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Review Article

Bats: The silent carriers of deadly viruses- A hidden threat to animal and human health

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Abstract

Emerging infectious diseases (EIDs), especially those of viral origin, pose significant threats to global health, biodiversity, and economies. A substantial proportion of these zoonotic disease outbreaks including SARS, MERS, Ebola virus and Nipah virus infections originated from bats, which act as asymptomatic reservoirs despite harboring highly pathogenic viruses. Bats' unique physiological traits such as flight, long lifespan, social behavior and broad geographic range, coupled with their distinctive immune strategies particularly dampened inflammatory responses allow for viral persistence without disease manifestation. This review explores how these immunological and ecological factors enable bats to maintain and transmit viruses, with emphasis on mechanisms of viral persistence, such as lowlevel replication, immune tolerance, latency and tissue tropism. It highlights the major viral families associated with bats, such as *Coronaviridae*, *Filoviridae* and *Paramyxoviridae*, and discusses the ecological and anthropogenic factors driving spillover risks, including habitat loss, climate change, wildlife trade and live animal markets. A "One Health" approach integrating human, animal and environmental health is critical for surveillance, prevention and response. The review also outlines future research directions including bat microbiome studies, predictive behavioural modelling and communitybased bio-surveillance, to mitigate the threat of future pandemics stemming from batborne viruses while preserving bat conservation and ecosystem balance.

Keywords: Bats, Emerging infectious diseases (EIDs), Immunological tolerance, Viral spillover, Zoonotic viruses,

Highlights

- Bats serve as asymptomatic reservoirs for highly pathogenic zoonotic viruses including SARS, MERS, Ebola and Nipah.
- Unique immunological traits in bats, such as dampened inflammatory responses, enable viral persistence without disease
- Major viral families associated with bats include *Coronaviridae*, *Filoviridae*, and *Paramyxoviridae*.
- Ecological and human-driven factors like habitat loss and wildlife trade increase the risk of viral spillover from bats.
- A One Health approach is essential for monitoring, preventing and responding to bat borne emerging infectious diseases.

INTRODUCTION

Emerging infectious diseases (EIDs), which were caused by viruses, have increasingly threatened global health, biodiversity, and economies now a days. A striking proportion of major zoonotic diseases including severe acute respiratory syndrome coronavirus (SARS-CoV), Middle East respiratory syndrome coronavirus (MERS-CoV), Ebola virus and Nipah virus originate from wildlife. Notably, they all share a common host: bats, which serve as their natural reservoirs (Epstein et al., 2006; Field et al., 2011; Menachery et al., 2015; Cunningham et al., 2017; Goldstein et al., 2018; Cui et al., 2019; Lecis et al., 2019; Epstein et al., 2020; Weinberg & Yovel, 2022; Wang et al., 2023). Despite their association with some of the world's most pathogenic viruses, bats rarely exhibit clinical signs and remain as "asymptomatic" or "silent" carriers (Robertson et al., 2004; Calisher et al., 2006; Mandl et al., 2015; Hayman, 2016; Banerjee et al., 2019a; Irving et al., 2021; Nagaraja et al., 2022). The paradox remains unresolved, continuing to challenge experts in virology, immunology and ecology.

With over 1400 species, bats are the second largest order of mammals and are present in every continent (Voigt & Kingston, 2015; Burgin et al., 2018; Hao et al., 2024). Their unique biological features such as powered flight, long lifespan, high metabolic rate, roosting behaviour and wide geographical range make an ideal interface for viral maintenance, evolution and transmission (Calisher et al., 2006; Simmons et al., 2008; Speakman, 2008; Beena & Saikumar, 2019). However, what make bats apart is not just their

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ecological traits, but their unique immune system, which appears to fight rather than showing symptoms of viral infections (Gonzalez et al., 2024). Unlike most of mammalian responses which aim to eliminate pathogens with inflammation, bats have evolved dampened inflammatory pathways, allowing viral persistence with minimal pathology (Beena & Saikumar, 2019; Wickenhagen et al., 2024).

Understanding the mechanisms by which bats give shelter and transmit high-risk viruses without showing symptoms of disease is crucial for predicting future outbreaks and preventing zoonotic spillovers (Wu, 2021; Gonzalez et al., 2024). Due to deforestation, climate change and habitat encroachment human-animal interface intensifies and the risk of bat borne viral emergence grows more rapidly (Subudhi et al., 2019). This review aims to synthesize the latest insights into bat virology, focusing on their immunological tolerance, ecological adaptations and the epidemiological implications of their role as stealthy viral hosts within a "One Health" framework (Eby et al., 2023; Gonzalez et al., 2024).

While bats are recognized as key reservoirs for many emerging viruses, they are not the only animal hosts contributing to zoonotic disease transmission (Haydon et al, 2002). Other wildlife such as rodents, birds, primates and insects, also serve as important viral reservoirs shown in Fig. 1 (Chu et al., 2010). Rodents, for instance, harbour Hantaviruses and Arenaviruses, often transmitting them through urine and feces. Birds, especially waterfowl, play a major role in the ecology of Influenza viruses, driving the evolution of avian flu strains. Primates have been linked to viruses like Simian Immunodeficiency Virus (SIV), which crossed into humans as HIV. Additionally, insects such as mosquitoes act as vectors for viruses including Dengue, West Nile and Zika, posing significant global health threats (Schountz et al., 2017). Understanding the diverse reservoirs beyond bats is critical for comprehensive surveillance and control of emerging infectious diseases.

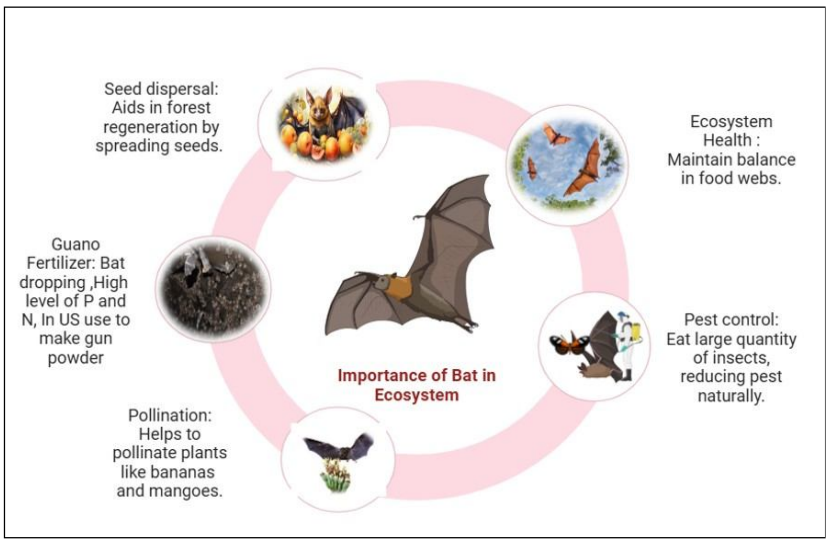


Fig. 1. Ecological importance of bats in ecosystem maintenance (Figure created by the authors using BioRender.)

Bat biology and ecology: A perfect storm for viral maintenance

Bats have unique physiological traits that make them efficient viral reservoirs. Representing the order *Chiroptera*, bats are the only mammals capable of long sustained flight, a trait that has shaped their physiology in unique ways. Their increased metabolic rate which is required for flight, has led to the evolution of enhanced DNA repair mechanisms and efficient oxidative stress control, which may incidentally contribute to viral tolerance (Schountz et al., 2017; Irving et al., 2021).

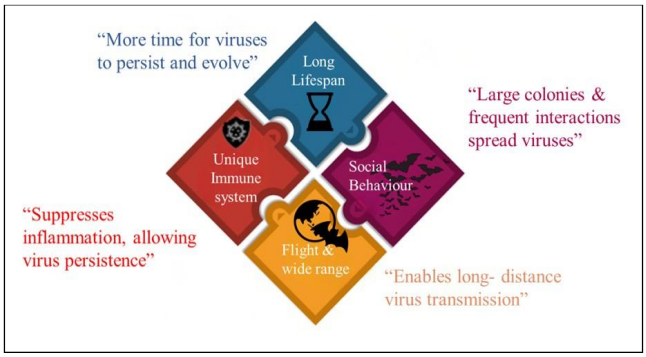


Fig. 2. Unique traits of bats as viral reservoirs (Figure created by the authors using BioRender.)

Bats live in large social colonies. This gregarious roosting behaviour facilitates both intraspecies and interspecies viral transmission. As shown in Fig. 2 their migration, hibernation and breeding further modulate immune function and viral dynamics within populations (Smith & Wang, 2013). These all contribute in virus shedding and increasing the risk of transmission to humans or livestock at particular times of the year.

Bats have long lifespan relative to their body size, with some species living over 30 years. This long lifespan provides a prolonged window for viral maintenance and

transmission across generations (Brook & Dobson, 2015). Moreover, their global distribution except on the polar regions and feeding behaviour (insectivorous, frugivorous, nectarivorous and hematophagous species) bring them into contact with a wide array of hosts, ecosystems and potential viral exchange pathways (Jones et al., 2002; Kunz et al., 2005; Teeling et al., 2005).

In this world where everything changed now a days, human activities like deforestations, urbanization, agricultural expansion make close human-bat interfaces, which make easy to transmit viruses and bats amplify their role as viral reservoirs and spillover agents (Plowright et al., 2017). Their biology is not merely a background factor but a driving force in the ecology of emerging viruses.

Immunological tolerance: how bats coexist with viruses

Unlike other mammals that often develop clinical signs and disease in response to viral infections, bats have evolved their immune adaptations that make them to coexist with viruses asymptomatically. This phenomenon is not merely a passive tolerance but a strategically regulated immune response, which dampened the inflammation while maintaining sufficient antiviral defence.

Innate immune adaptations: Bats exhibit constant expression of type I interferons (IFNs), particularly IFN-α, even in the absence of infection. This continuous lowlevel antiviral state makes them to early control viral replication without inflammatory response. However, key signalling components which dampened inflammation such as stimulator of interferon genes (STING) and inflammasome pathways (NLRP3) are altered in bats (Xie et al., 2018; Fu et al., 2023). This prevents the over expression of immune response and tissue pathology that often accompanies viral infections in other mammals (Zhou et al., 2011; Cowled et al., 2012; Zhou et al., 2014; Brooke & Dobson, 2015; Banerjee et al., 2016; Zhou et al., 2016; Banerjee et al., 2017; Schountz et al., 2017; Xie et al., 2018; Ahn et al., 2019; Banerjee et al., 2019b).

Constitutive interferon response: In addition to their unique innate immune adaptations, bats possess highly efficient mechanisms for viral detection and interferon signalling. When viruses invade host cells, they release Toll like receptors recognized by Pattern Recognition Receptors (PRRs) (Yoneyama et al., 2004; Kato et al., 2006; Takeuchi & Akira, 2010; Irving et al., 2021; Das et al., 2025). As shown in Fig. 3 for RNA viruses, Toll like receptors (TLR7/8 and TLR3) detect single and double-stranded RNA in endosomes, while Retinoic acid inducible gene 1 (RIG-I) and Melanoma differentiation associated gene 5 (MDA5) identify viral RNA in the cytoplasm (Irving et al., 2021; Das et al., 2025). These PRRs converge on the mitochondrial antiviral signalling protein (MAVS), which activates downstream kinases such as TBK1 and transcription factors IRF3 and IRF7 (Das et al., 2025). This signalling cascade results in the rapid production of type I and III interferons (IFN-α, IFN-β, IFN-ω, IFN-λ, IFN-κ), initiating a robust antiviral response (Brooke & Dobson, 2015; Schountz et al., 2017). Upon secretion, interferons bind to their cognate receptors on neighbouring cells, triggering the JAK-STAT pathway. This activates JAK1 and TYK2, which phosphorylate STAT1 and STAT2. Together with IRF9, these form the ISGF3 complex that translocate to the nucleus and binds to interferon-stimulated response elements (ISREs), inducing the expression of hundreds of interferon-stimulated genes (ISGs) as shown in Fig. 4 (Seth et al., 2005; Chau et al., 2008; McNab et al., 2015; Irving et al., 2021; Das et al., 2025). These ISGs encode antiviral proteins that inhibit viral replication, amplify immune signalling and reinforce the antiviral state. In contrast, DNA viruses are detected by cytosolic DNA sensors as shown in Fig. 5 such as cGAS, DAI and PYHIN proteins (Schoggins et al., 2011, Hoffmann et al., 2019; Schuhenn et al., 2022). The cGAS-STING pathway is particularly central; upon sensing viral DNA, cGAS produces cGAMP, a second messenger that activates STING on the endoplasmic reticulum. STING

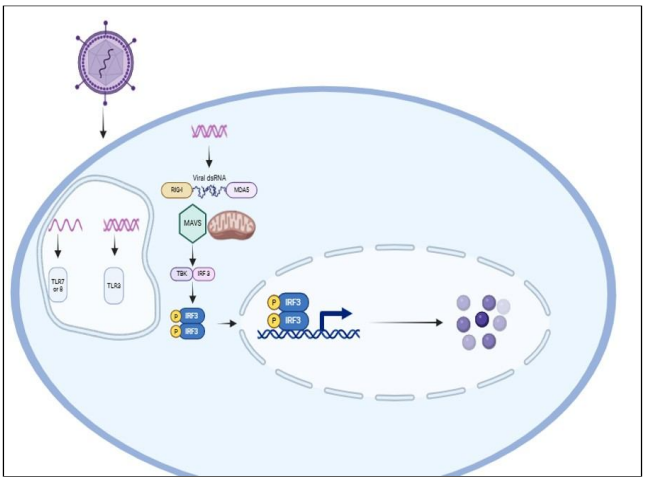


Fig. 3. Detection of viral RNA by pattern recognition receptors leading to interferon production (Figure created by the authors using BioRender.)

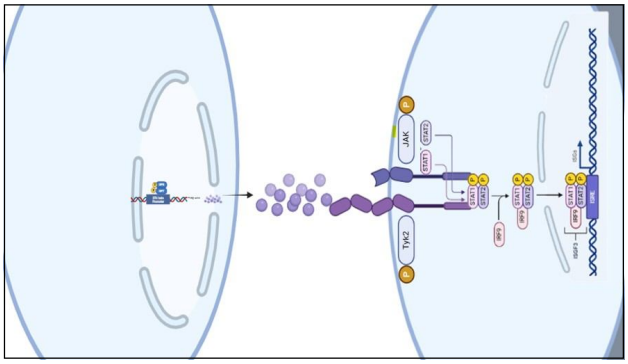


Fig. 4. JAK-STAT pathway activation by interferons in antiviral immunity (Figure created by the authors using BioRender.)

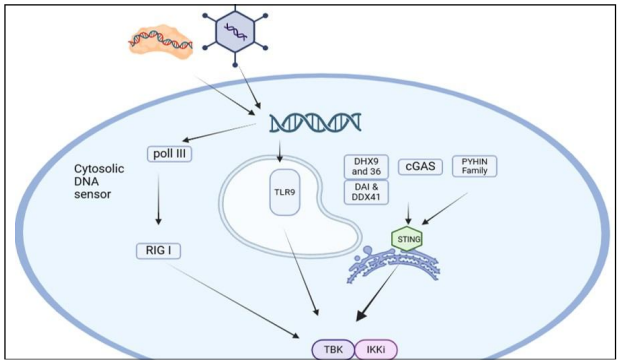


Fig. 5. cGAS-STING pathway activation by cytosolic DNA (Figure created by the authors using BioRender.)

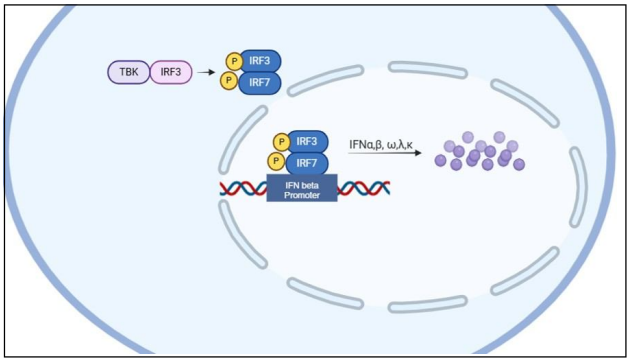
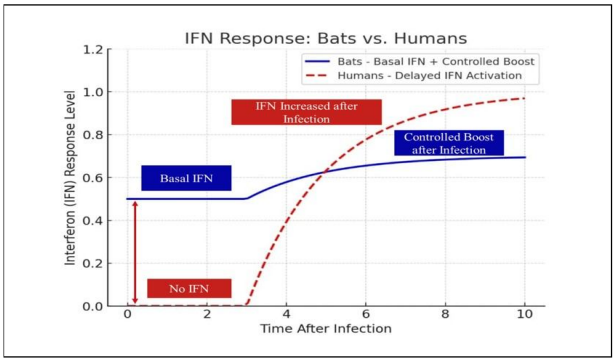


Fig. 6. Interferon signaling triggered by cGAS-STING pathway activation (Figure created by the authors using BioRender.)



Graph 1. Comparison of baseline and induced interferon responses in Bats vs. Humans

then recruits TBK1 and IKKi, activating IRF3 and NF-κB to promote the expression of type I interferons as shown in Fig. 6 and pro-inflammatory cytokines (Brooke & Dobson, 2015; Schountz et al., 2017). In bats, while these fundamental mechanisms are conserved, key regulators such as STING and components of the inflammasome (e.g., NLRP3) exhibit unique alterations that suppress excessive inflammation (Clayton & Munir, 2020; Irving et al., 2021). This finely tuned immune balance allows bats to mount early and efficient antiviral responses as shown in Graph 1 while minimizing immunopathology, contributing to their exceptional tolerance to viral infections.

Dampened inflammatory response

Bats, unlike many other mammals, exhibit a unique form of immunological tolerance that allows them to coexist with viruses without developing disease. While their innate immune system actively detects viral RNA and DNA through receptors such as TLR3, TLR7, TLR8, TLR9, cGAS and PYHIN proteins as shown in Fig. 7, the downstream inflammatory response is tightly regulated (Beena and Saikumar, 2019; Bertheloot et al., 2021; Wickenhagen et al., 2024). Although

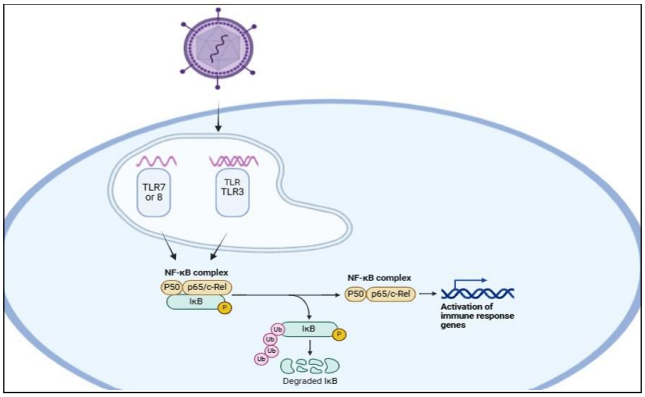


Fig. 7. TLR-mediated recognition of viral RNA and activation of NF-κB pathway (Figure created by the authors using BioRender.)

activation of these receptors typically leads to NF-κB translocation and the production of cytokines like TNF-α, IL-8 and IL-1β via pathways such as cGAS-STING and the NLRP3 inflammasome, bats suppress these inflammatory outputs (Beena & Saikumar, 2019;

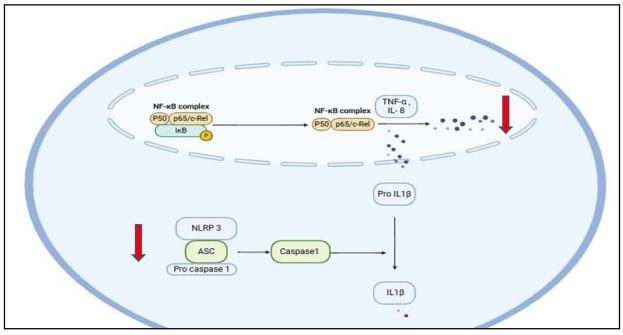


Fig. 8. Activation of pro-inflammatory cytokines via NF-κB and NLRP3 inflammasome (Figure created by the authors using BioRender.)

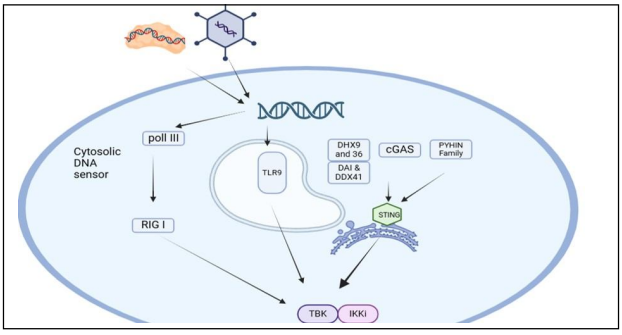


Fig. 9. DNA sensing via cGAS-STING pathway leading to inflammatory cytokine production (Figure created by the authors using BioRender.)

Table 1. Comparison of bats and human adaptive immunity

Feature	Bats	Humans
Antibody Levels	Low baseline, rapid response when needed	Higher baseline, strong response
Treg (Regulatory T-Cells)	Increased, suppress inflammation	Lower, more inflammation
CD8+ T-Cell Cytotoxicity	Reduced, limits tissue damage	Strong, can cause immunopathology

Bertheloot et al., 2021; Wickenhagen et al., 2024). They achieve this through reduced activation of NF-κB and dampened NLRP3 inflammasome activity as shown in Fig. 8, thereby minimizing tissue-damaging inflammation and the cGAS–STING pathway is illustrated in Fig. 9. This balance enables bats to maintain effective antiviral defences while avoiding immunopathology, a key feature of their viral tolerance (Beena & Saikumar, 2019; Bertheloot et al., 2021; Wickenhagen et al., 2024).

Adaptive immune modulation: While the adaptive immune system in bats is functional, studies suggest that only T cell responses are decreasing and become less inflammatory compared to human as shown in Table 1. This modulation is believed to contribute to prolonged viral persistence with minimal immunopathology (Schountz et al., 2017). Regulatory T cells may also play a role in suppressing excessive immune activation, further enabling bats to act as tolerant hosts (Lu et al., 2019; Banerjee et al., 2020; Zhou et al., 2023; Wickenhagen et al., 2024).

Reduced immunopathology: tolerance over resistance: Bats appear to prioritize immune tolerance over resistance. They use a survival strategy that allows viruses to persist at non-lethal levels. Rather than eliminating the pathogen entirely, bats accept coexistence mechanism and maintain balance relationship and allow viruses to grow within them but in balance way without causing harm themselves. This approach makes significant difference from the immune strategies observed in humans and other mammals, where resistance often involves robust inflammation and collateral tissue damage (Irving et al., 2021).

Evolutionary perspective: These immunological responses likely evolved with the demands of flight-related metabolism, where avoiding inflammation was crucialfor preventing damage from increasing oxidative stress. Over the time, bats have co-adapted with viruses, leading to mutual tolerance and reduced virulence within the host. However, when these viruses spill over into non-adapted hosts like humans the absence of such tolerance often results in severe disease as shown in Table 2 (Letko et al., 2020a; Letko et al., 2020b; Irving et al., 2021; Seifert et al., 2022; Letko, 2024).

Major viral families associated with bats

Surprisingly, bats are natural hosts for diversity of viruses, and many of them have high zoonotic potential. Their role in the emergence of some of the deadliest outbreaks which creates havoc. Viruses associated with bats span multiple families, with many of them capable of crossing species barriers and causing outbreaks in domestic animals and humans (Solari et al., 2009). Available databases from 69 countries have identified over 4100 bat-associated viruses across 196 bat species, spanning 23 viral families (Lei & Dong, 2016). Notably, 43% of emerging and re-emerging pathogens, including bioterrorism agents (Category A, B, and C),

Table 2. Reservoir and spillover dynamics of bat-origin viruses

Virus	Bat Reservoir	Intermediate Host(s)	Spillover Pathway	Associated Human Disease
SARS-CoV& SARS-CoV 2	Horseshoe bats (*Rhinolophus* spp.)	Civets & Pangolins	Via intermediate hosts (Pangolins suspected in SARS-CoV 2)	Severe Acute Respiratory Syndrome (SARS)
MERS-CoV	Egyptian fruit bats (*Rousettus* spp.)	Camels	Via intermediate hosts (Camel)	Middle East Respiratory Syndrome (MERS)
Nipah Virus	Pteropus fruit bats	Pigs	Contaminated fruit or livestock	Encephalitis, Respiratory Illness
Hendra Virus	Flying foxes (*Pteropus* spp.)	Horses	Via horses	Encephalitis, Respiratory Disease
Ebola Virus	Various bat species	Possibly primates	Direct contact or via primates	Hemorrhagic Fever
Marburg Virus	Egyptian fruit bats (*Rousettus aegyptiacus*)	None Known		-Severe Hemorrhagic Fever
Rabies Virus	Various bat species	None (Direct Transmission)	Direct bite	Fatal Encephalitis

have been detected in various bat species (Smith & Wang, 2013; Williams et al., 2021). Additionally, more than 200 viruses have been reported in bats, with the majority being RNA viruses, known for their high mutation and recombination rates(Li et al., 2005; Donaldson et al., 2010; Ge et al., 2013; Smith & Wang, 2013; Hu et al., 2017; Lam et al., 2020; Li et al., 2021; Nabi et al., 2021; Williams et al., 2021). Remarkably, 59 out of 60 bat-associated viruses exhibit extensive genetic diversity, allowing them to adapt and spill over into new hosts as shown in Table 2 (Beena & Saikumar, 2019).

Mechanisms of viral persistence in bats

Bats survive with viruses over long period of time without showing symptoms make them asymptomatic or silent viral reservoirs (Mackenzie & Jeggo, 2013; Plowright et al., 2017). Several closely related mechanisms like immunological, physiological and ecological helps in viral persistence, leading to spillover risk when ecological balance is disrupted (Schountz et al., 2017; Beena & Saikumar, 2019).

Persistent low level viral replication: Some viruses exist in a subclinical, low-replication state in bats due to constant interferon stimulation which allows viruses to be maintained in tissues such as the intestines, kidneys or salivary glands without triggering pathology or being completely eliminated (Luis et al., 2013; Letko et al., 2020b). For examples coronaviruses and paramyxoviruses replicate at low levels without triggering a strong immune response (Luis et al., 2013; Letko et al., 2020a).

Immunological equilibrium: Bats coexist with viruses by maintaining a non-inflammatory antiviral state and also avoid excessive immune activation modulating immune mechanisms like downregulation of inflammasomes activity (NLRP3), dampened STING pathways, and modulated interferon responses, which in other mammals would lead to disease (Letko et al., 2020a; Irving et al., 2021).

Viral latency and reactivation: Physiological stress (e.g., pregnancy, migration and food scarcity) reactivates some viruses such as herpesviruses and paramyxoviruses which may exist in a latent state and ultimately leads to viral shedding, which often align with periods of increased bat–human interaction or colony dynamics (Letko et al., 2020b).

Tissue tropism and viral niches: Specific viruses may preferentially infect immune-privileged or low-immunosurveillance tissues (e.g., central nervous system and reproductive tract), enabling long-term persistence without detection (Beena & Saikumar, 2019). For instance, lyssaviruses may persist in salivary glands, facilitating transmission during feeding or grooming (Beena & Saikumar, 2019).

Co-evolution and host-virus balance: Over evolutionary time, many bat species have co-evolved with their viral passengers, leading to attenuated viral replication and reduced host damage (Plowright et al., 2017). This balance is often finely tuned in the natural bat host. The virus may have minimal impact, but when introduced into a novel host (human or livestock),

virulence often increases due to lack of co-adaptation (Plowright et al., 2017).

Surveillance and prevention strategies for bat borne viruses

Increasing threat of zoonotic diseases from bats highlights the urgent need for advance surveillance system, targeted research and preventive public health strategies. Bats conservation with human health is essential because it play vital role in ecology as shown in Fig. 1, including insect control and pollination.

One health approach: An integrated One Health framework, which recognizes the interconnectedness of human, animal and environmental health, is key to preventing spillover. Collaborative efforts between veterinarians, ecologists, virologists and public health experts are critical in monitoring and mitigating emerging threats (Eby et al., 2023; Gonzalez et al., 2024).

Viral surveillance in bats: Enhanced molecular surveillance programs including metagenomic sequencing and RT-PCR are crucial for detecting known and novel viruses in bat populations. Monitoring should focus on highrisk regions, particularly where habitat disturbance or wildlife–human interfaces are expanding (Gonzalez et al., 2024).

Spillover hotspot mapping: Geospatial modelling tools can help predict and identify spillover hotspots by integrating ecological data, bat distribution, land use changes and human population density. This aids in targeted interventions and resource allocation (Gonzalez et al., 2024).

Public awareness and risk communication: Educating communities, particularly those involved in bat hunting, guano collection or wildlife trade, about safe practices can reduce zoonotic risk. Community-based programs emphasizing safe handling, hygiene and wildlife protection have shown success in several regions (Gonzalez et al., 2024).

Safe agricultural practices: Buffer zones between bat habitats and livestock farms, protective barriers around fruit trees, and restricting bat access to farm water sources can limit viral spillover to domestic animals.

Bat conservation with safety measures: Conservation efforts should avoid direct interference with bat colonies and instead focus on preserving natural habitats to minimize forced human-bat contact. Bats should not be culled, as such actions may increase stress and viral shedding, worsening the risk (Banerjee et al., 2020).

Case studies

Marburg virus disease outbreak: In 2024, Rwanda experienced its first recorded Marburg virus outbreak, confirmed on September 27, with healthcare workers in Kigali among the affected. The virus, linked to Egyptian fruit bats (*Rousettus aegyptiacus*), led to a high fatality rate, prompting swift containment efforts. Authorities monitored 3,000 contacts, initiated quarantine measures, and received 700 vaccine doses for trial, prioritizing healthcare workers and high-risk individuals. The outbreak was declared over on December 20, 2024, after 42 days without new cases. This event highlights the ongoing threat of filoviruses and the importance of early detection, rapid response, and international collaboration in preventing further spread.

Comparative analysis of a viral sensor RIG-I in humans and bats: Investigated RIG-I function in humans, *Myotis daubentonii* (microbat) and *Rousettus aegyptiacus* (megabat). Gene Cloning→ Sequence Comparison → IFN Response Testing → SARS-CoV-2 Recognition

Future directions and research gaps in bat virology

Predictive behavioral models: These models use tracking data, ecological patterns, climate variables, and machine learning algorithms to predict bat movement, roosting behavior, foraging routes and seasonal shifts. By anticipating when and where bats are most likely to interact with humans, livestock, or wildlife, these models help forecast spillover risks and guide targeted interventions.

Bat microbiome exploration: This area focuses on mapping the bacterial, viral, fungal and archaeal communities that naturally live in bats. Understanding how the bat microbiome influences immunity, viral persistence and tolerance can reveal why bats host many viruses without disease symptoms. It also helps identify novel microbes, track pathogen-microbiota interactions and explore microbiome-based disease control strategies.

Community based bio surveillance: This strategy uses local communities, citizen scientists, forest workers and wildlife caretakers for early detection of unusual bat behavior, morbidity, mortality or human–animal contact. Equipped with simple reporting tools (mobile apps, rapid tests), community bio surveillance

strengthens real-time outbreak warning systems, especially in remote regions where laboratory surveillance is limited.

Bat-compatible immunization: A conservation- and ecology-friendly approach to reduce viral transmission at its source. This includes developing oral vaccines, self-disseminating viral vectors or bait-based immunization strategies that can immunize bats without capturing or stressing them. The goal is to interrupt viral amplification within bat colonies while preserving bat health and ecological roles.

Enhancing transmission barriers: These are interventions that reduce the likelihood of viruses crossing from bats to domestic animals or humans. Strategies include improved farm biosecurity near bat habitats, physical barriers such as netting over fruit orchards, environmental modifications to minimize shared resources, and behavioral education for communities. The aim is to strengthen each point in the transmission chain, making spillover biologically and behaviorally less likely.

Conflict of interest: The authors declare no conflict of interest.

Author's contributions: FAP: Conceived the review and wrote the manuscript; ACP, SPA: Contributed to literature search and manuscript editing; NMR, RAM, VRN: Reviewed and approved the final manuscript.

Data availability statement: All data generated or analyzed during this study are included in this published article.

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