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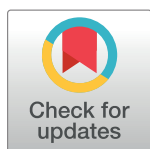
Bat pathogens hit the road: But which one?

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Current evidence suggests that environmental changes and interactions between wildlife, livestock, and humans contribute to the spillover of infectious agents from bats to other hosts [1]. An increasing number of studies investigating the diversity and infection dynamics of bat pathogens has recently been published; however, how these infectious agents are transmitted both within bat populations and to other hosts, including humans, often remains unknown. Here, we summarize current knowledge on direct and indirect transmission routes of bat infectious agents of public health concern (Fig 1). Although bats are recognized as major reservoir hosts of emerging infectious diseases, we highlight that a significant knowledge gap on transmission mechanisms remains and needs further exploration.



Bat bites: The exception rather than the rule?

Although bat bites may be the main transmission route coming to mind, pathogen transmission involving bat bites has been documented mostly for rabies virus (Rhabdoviridae). The common vampire bat (*Desmodus rotundus*) can, for instance, naturally transmit rabies to other species when biting to feed on blood, particularly to livestock and sometimes to humans [2]. *Mycoplasma* has also been detected in common vampire bat blood and saliva and might be transmitted between bats, for instance, during aggressive behaviors [3]. Obligate blood-feeding bats are, however, restricted to Central and South America and represent only a very small proportion of the bat species diversity (<0.005%; 3/1,200). Most bat species do not naturally bite humans unless intentional contacts occur (e.g., veterinarian and field biologists involved in bat capture and handling, people trying to remove bats from houses).

Contact with bat body fluids (saliva, urine, and feces) is increasingly recognized as an important mechanism of pathogen spillover to humans. Human encroachment into bat habitats as well as increasing urbanization, which facilitates bat roosting in artificial structures, are likely to increase contact with bat body fluids. For example, Nipah virus (Paramyxoviridae) human infection cases reported in Bangladesh were associated with the consumption of raw sap from date palm trees contaminated with fruit bat saliva and urine [4]. In the case of Marburg virus (Filoviridae), experimental studies indicate that bat-to-bat transmission may occur via saliva and aerosols, suggesting that the virus may be transmitted to other hosts by a similar mechanism [5,6]. This hypothesis is supported by investigations revealing that most humans infected with Marburg virus had entered bat (*Rousettus aegyptiacus*) caves before becoming sick and reported regular contacts with bats or their secretions [7].

Hunting, preparation, and consumption of bats as bushmeat have also been pointed out as a potential source of infection, especially for Ebola virus. For instance, the putative first human case of the 2007 Ebola outbreak in the Democratic Republic of Congo would have bought freshly killed bats for consumption [8]. The fruit bat *Eidolon helvum*, which is the most frequently hunted and traded bat species in many African countries (e.g., more than 120,000 *E. helvum* are sold yearly in markets in Ghana [9]), has been shown to be infected with Henipa-

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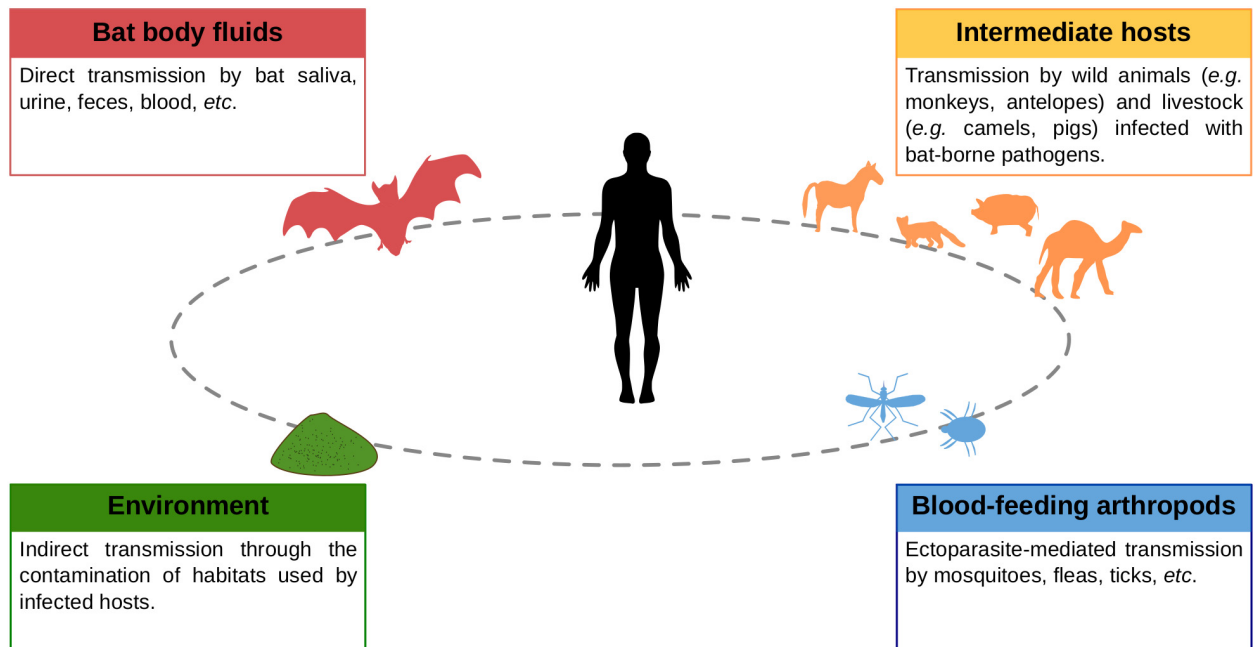


Fig 1. Possible transmission routes of bat-borne pathogens to humans.

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related viruses. This highlights the substantial exposure of local hunters and consumers to viruses of potential zoonotic importance [10].

Can other animals transmit bat-borne pathogens?

Infection of wild animals such as apes, monkeys, and antelopes with bat-borne infectious agents may also play a role in the transmission chain to humans, such as for Ebola virus [11]. In the case of the severe acute respiratory syndrome (SARS) coronavirus, civets (*Paguma larvata*) got infected with a virus circulating in horseshoe bats (*Rhinolophus* sp.) and would have then acted as an intermediate amplifying host [12]. Natural bat predation by other animals (e.g., monkeys, domestic cats) and its consequences on infectious agents transmission are poorly documented [13,14] but could also favor spillover opportunities to other hosts.

In addition to wild animals, the role of livestock as intermediate and amplifying hosts between wild animals and humans has been clearly demonstrated in several outbreaks, such as for Filovirus and Henipavirus [15,16]. Indeed, in Malaysia, the growth of commercial pig farms with fruit trees on the farm has created an environment where bats could drop partially eaten fruits contaminated with Nipah virus into pig stalls [4,17].

In contrast to rapid and short-time spillover events, long-time and silent circulation of viruses in livestock before transmission to humans may also occur, as is strongly suspected for the ongoing outbreak of Middle East respiratory syndrome (MERS). Although bats are likely to be a source of MERS-like coronaviruses, dromedary camels (*Camelus dromedaries*) act as the natural reservoir host in which the MERS coronavirus could have circulated for more than 30 years before its first detection in humans [18]. Other animals such as llamas (*Lama glama*) and wild boars (*Sus scrofa*) have shown susceptibility to MERS coronavirus infection [19], suggesting a large host species range. The endemic human coronavirus 229E may also constitute a descendant of camelid-associated viruses [20] and further supports that livestock plays a key role in the long-time establishment of bat-borne viruses in humans.

Are blood-feeding arthropods involved in bat-borne pathogen transmission?

A large diversity of arthropods, such as mosquitoes, mites, flies, fleas, and ticks [21], can be found in habitats occupied by bats, particularly in cave systems. Some bat ectoparasites (e.g., fleas and ticks) might incidentally bite humans [22], but ectoparasite-mediated transmission of bat-borne infectious agents to humans is difficult to demonstrate and has rather been speculated, such as for the transmission of Ebola virus [23]. Nevertheless, the presence of the bacterium *Bartonella mayotimonensis*, the etiologic agent of endocarditis in humans, both in bat blood and fleas, suggests that transmission to humans by flea bites or their fecal droppings may occur [24]. With the advance of metagenomic technologies, a large diversity of potentially zoonotic bacteria (e.g., *Rickettsia*, *Bartonella* [25]) have been described in bat ectoparasites, but such investigations remain scarce for other infectious agents, such as haemosporidian parasites and viruses [26]. Dengue virus (DENV) was recently detected simultaneously in bat flies (Streblidae) and in their host (*Desmodus rotundus*), although DENV transmission from bat flies to humans has never been reported [27]. To date, the role of blood-feeding arthropods in pathogen spillover to humans therefore remains highly speculative.

Does environmental transmission occur?

Environmental transmission or indirect transmission through the contamination of habitats used by infected hosts has been described as a major mechanism in the epidemiology of wildlife diseases. For bat infectious agents, a limited number of experimental and field studies have been performed to assess their persistence in the environment. Henipaviruses can persist in liquids and on solid surfaces for several days under laboratory conditions and filoviruses for several weeks [28,29]. Bat-borne *Leptospira* could be a source of contamination to other hosts, as this bacterial genus is known to persist in moist environments [30]. Transmission may also occur by bat guano (i.e., accumulation of bat excrement in the environment). Indeed, guano from cave-dwelling bats is commonly used in agriculture as fertilizer worldwide [31]. Reports of human infection with bat guano are usually restricted to histoplasmosis, also known as “cave disease,” a lung infection caused by a fungus (*Histoplasma capsulatum*). The detection of coronavirus RNA in bat guano has been demonstrated [32], although there was no evidence of long-time maintenance of infectious viral particles by virus isolation. Longitudinal sampling of environmental material (water, guano, and soil) exposed to bat secretions for the detection, quantification, and isolation of infectious agents is needed to better assess the risk associated with this transmission route.

What can we learn from bat-to-bat transmission?

Transmission of infectious agents is highly dynamic in bats and is associated with significant changes in bat population structure (e.g., birth pulse in maternity colonies) [1]. Periods of high prevalence of infected bats with Hendra and Marburg viruses have been shown to coincide with the timing of infectious agent spillover to other hosts [1,33]. Although several studies have focused on these aspects, a precise assessment of the diversity of transmission routes involved in disease epidemiology in bats is still lacking, especially when considering the extreme diversity of bat species and associated ecological and biological features. Such information is not only relevant from a fundamental perspective but can provide major information for the development of biosafety measures, therefore limiting emergence risk.

Although communication and education on the risk associated with bat-borne pathogens has increased over the past decade, the benefits of bats in ecosystem functions (e.g., pollination,

soil fertilization, and crops pest control) tend to be disregarded [34]. Gaining knowledge on disease epidemiology and bat ecology is critical to fully assess the challenges associated with human health and bat conservation. In this context, implementation of One Health approaches seems essential and beneficial for a sustainable development, particularly for populations living in hotspots of bat-borne disease emergence [35].

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References

1. Plowright RK, Eby P, Hudson PJ, Smith IL, Westcott D, Bryden WL, et al. Ecological dynamics of emerging bat virus spillover. *Proc R Soc B Biol Sci.* 2015; 282: 20142124.
2. Streicker DG, Allgeier JE. Foraging choices of vampire bats in diverse landscapes: potential implications for land-use change and disease transmission. *J Appl Ecol.* 2016; 53: 1280–1288. <https://doi.org/10.1111/1365-2664.12690> PMID: 27499553
3. Volokhov D V, Becker DJ, Bergner LM, Camus MS, Orton RJ, Chizhikov VE, et al. Novel hemotropic mycoplasmas are widespread and genetically diverse in vampire bats. *Epidemiol Infect.* 2017; 145: 3154–67. <https://doi.org/10.1017/S095026881700231X> PMID: 29061202
4. Luby S, Rahman M, Hossain M, Blum L, Husain M, Gurley E, et al. Foodborne transmission of Nipah virus, Bangladesh. *Emerg Infect Dis.* 2006; 12: 1888–1894. <https://doi.org/10.3201/eid1212.060732> PMID: 17326940
5. Amman BR, Jones ME, Sealy TK, Uebelhoer LS, Schuh AJ, Bird BH, et al. Oral shedding of Marburg virus in experimentally infected Egyptian fruit bats (*Rousettus aegyptiacus*). *J Wildl Dis.* 2015; 51: 113–124. <https://doi.org/10.7589/2014-08-198> PMID: 25375951
6. Schuh AJ, Amman BR, Sealy TK, Spengler JR, Nichol ST, Towner JS. Egyptian rousette bats maintain long-term protective immunity against Marburg virus infection despite diminished antibody levels. *Sci Rep.* 2017; 7: 8763. <https://doi.org/10.1038/s41598-017-07824-2> PMID: 28821722
7. Adjemian J, Farnon EC, Tschioke F, Wamala JF, Byaruhanga E, Bwire GS, et al. Outbreak of Marburg hemorrhagic fever among miners in Kamwenge and Ibanda districts, Uganda, 2007. *J Infect Dis.* 2011; 204: S796–S799. <https://doi.org/10.1093/infdis/jir312> PMID: 21987753
8. Leroy EM, Epelboin A, Mondonge V, Pourrut X, Gonzalez J-P, Muyembe-Tamfum J-J, et al. Human Ebola outbreak resulting from direct exposure to fruit bats in Luebo, Democratic Republic of Congo, 2007. *Vector-Borne Zoonotic Dis.* 2009; 9: 723–728. <https://doi.org/10.1089/vbz.2008.0167> PMID: 19323614
9. Kamins AO, Restif O, Ntiama-Baidu Y, Suu-Ire R, Hayman DTS, Cunningham AA, et al. Uncovering the fruit bat bushmeat commodity chain and the true extent of fruit bat hunting in Ghana, West Africa. *Biol Conserv.* 2011; 144: 3000–3008. <https://doi.org/10.1016/j.biocon.2011.09.003> PMID: 22514356
10. Weiss S, Nowak K, Fahr J, Wibbelt G, Mombouli J-V, Parra H-J, et al. Henipavirus-related sequences in fruit bat bushmeat, Republic of Congo. *Emerg Infect Dis.* 2012; 18: 1536–1537. <https://doi.org/10.3201/eid1809.111607> PMID: 22935105
11. Leroy EM, Rouquet P, Formenty P, Souquière S, Kilbourne A, Froment J-M, et al. Multiple Ebola virus transmission events and rapid decline of central African wildlife. *Science.* 2004; 303: 387–390. <https://doi.org/10.1126/science.1092528> PMID: 14726594
12. Hu B, Zeng L, Yang X, Ge X, Zhang W, Li B, et al. Discovery of a rich gene pool of bat SARS-related coronaviruses provides new insights into the origin of SARS coronavirus. *PLoS Pathog.* 2017; 13: e1006698. <https://doi.org/10.1371/journal.ppat.1006698> PMID: 29190287
13. Tapanes E, Detwiler KM, Cords M. Bat predation by Cercopithecus monkeys: implications for zoonotic disease transmission. *Ecohealth.* 2016; 13: 405–409. <https://doi.org/10.1007/s10393-016-1121-0> PMID: 27138290
14. Delpietro H, Konolsaisen F, Marchevsky N, Russo G. Domestic cat predation on vampire bats (*Desmodus rotundus*) while foraging on goats, pigs, cows and human beings. *Appl Anim Behav Sci.* 1994; 39:141–150.
15. Glennon EE, Restif O, Sbarbaro SR, Garnier R, Cunningham AA, Suu-Ire RD, et al. Domesticated animals as hosts of henipaviruses and filoviruses: A systematic review. *Vet J.* 2018; 233: 25–34 <https://doi.org/10.1016/j.tvjl.2017.12.024> PMID: 29486875

16. Field H, Young P, Yob JM, Mills J, Hall L, Mackenzie J. The natural history of Hendra and Nipah viruses. *Microbes Infect.* 2011; 3: 307–314.
17. Pulliam JRC, Epstein JH, Dushoff J, Rahman SA, Bunning M, Jamaluddin AA, et al. Agricultural intensification, priming for persistence and the emergence of Nipah virus: a lethal bat-borne zoonosis. *J. R. Soc. Interface.* 2012; 9: 89–101. <https://doi.org/10.1098/rsif.2011.0223> PMID: 21632614
18. Müller MA, Corman VM, Jores J, Meyer B, Younan M, Liljander A, et al. MERS Coronavirus neutralizing antibodies in camels, Eastern Africa, 1983–1997. *Emerg Infect Dis.* 2014; 20: 2093–2095. <https://doi.org/10.3201/eid2012.141026> PMID: 25425139
19. Vergara-Alert J, van den Brand JMA, Widagdo W, Muñoz M, Raj S, Schipper D, et al. Livestock susceptibility to infection with Middle East Respiratory Syndrome Coronavirus. *Emerg Infect Dis.* 2017; 23: 232–240. <https://doi.org/10.3201/eid2302.161239> PMID: 27901465
20. Corman VM, Eckerle I, Memish ZA, Liljander AM, Dijkman R, Jonsdottir H, et al. Link of a ubiquitous human coronavirus to dromedary camels. *Proc Natl Acad Sci USA.* 2016; 113: 9864–9869. <https://doi.org/10.1073/pnas.1604472113> PMID: 27528677
21. Obame-Nkoghe J, Leroy E-M, Paupy C. Diversity and role of cave-dwelling hematophagous insects in pathogen transmission in the Afrotropical region. *Emerg Microbes Infect.* 2017; 6: e20. <https://doi.org/10.1038/emi.2017.6> PMID: 28400590
22. Dick CW, Patterson BD. Bat flies—obligate ectoparasites of bats. In: Morand S, Krasnov BR, Poulin R, editors. *Micromammals and macroparasites: from evolutionary ecology to management.* Springer; 2006. pp. 179–194.
23. Monath T.P. Ecology of Marburg and Ebola viruses: speculations and directions for future research. *J Infect Dis.* 1999; 179(Suppl 1): S127–38.
24. Veikkolainen V, Vesterinen EJ, Lilley TM, Pulliainen AT. Bats as reservoir hosts of human bacterial pathogen, *Bartonella mayotimonensis*. *Emerg Infect Dis.* 2014; 20: 960–967. <https://doi.org/10.3201/eid2006.130956> PMID: 24856523
25. Wilkinson DA, Duron O, Cordonin C, Gomard Y, Ramasindrazana B, Mavingui P, et al. The Bacteriome of Bat Flies (Nycteribiidae) from the Malagasy region: a community shaped by host ecology, bacterial transmission mode, and host-vector specificity. *Appl Environ Microbiol.* 2016; 82: 1778–1788. <https://doi.org/10.1128/AEM.03505-15> PMID: 26746715
26. Goldberg TL, Bennett AJ, Kityo R, Kuhn JH, Chapman CA. Kanyawara Virus: A novel Rhabdovirus infecting newly discovered Nycteribiid bat flies infesting previously unknown Pteropodid bats in Uganda. *Sci Rep.* 2017; 7: 5287. <https://doi.org/10.1038/s41598-017-05236-w> PMID: 28706276
27. Abundes-Gallegos J, Salas-Rojas M, Galvez-Romero G, Perea-Martínez L, Obregón-Morales CY, Morales-Malacara JB, et al. Detection of Dengue virus in bat flies (Diptera: Streblidae) of common vampire bats, *Desmodus rotundus*, in Progreso, Hidalgo, Mexico. *Vector-Borne Zoonotic Dis.* 2018; 18: 70–73. <https://doi.org/10.1089/vbz.2017.2163> PMID: 29232534
28. Piercy TJ, Smither SJ, Steward JA, Eastaugh L, Lever MS. The survival of filoviruses in liquids, on solid substrates and in a dynamic aerosol. *J Appl Microbiol.* 2010; 109: 1531–1539. <https://doi.org/10.1111/j.1365-2672.2010.04778.x> PMID: 20553340
29. Fogarty R, Halpin K, Hyatt AD, Daszak P, Mungall BA. Henipavirus susceptibility to environmental variables. *Virus Res.* 2008; 132: 140–144. <https://doi.org/10.1016/j.virusres.2007.11.010> PMID: 18166242
30. Thibeaux R, Geroult S, Benezech C, Chabaud S, Soupé-Gilbert M-E, Girault D, et al. Seeking the environmental source of Leptospirosis reveals durable bacterial viability in river soils. *PLoS Negl Trop Dis.* 2017; 11: e0005414. <https://doi.org/10.1371/journal.pntd.0005414> PMID: 28241042
31. Mildenstein T. and De Jong C. (2011). Natural history, ecological and socio-economic value of bats. In: *FAO. Investigating the role of bats in emerging zoonoses: Balancing ecology, conservation and public health interests.* Newman SH, Field HE, de Jong CE, Epstein JH, editors. Vol. 12, *FAO Animal Production and Health Manual n°12.* Rome, Italy; 2011. p 63.
32. Wacharapluesadee S, Sintunawa C, Kaewpom T, Khongnomnan K, Olival KJ, Epstein JH, et al. Group C Betacoronavirus in bat guano fertilizer, Thailand. *Emerg Infect Dis.* 2013; 13: 1349–1351.
33. Amman BR, Carroll SA, Reed ZD, Sealy TK, Balinandi S, Swanepoel R, et al. Seasonal pulses of Marburg virus circulation in juvenile *Rousettus aegyptiacus* bats coincide with periods of increased risk of human infection. *PLoS Pathog.* 2012; 8: e1002877. <https://doi.org/10.1371/journal.ppat.1002877> PMID: 23055920
34. López-Baucells A, Rocha R, Fernández-Llamazares Á. When bats go viral: negative framings in virological research imperil bat conservation. *Mamm Rev.* 2018; 48: 62–66.
35. Wood JLN, Leach M, Waldman L, MacGregor H, Fooks AR, Jones KE, et al. A framework for the study of zoonotic disease emergence and its drivers: spillover of bat pathogens as a case study. *Philos Trans R Soc B Biol Sci.* 2012; 367: 2881–92.