enabling cross-species transmission. Additional mutations may help the virus evade host immune responses, improve the efficiency of replication, or enhance transmission between human hosts [53,54]. Critically, the evolutionary distance between an animal virus and a pandemic-capable human virus can sometimes be surprisingly short, as just one or two mutations may be sufficient for a virus to gain the traits required to infect and spread in human populations.

However, the timing and likelihood of such evolutionary leaps are not dictated by virology alone. They are deeply influenced by the ecological and epidemiological contexts in which humans and animals interact. Factors such as the frequency, duration, and nature of contact between people and wildlife or livestock, shaped by land use changes, animal husbandry practices, and cultural behaviors (many of which are described above), create the pathways through which zoonotic viruses are exposed to selective pressures that favor human adaptation. Unfortunately, these spatiotemporal patterns of human–animal interaction remain inadequately studied and poorly integrated into viral emergence forecasting models [55,56].

Ongoing surveillance efforts, particularly in regions with a high prevalence of human–animal interaction, have identified several viral families of concern. Among them are bat-borne coronaviruses, such as those in the SARS-related and HKU lineages; henipaviruses (e.g., Nipah and Hendra); as well as highly pathogenic avian influenza (HPAI) strains such as H5N1 (Clade 2.3.4.4b). Genetic analyses show that some of these viruses already possess partial or full compatibility with human physiology, such as binding to human-like receptors; this suggests that they are evolutionarily positioned just steps away from becoming threats to humans [57,58]. These findings underscore the urgent need for globally coordinated field-based surveillance, virological characterization, and upstream interventions that prevent zoonotic spillover before these viruses evolve into the next pandemic threat.

5. Future Projections to 2050 and Beyond

The risk of viral zoonotic spillover in the coming decades will be shaped by a convergence of ecological, climatic, demographic, and political trends. As human societies continue to modify their environments, the natural buffers that once separated wildlife from people are rapidly eroding. By 2050, projections suggest that over half of the remaining wild landscapes in South America and Asia will have been transformed by agriculture, infrastructure, and urban development [59]. These land-use changes heighten the likelihood of contact between humans, livestock, and wildlife reservoir hosts of viral infections. Without proactive planning and ecosystem protections, the spatial spread of human activity will continue to generate new interfaces for pathogen exchange.

Climate change will further compound these risks. Increasing temperature and precipitation regimes will continue to alter the distribution of species, thus destabilizing ecosystems and enabling disease vectors such as mosquitoes and ticks to move into new territories [60,61]. In parallel, extreme weather events—droughts, floods, and heatwaves—will continue to stress both wildlife populations and public health systems, increasing the chances of pathogen spillover and diminishing our ability to respond effectively. These climatic pressures will unfold concurrently with continued population growth and rapid urbanization, especially in low- and middle-income countries [62]. With the global popula-

tion projected to exceed 9 billion by 2050, expanding megacities will face the dual challenge of meeting development goals while maintaining environmental integrity and controlling zoonotic risk [63,64].

Despite these looming threats, technological and policy innovations offer pathways for mitigation, if they are equitably implemented. Advances in genomic surveillance, artificial intelligence, and integrated data systems are revolutionizing the way in which scientists detect, track, and predict emerging pathogens. However, these tools can only be effective within governance structures that support timely information sharing, cross-sectoral collaboration, and sustained public health investment. At present, fragmented global coordination and stark disparities in access to technology and funding may hinder the full potential of these innovations. As the world looks toward 2050 and beyond, the trajectory of zoonotic disease emergence will depend not only on the natural systems we disrupt, but also on the human systems we choose to strengthen.

6. Strategies for a Safer Future

Preventing future pandemics demands a comprehensive, proactive approach that is rooted in the One Health paradigm, which emphasizes the deep interdependence of human, animal, and environmental health [65]. By acknowledging that the health of people is closely associated with the health of animals and the ecosystems we share, One Health offers a framework for integrated action that tackles emerging pandemic threats. Rather than reacting to outbreaks after they occur, this strategy focuses on understanding and disrupting the conditions that allow zoonotic pathogens to emerge and spread in the first place.

A fundamental component of this approach is enhancing One Health systems by implementing integrated surveillance and data-sharing platforms. Coordinated data sharing across human health and the veterinary and environmental sectors could enable the early detection of threats at the animal–human interface [66]. For example, joint monitoring programs that track HPAI in poultry and wild birds alongside hospital admissions for human respiratory illnesses could facilitate the early identification of spillover signals [67]. Institutionalizing collaboration between veterinarians, ecologists, medical professionals, and policy makers, such as through national One Health task forces (see lessons learned from Kenya [68,69], Bangladesh [70], and Thailand [71,72] as examples), would place value on cross-sectoral collaboration above sectoral siloing [73].

Equally critical is land use planning and the protection of biodiversity. Preserving intact ecosystems and maintaining natural buffer zones between wildlife habitats and areas of human activity will reduce the likelihood of pathogen spillover [74]. In Malaysia, for instance, the fragmentation of bat habitats due to deforestation has been linked to the increased transmission of Nipah virus to pigs and humans [75,76]. Strategic zoning, sustainable forestry practices, and the strict enforcement of environmental regulations can reduce the human encroachment and maintain ecological balances that reduce the risk of viral zoonotic disease spillover.

Another high-risk interface for zoonotic spillover is the wildlife trade and live animal markets, where diverse animal species are brought into close proximity. This unnatural mingling increases the likelihood of viral exchange, recombination, and spillover to humans, especially in environments with poor sanitation, limited oversight, and minimal veterinary screening. Wildlife trade, both legal and illegal, frequently involves the capture, transport, and sale of animals such as bats, primates, rodents, and civets—many of which are known or suspected reservoirs of novel viruses. Reforming these sectors will require a multifaceted approach, including the enforcement of existing wildlife protection laws, the identification and regulation of high-risk species on wildlife farms and at markets, and

the implementation of improved hygiene and animal care protocols. Equally important is the need to establish surveillance systems that monitor not just the animals being sold but the handlers, traders, and supply chains involved, many of which operate informally and elevate the risk of spillover events, infection, and uncontrolled transmission.

Enhancing agricultural biosecurity will also play a major role in preventing the amplification of zoonotic disease. Intensive animal farming creates ideal conditions for viral mutation and transmission, especially when pathogens from wildlife are introduced into farmed livestock populations. Measures such as reducing the density of stocking, eliminating non-therapeutic antibiotic use (which can promote antimicrobial resistance) and training farmers to be antimicrobial stewards, and implementing real-time farm-level disease surveillance can reduce risks. For example, enhanced biosecurity protocols in European pig farms have successfully lowered the risk of swine influenza outbreaks [77].

The threat of zoonoses is further exacerbated by changing climatic regimes worldwide. Investing in climate-resilient infrastructure, common-sense adaptation strategies at the One Health interface, and sustainable agriculture can mitigate these pressures. In East Africa, climate-smart farming practices have helped farmers adapt to shifting rainfall patterns, preserving livelihoods while reducing ecosystem degradation [78,79]. Additionally, public health systems must be equipped to adapt to new disease ecologies, including emerging vector-borne threats in regions previously unaffected.

Finally, effective One Health interventions must be community-led to ensure sustainability, cultural relevance, and equitable outcomes for all. Local communities are often the first to encounter and respond to emerging viral zoonotic threats, yet their knowledge, priorities, and adaptive strategies are frequently overlooked in top-down approaches. Engaging communities as active partners, not passive recipients, enables the co-design of interventions that align with local practices, beliefs, and resource realities. Ultimately, centering One Health around local leadership and participation ensures that interventions are grounded in the lived experiences of those most vulnerable to viral zoonotic spillover.

Viral zoonotic spillover is not an anomaly—it is a foreseeable consequence of unsustainable human activities. Accelerating deforestation, climate disruption, intensive industrial agriculture, and deep-rooted social inequities worldwide have converged to erode the ecological boundaries that once buffered humans from wildlife-borne pathogens. We are at a pivotal moment in history. Preventing the next pandemic requires more than reactive measures; it demands a proactive shift toward the One Health framework. By strengthening early warning systems, addressing the main reasons for spillover, and redefining our relationship with the natural world, we can chart a more resilient and equitable future. The opportunity to act remains, but the margin for delay is woefully and rapidly shrinking.

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