

Henipaviruses at the Interface Between Bats, Livestock and Human Population in Africa: A Review

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Abstract

Nipah virus (NiV) and Hendra virus (HeV) are closely related members within the genus *Henipavirus*, family *Paramyxoviridae*, for which fruit bats serve as the reservoir. The initial emergence of NiV infections in pigs and humans in Malaysia, and HeV infections in horses and humans in Australia, posed severe impacts on human and animal health, and continues threatening lives of humans and livestock within Southeast Asia and Australia. Recently, henipavirus-specific antibodies have also been detected in fruit bats in a number of sub-Saharan African countries and in Brazil, thereby considerably increasing the known geographic distribution of henipaviruses. Africa is progressively being recognized as a new high prevalence zone for henipaviruses, as deduced from serological and molecular evidence of past infections in Madagascar, Ghana, Republic of Congo, Gulf of Guinea, Zambia, Tanzania, Cameroon, and Nigeria lately. Serological data suggest henipavirus spillover from bats to livestock and human populations in Africa without reported clinical disease in any of these species. All virus isolation attempts have been abortive, highlighting the need for further investigations. The genome of the Ghanaian bat henipavirus designated Ghana virus (GhV), which was detected in a pteropid *Eidolon helvum* bat, is the only African henipavirus that has been completely sequenced limiting our current knowledge on the genetic diversity and pathogenesis of African henipaviruses. In this review, we summarize the available data on the circulation of henipaviruses in Africa, discuss potential sources for virus spillover, and highlight existing research gaps.

Keywords: henipavirus, paramyxovirus, zoonotic, fruit bat, livestock, human

Introduction

THE GENUS *HENIPAVIRUS* within the order of *Mono-negavirales*, family of *Paramyxoviridae* comprises five species that have all been detected within the past 25 years. Of these, Hendra virus (HeV) and Nipah virus (NiV) are closely related novel emerging zoonotic RNA viruses, to which three species have been added more recently, namely Cedar virus (CedV), Ghana virus (GhV), and Mojiang virus (MojV). With the extension of the known geographic dis-

tribution of henipaviruses outside Southeast Asia and Australia into Africa and lately also into Brazil, the global attention and relevance of these viruses has considerably increased.

Thus the objectives of this review are to summarize the existing data on the molecular and serological evidence confirming the circulation of henipaviruses in Africa and their spillover from bats to livestock and humans, and second to discuss possible risk factors associated with the emergence and spillover of henipavirus infection in Africa.

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Morphology and Genome Organization of Henipaviruses

Henipaviruses harbor a nonsegmented, single-stranded negative sense RNA genome consisting of a helical nucleocapsid encased in an envelope, forming spherical to pleomorphic virus particles. Their genome codes for six major structural proteins from the 3' to 5' terminal (Fig. 1); nucleoprotein (N), phosphoprotein (P), matrix protein (M), fusion glycoprotein (F), attachment glycoprotein (G), and large polymerase protein (L) (Wang et al. 2000, 2001, Bellini et al. 2005, ICTV 2011, Rota and Lo 2012, Afonso et al. 2016). The P gene encodes for accessory proteins or nonstructural proteins designated C, V, and W, which can be translated by the use of alternative translation starts or by messenger RNA (mRNA) editing mechanisms and which are able to compromise the host's immune system (Yoneda et al. 2010, Basler 2012).

The N, M, and L genes of NiV and HeV are highly conserved and are exploited for molecular diagnostic (PCR) purposes. The nucleotide homologies between NiV and HeV are 79% for the N gene, 77% for the M gene, and 87% for the L gene (Harcourt et al. 2000, Wang et al. 2001). Meanwhile, the amino acid sequence identity between the N proteins of NiV and HeV is 92%, whereas the G proteins of both viruses display an amino acid sequence identity of 83% (Harcourt et al. 2000), which is relevant for serological diagnostic assays.

The cellular receptor used by the different representatives of this virus family may influence the virulence, pathogenesis, and pathogenicity according to the respective tissue distribution of the receptor. The viral surface G protein facilitates the binding of the virus to the cellular surface, which is mediated by cellular ephrin B2 and ephrin B3 in the case of NiV and HeV

(Bonaparte et al. 2005, Negrete et al. 2005, Xu et al. 2012), only ephrin B2 in the case of CedV (Marsh et al. 2012) and most probably GhV (Lee et al. 2015), whereas the cellular receptor for the MoV G protein is still to be elucidated, because the ephrin receptor binding motif is absent in this protein (Rissanen et al. 2017). The fusion protein, F₀, is synthesized as an inactive precursor that requires cleavage by a host cell protease to become active subunits F₁ and F₂. Thus these subunits mediate the fusion of the virion membrane with the plasma membrane of the host cell (Wang et al. 2001, Diederich et al. 2005).

Although antibodies against the N protein are generated early after infection because of the abundant expression of this protein (Chua et al. 2000, Harcourt et al. 2000), the G protein is expressed on the surface of infectious viral particles and thus induces neutralizing antibodies (Zhu et al. 2006). Although the serum neutralization test that is considered the gold standard in henipavirus serology requires Biosafety Level 4 (BSL-4) facilities, N and G proteins are broadly used as suitable antigens for serological screening by enzyme-linked immunosorbent assay (ELISA) (Tamin et al. 2002, McNabb et al. 2014, Fischer et al. 2018). After the implementation of a commercial vaccine against HeV infections in horses in Australia that is based on the soluble HeV G protein, the parallel determination of antibodies against HeV N and G proteins can be used for the differentiation between infected and vaccinated animals (DIVA approach).

Henipaviruses in Southeast Asia, Australia, and China

NiV and HeV can cause severe respiratory illness, encephalitis, and neurodegenerative diseases in humans and

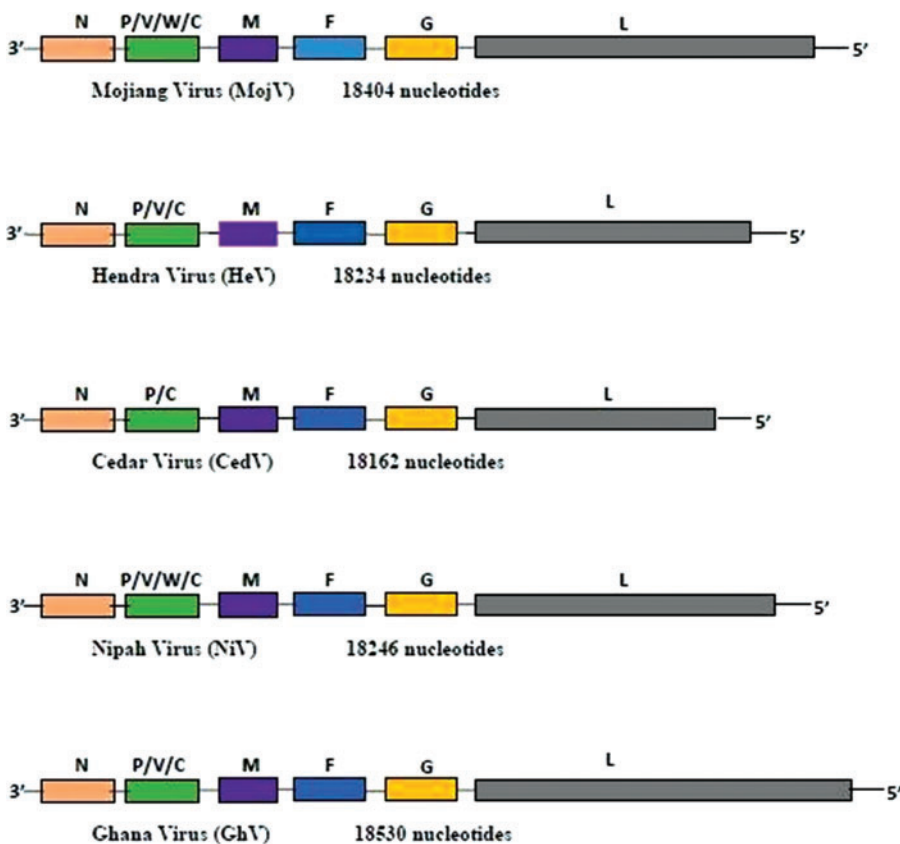


FIG. 1. Organization of henipavirus genes. F, fusion glycoprotein; G, attachment glycoprotein; L, large polymerase protein; M, matrix protein; N, nucleoprotein; P, phosphoprotein; V/C/W, nonstructural proteins. Color images are available online.

animals with case fatality rates reaching up to 40–75% (Selvey et al. 1995, Chua et al. 1999, Chua 2003, McCormack 2005, Eaton et al. 2006, ProMED-mail 2011). Because of their zoonotic potential, broad host range, and high virulence and also the current absence of vaccines and therapeutics, both viruses have been classified as BSL-4 agents as the only members of the *Paramyxovirus* family. Fruit bats of the genus *Pteropus*, suborder *Megachiroptera*, are widely described as the natural reservoir for henipaviruses (Young et al. 1996, Halpin et al. 1999, 2011, Enserink 2000, Field et al. 2001, Yob et al. 2001), except MojV, which is considered to have a rodent reservoir host, *Rattus flavipectus* (Wu et al. 2014).

HeV first emerged in 1994 in Hendra a suburb of Brisbane, Australia, leading to an outbreak of severe respiratory disease in 21 horses of which 14 died, and including the fatal infection of a horse trainer (Murray et al. 1995a, 1995b, Nowak 1995, Selvey et al. 1995). Since its initial detection in Australia, HeV spillover from flying foxes to horses has regularly occurred, with an increase in the disease events in 2011–2012 (Halpin et al. 1999, 2000, 2011, Marsh et al. 2010). Until now 55 events have been reported, resulting in the death and killing of 97 horses (Marsh et al. 2010, Ball et al. 2014, Kohl et al. 2018) and 1 dog (Halim et al. 2015, Kirkland et al. 2015). Of the seven human infections, four were fatal (ProMED-mail 2011). The licensing of a HeV vaccine for horses in Australia in 2012 has decreased the infection risk for horses and horse owners as long as horses are properly vaccinated (Middleton et al. 2014, Goyen et al. 2017, Manyweathers et al. 2017).

NiV was first identified during a major outbreak of an acute respiratory disease in pigs in Sungai Nipah, Malaysia, between 1998 and 1999, which resulted in the death of 105 persons/pig-farm workers among 265 human infections and the extirpation of 1.1 million pigs, which were considered to act as intermediate hosts (Centers for Disease Control and Prevention [CDC] 1999, Chua et al. 1999, Parashar et al. 2000, AbuBakar et al. 2004). This was followed by a related smaller outbreak in Singapore in 1999 (Chew et al. 2000). Again, flying foxes were identified as the reservoir host of this virus (Chua et al. 2000, 2002, Enserink 2000, Yob et al. 2001).

Since 2001, NiV spillover infections from bats to humans are being reported from Bangladesh and India, where, without any involvement of pigs in the transmission cycle, humans became infected through the consumption of NiV contaminated date palm sap (Luby et al. 2006, 2009, Rahman and Chakraborty 2012, Islam et al. 2016). Sequence analysis revealed a high degree of similarity between the NiV strains circulating in Bangladesh and India (AbuBakar et al. 2004, Harcourt et al. 2005). Very recently, another NiV outbreak was reported in India and led to widespread public anxiety (Paul 2018), underlining the importance of public relations regarding zoonotic diseases. During these outbreaks, human-to-human infections occurred mostly by direct contact with infected patients or by contact with contaminated surfaces in hospitals and homes (Gurley et al. 2007, Sazzad et al. 2013, Chakraborty et al. 2016).

In the following years, NiV infections have also been detected in livestock species such as cattle, goats, and pigs in Bangladesh (Chowdhury et al. 2014), whereas the infection of dogs had already been reported in Malaysia in 2009 (Mills et al. 2009). Furthermore, the first NiV infection of horses was observed in the Philippines in 2014, and horse-to-

human infections were postulated to have occurred through handling and consumption of horse meat, whereas human-to-human infections occurred by direct contact with infected subjects (Ching et al. 2015).

Ever since the emergence of NiV and HeV, studies on henipaviruses have extensively been conducted in Southeast Asia and Australia. In fact, fruit bats in Malaysia (Yob et al. 2001), Cambodia (Olson et al. 2002, Reynes et al. 2005), Thailand (Wacharapluesadee et al. 2005, 2016), Indonesia (Sendow et al. 2010, 2013), Vietnam (Hasebe et al. 2012), Papua New Guinea (Breed et al. 2010, 2013, Field et al. 2013), China (Li et al. 2008), and India (Yadav et al. 2012, 2018) were tested positive for the presence of NiV or HeV-specific antibodies and/or henipavirus-related RNA, whereas only HeV RNA and HeV-specific antibodies were detected in pteropid fruit bats in Australia (Field et al. 2011, Smith et al. 2011, Edson et al. 2015).

Results from studies in Australia indicated that urine is the most plausible source of HeV infection from bats to bats and bats to horses (Smith et al. 2011, Barr et al. 2015, Edson et al. 2015) and that virus excretion rather occurs periodically than continuously (Field et al. 2011). In the course of these screening efforts, CedV was detected and successfully isolated from *Pteropus alecto* fruit bats in Australia (Marsh et al. 2012). The lack of the alternative editing of the P gene, resulting in the translation of the V gene, may contribute to its majorly reduced, if not absent, pathogenicity in bats as well as in ferrets and guinea pigs after experimental exposure (Marsh et al. 2012).

Sequence analysis revealed nucleotide homologies between CedV and NiV or HeV to be 59% and 58% for N, 60% in both cases for M, and 50% in both cases for L (Marsh et al. 2012), which is considerably lower than the similarities between these proteins of HeV and NiV. Moreover, the considerably lower antigenic similarity of the CedV G protein and the G proteins of HeV or NiV (29% and 30%, respectively) results in a lack of cross-reactivity of antibodies raised against HeV G or NiV G proteins with CedV G (Marsh et al. 2012). Shortly afterward, another member of the *Henipavirus* genus designated MojV was detected in rats (*R. flavipectus*) in China in the course of a molecular screening of bats and rodents after fatal respiratory infections in three mine workers in the Yunnan Province (Wu et al. 2014).

Sequence analysis revealed nucleotide homologies between MojV and the other known henipaviruses to be 53–57% for N, 60–63% for M and 56–59% for L (Wu et al. 2014), which is again considerably lower than the similarities between these proteins of HeV and NiV (Harcourt et al. 2000, Wang et al. 2001), but comparable with the similarities between HeV or NiV and CedV (Marsh et al. 2012). Virus isolation attempts remained unsuccessful in this study (Wu et al. 2014).

Of interest, virus isolation attempts have been highlighted in several studies across Southeast Asia and Australia, but successful isolations were only reported for HeV in Australia (Marsh et al. 2010, Smith et al. 2011) and NiV in Malaysia (Chua et al. 1999, 2001, 2002, AbuBakar et al. 2004) and Bangladesh (Harcourt et al. 2005). Of late, antibodies against henipaviruses were also detected in bats in Brazil (De Araujo et al. 2017), thereby expanding the geographic distribution of henipaviruses to new territories. However, Africa is becoming another hotspot for the circulation of henipaviruses, for

example, from the indigenous *Eidolon helvum* bat that is widely distributed across the continent.

Serological and Molecular Evidence of Henipaviruses in Bats and Potential Spillover into Livestock and the Human Population in Africa

An ample number of studies in Madagascar (Iehlé et al. 2007), Ghana (Hayman et al. 2008, Drexler et al. 2009, 2012), the Republic of Congo (Weiss et al. 2012), Gulf of Guinea (Peel et al. 2012), Zambia (Muleya et al. 2013), Tanzania (Peel et al. 2013), Cameroon (Pernet et al. 2014), and Nigeria (Olufemi et al. 2015) have effectively revealed the presence of

henipavirus-specific antibodies and henipavirus-related RNA in African fruit bats. Some of these studies have shown that there has also been exposure of pigs, horses, and humans to henipaviruses in Africa suggesting spillover events from bats to livestock and to human populations (Hayman et al. 2011, Pernet et al. 2014, Olufemi et al. 2015). Figure 2 illustrates the locations in sub-Saharan Africa where henipavirus-specific antibodies or henipavirus-related RNA were detected so far.

The first molecular evidence of henipavirus infection in bats in Africa was reported in a West African country, Ghana, in which fruit bats of the species *E. helvum* were sampled for their fecal droppings. A total of 215 fecal samples were obtained from an estimated colony of ~400,000 bats in the

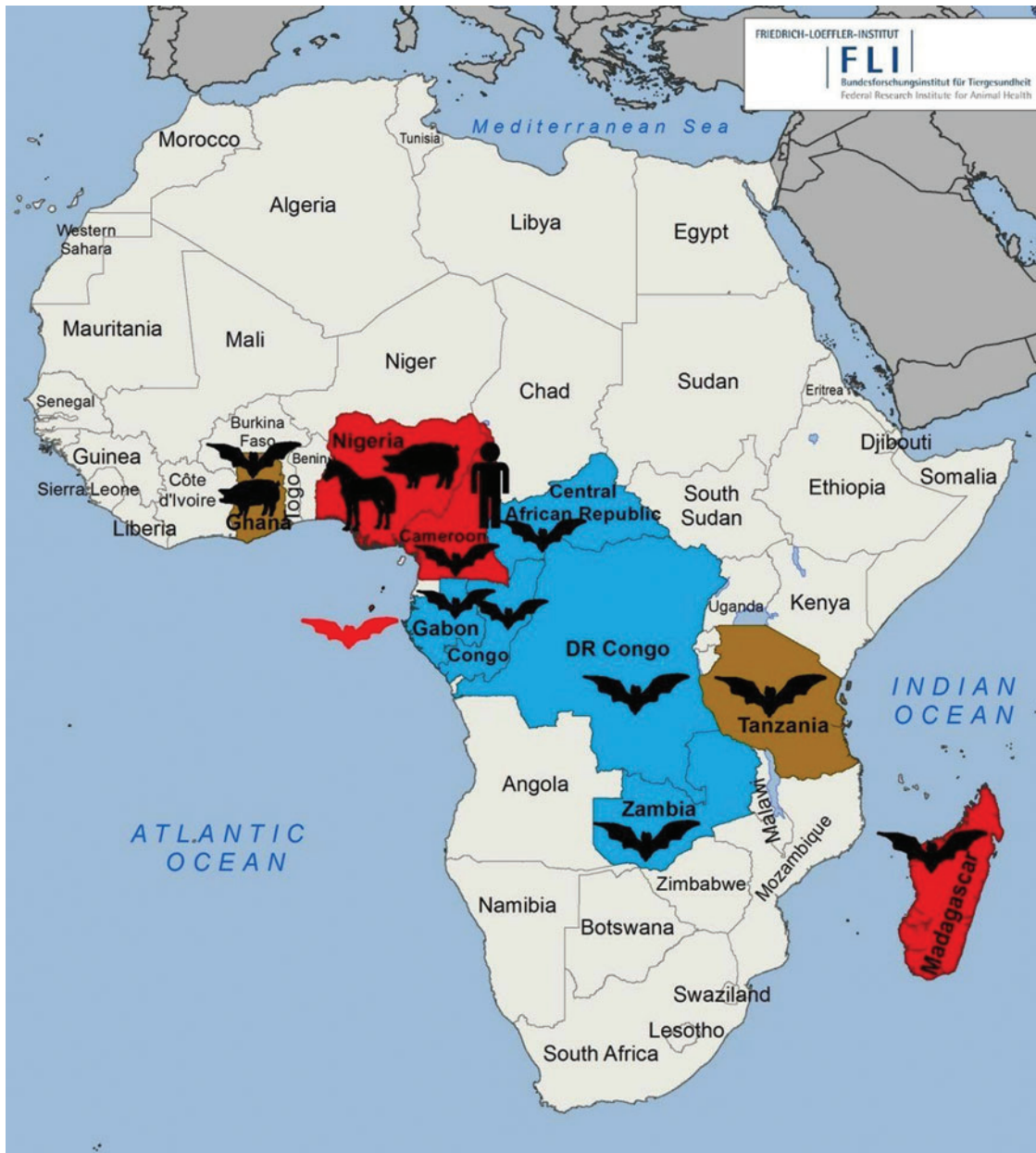


FIG. 2. Serological and molecular evidence of henipavirus infections in sub-Saharan Africa. *Red*: countries with positive results in serological screening; *brown*: countries with positive results in serological and PCR screening; *blue*: countries with positive results in PCR screening. Color images are available online.

Zoological Garden of Kumasi, Ghana (Drexler et al. 2009). Three of 215 were confirmed positive by a broad-spectrum RT-PCR targeting the L-gene of henipavirus, morbillivirus, and respirovirus (Tong et al. 2008). Sequencing of the amplicons revealed that the three viral sequences were closely related to the so far known henipaviruses but one was more closely to NiV. However, virus isolation was unsuccessful (Drexler et al. 2009).

A serological study in the same country revealed henipavirus-specific antibodies in Ghanaian fruit bats (Hayman et al. 2008), whereas a later study in 2011 confirmed a seroprevalence of 5% in 97 domestic pigs tested by Luminex binding assay but with no cross-neutralizing antibodies to NiV or HeV, suggesting previous exposure of Ghanaian pigs to serologically related but distinct henipaviruses (Hayman et al. 2011).

The entire genome of an African henipavirus, GhV, was successfully sequenced in a study that involved sampling of bats in Ghana, Republic of Congo, Gabon, the Central African Republic (RCA), and the Democratic Republic of Congo (DRC) (Drexler et al. 2012).

The first serological evidence of henipavirus-specific antibodies in African horses was revealed during a cross-sectional survey of horses and pigs in Zaria and environs in Kaduna state, Nigeria (Olufemi et al. 2015). A total of 200 and 310 sera were sampled from horses and pigs, respectively. All samples were analyzed using an indirect ELISA based on HeV-sG antigen (CSIRO Australia). The species-specific seroprevalence was 15.5% and 20% for horses and pigs, respectively. It was noticed that horses managed under intensive system, used for sports and traditional purposes, consumed homemade food, consumed well water, and were kept outdoors were at higher risk to henipavirus infection. The highest risk factors for pigs to contract a henipavirus infection included import, intensive management with homemade feed and well water, and being kept outdoors without a feed storage plan (Olufemi et al. 2015). However, results from this study should be interpreted carefully because the study lacks confirmatory testing, for example, by Western blot or immunofluorescence assay detecting antibodies against other viral antigens such as the nucleoprotein.

Moreover, the first evidence of henipavirus spillover into human populations of Africa was detected in Cameroon (Pernet et al. 2014). In this study, sera were sampled from 44 *E. helvum* fruit bats and 497 humans. These samples were subjected to a vesicular stomatitis virus (VSV)-based pseudoparticle seroneutralization assay to detect NiV (cross-) neutralizing antibodies. A seroprevalence of 48% and 3–4% was observed in bats and humans, respectively. Consequently, the seropositive human sera were found almost exclusively in individuals involved in butchering bats for bushmeat and residing in proximity to areas undergoing deforestation (Pernet et al. 2014). Furthermore, another study conducted in Brazzaville, Republic of Congo, aimed at investigating the risk of zoonotic disease emergence through hunting of bats and preparation and consumption of bushmeat. A total of 339 samples collected from 42 *E. helvum* bats destined for human consumption were obtained from local hunters at the market. All samples were tested by a broad-spectrum RT-PCR targeting the L-gene of respirovirus, morbillivirus, and henipavirus (Tong et al. 2008), and by a quantitative RT-PCR (RT-qPCR; Weiss et al. 2012) that was used to determine the viral load in the tissues. Henipavirus-

related sequences were detected in 15 samples from 11 individual bats and virus load ranged from 1.1×10^2 to 3.4×10^4 copies per tissue sample of $\sim 0.3 \text{ cm}^3$ and 4 samples could not be quantified because of low viral load in tissues (Weiss et al. 2012).

In East Africa, during an epidemiological study to screen for paramyxoviruses in frugivorous *E. helvum* bats in Zambia, 312 bats were captured at the Kazanka National Park from which the corresponding number of spleen samples were collected (Muleya et al. 2013). Samples were tested for paramyxovirus-related sequences using a semi-nested RT-PCR (Tong et al. 2008) and further sequenced and phylogenetic analysis performed. Among the seven novel paramyxovirus sequences detected, five were closely related to the genus *Henipavirus*. The presence of these viruses in bats, livestock, and human populations in Africa poses a potential public health risk although no outbreak is yet reported within this continent and as such continuous surveillance of these viruses in bat–livestock–human populations is primordial. Table 1 presents an overview of serological and molecular studies performed so far in Africa.

Possible Risk Factors Associated with Henipavirus Emergence and Spillover in Africa

Disease emergence results from the dynamic interactions between pathogen, animal, and/or human hosts and the perpetually changing environment. These interactions are at the core of disease emergence; therefore, understanding these drivers and impacts will allow an evidence-based risk assessment and the development of mitigation strategies that will enable an effective and timely response to new disease outbreaks (Wang and Cramer 2014).

The frugivorous bat species *E. helvum* is highly abundant particularly across the sub-Saharan region and also present on some offshore and isolated islands (Thomas and Henry 2013). Fruit bat colonies undergo annual transcontinental migration after the rainfall gradient to suitable feeding grounds or the seasonal changes in food availability, with reports of individual bats covering >2500 km yearly (Richter and Cumming 2008, Ossa et al. 2012, Fahr et al. 2015). Generally, they roost in urban settlements and feed in close proximity to human and livestock populations, thereby increasing the possibility of disease agents such as henipaviruses to cross species barriers and infect new hosts, resulting in putatively harmful or even fatal disease outbreaks (Peel et al. 2013).

In addition, husbandry practices and management in developing nations in Africa allow close contact between bats and livestock populations because animals are mostly kept free-ranging. There is a high probability for bats to contaminate their food, pasture, and water with secretions and excretory products thus culminating to infection (Peel et al. 2013, Olufemi et al. 2015).

Moreover, deforestation causes habitat fragmentation and severely impacts natural habitats of bats, forcing them to further migrate toward urban centers and thereby increasing the possibility of contact with domestic animals and humans, potentially leading to cross-species transmission of viral agents (Weiss and McMichael 2004, Wolfe 2005, Lloyd-Smith et al. 2009, Murray and Daszak 2013). The altered habitat may also influence the density of the local bat population, thereby affecting the spillover risk (Plowright et al. 2015). Bat migration toward urban centers could also alter

TABLE 1. OVERVIEW OF SEROLOGICAL AND MOLECULAR STUDIES PERFORMED IN AFRICA ON THE PRESENCE OF HENIPAVIRUSES IN DIFFERENT HOST SPECIES

Locations	Host species	No. of animals	Samples	No. of samples	Study design	Diagnostic assay	Sampling period	Antibody prevalence	Infection prevalence (PCR)	References
Madagascar	Fruit bats: <i>Pteropus rufus</i> , <i>Eidolon dupreanum</i> , <i>Rousettus madagascariensis</i>	Not specified	Sera	427	Cross-sectional study	ELISA; SNT	2003–2005	23/427 (5.4%) were positive for both NiV and HeV with ELISA; 3/427 were positive with SNT	N/A	Iehlé et al. (2007)
Republic of Congo	Fruit bats: <i>Eidolon helvum</i>	42	Urine, sera, tissues	339	Cross-sectional study	PCR (L gene) and qPCR	2009	N/A	15 samples 11 bats +ve by PCR	Weiss et al. (2012)
Nigeria	Pigs, horses	510: 310 pigs and 200 horses	Sera	510	Cross-sectional survey	Indirect ELISA; HeV sG iELISA	2015	Species-specific seroprevalence was 20% ($n=310$ pigs) and 15.5% ($n=200$ horses)	N/A	Olufemi et al. (2015)
Ghana	Fruit bats: <i>E. helvum</i> , <i>Epomophorus gambianus</i> , <i>Epomops franqueti</i> , <i>Epomops buettikoferi</i> , <i>Hypsignathus monstrosus</i> , <i>Nanorycteri veldkampii</i>	206: 59, 89, 29, 7, 18, 4, respectively	Sera	206	Cross-sectional study	Luminex multiplex microspheres assay or LBA and VNT	2007	Species-specific seroprevalence for LBA: <i>E. helvum</i> , 22% (13/59, 95% CI: 11–33) for HeV and 39% (23/59, 95% CI: 27–51) for NiV. <i>E. gambianus</i> , 1% (1/89, 95% CI: 0–3) for NiV. <i>H. monstrosus</i> , 6% (1/18, 95% CI: 0–16) for NiV. The others were negative. VNT seropositivity was 30% (7/13 of the luminex +ve samples from <i>E. helvum</i>)	N/A	Hayman et al. (2008)
Ghana	Domestic pigs	97	Sera	97	Cross-sectional study	LBA	2007	Seroprevalence was 5% ($n=97$ pig sera) but with no cross-neutralizing antibodies to NiV and HeV	N/A	Hayman et al. (2011)

(continued)

TABLE 1. (CONTINUED)

Locations	Host species	No. of animals	Samples	No. of samples	Study design	Diagnostic assay	Sampling period	Antibody prevalence	Infection prevalence (PCR)	References
Ghana	Fruit bats: <i>E. helvum</i>	A colony of bats ~400,000 bats	Feces	215	Not specified	RT-PCR (L-gene)	2008	N/A	3/215 yielded a positive RT-PCR	Drexler et al. (2009)
Ghana, Congo, RCA, DRC and Gabon	Fruit bats: several species	2616	Feces, swabs, sera, and tissues	Not specified	Not specified	RT-PCR and NGS	Not specified	N/A	66 Novel paramyxoviruses, among which henipavirus related to the African Gh-M74a	Drexler et al. (2012)
Equatorial Guinea: Gulf of Guinea	Fruit bats: <i>Eidolon helvum</i>	75	Sera	73	Cross-sectional serological study	Luminex multiplex binding assay, Inhibition assay and VNT	2010	Positive seroprevalence for henipavirus by luminex assay and confirmed using alternative assays	N/A	Peel et al. (2012)
Zambia	Frugivorous or fruit bats: <i>E. helvum</i>	312	Spleen	312	Cross-sectional study	Broad-spectrum seminested RT-PCR (L-gene)	2008–2011	N/A	8% (25/312) PCR +ve for paramyxovirus 7 new paramyxoviruses, 5 ~ henipaviruses, ~2 Afr	Muleya et al. (2013)
Cameroon	Fruit bats: <i>E. helvum</i> and humans	44 and 497, respectively	Sera	44 and 497, respectively	Cross-sectional study	VSV-based pseudoparticle seroneutralization assay with NiV-X-Nabs	2001–2007	Seropositivity was 48% (21/44 <i>E. helvum</i> <i>n</i> = 44) and 3–4% (human <i>n</i> = 497)	N/A	Pernet et al. (2014)
Tanzania	Fruit bats: <i>E. helvum</i>	263	Sera and urine	222 sera, 10 urine pools	Not specified	Luminex multiplex assay, VNT and hemi-nested RT-PCR (L-gene)	Not specified	Seroprevalence was 5% (11/222, 3–9%) by VNT	One PCR +ve pool urine samples of six bats sero -ve with luminex and VNT	Peel et al. (2013)

~, closely related to; Afr, African; CI, confidence interval; DRC, Democratic Republic of Congo; ELISA, enzyme-linked immunosorbent assay; HeV, Hendra virus; HeV sG iELISA, Hendra virus recombinant soluble G-glycoprotein indirect immunosorbent assay; LBA, Luminex binding assay; N/A, not applicable; NGS, Next Generation Sequencing; NiV, Nipah virus; qPCR, quantitative PCR; RCA, Central African Republic; SNT, serum neutralization test; VNT, virus neutralization test; VSV, vesicular stomatitis virus.

their feeding habits, which might subsequently affect their immune responses by limiting their ability to combat or clear the viruses they harbor and possibly increase the probability of virus spillover to other species (Plowright et al. 2015, 2017, Giles et al. 2018, Kessler et al. 2018, Páez et al. 2018).

Indeed, socioeconomic and cultural activities like bat hunting, sale, handling, butchering, and consumption as bushmeat is considered one of the primordial risk factors associated with henipavirus spillover to human populations in Africa (Weiss et al. 2012, Pernet et al. 2014). However, humans may also be infected through contact with environmental virus contamination by, for example, inhaling virus particles from bat secretions and excretions upon intrusion into bat roosting areas (Weiss et al. 2012). Although no specific disease symptoms have been associated with henipavirus infections in bats, pigs, and humans in Africa (Hayman et al. 2008, Drexler et al. 2009, Pernet et al. 2014), there is a possibility of underreporting of clinical cases connected with such infections. This is especially the case because febrile flu-like infections in humans that may also develop into encephalitis occur frequently in sub-Saharan Africa without further investigation into the infectious source. It is therefore important to continue the screening for such infections and to associate these virological results with clinical data of the sampled individuals.

Limits or Gaps in the Study of Henipaviruses in Africa

So far, GhV is the only African henipavirus that has been completely sequenced (Drexler et al. 2012). Not much is known on the real prevalence of henipavirus infection in Africa and only very little is known on the genomic diversity of henipaviruses circulating at the interface between bats, livestock, and humans in sub-Saharan Africa. All efforts to isolate African henipaviruses and even the attempt to generate a recombinant replication competent GhV have failed so far, making it impossible to really assess their pathogenic, antigenic, and zoonotic potential (Hayman et al. 2008, Drexler et al. 2009, Weiss et al. 2012) and their public health risk.

Cross-sectional serological studies provide no details on viral transmission dynamics within populations. However, valuable information on the presence or absence of virus infection may be obtained and consequently, further studies are required to understand virus–host interaction and mechanisms of cross-species transmission. Only one study indicated a potential spillover of an African henipavirus into the human populations in Cameroon without reporting on clinical cases (Pernet et al. 2014). It is worth mentioning that the human sera used in this study were archival samples collected between 2001 and 2003, thus suggesting that human exposure to henipaviruses or henipa-like viruses might have occurred before the first known report of a circulation of these viruses.

Therefore, more studies should be undertaken as henipaviruses with a higher pathogenicity might be circulating in Africa, possibly causing isolated clinical cases in humans and/or animals. Multidisciplinary studies on henipaviruses involving bats, livestock, and humans have not yet been conducted throughout Africa; the previous studies targeted just individual aspects.

So far, almost all serological screening and confirmatory tests have been performed using the glyco- and nucleopro-

teins of either HeV or NiV, thus possibly detecting cross-reactive antibodies that are not specifically targeting GhV. However, our present knowledge suggests that the applied diagnostic measures cannot fully identify the assumed diversity of circulating henipaviruses in Africa. Only one assay has been used to date that is able to specifically detect antibodies against GhV and to correlate these results to HeV or NiV-specific serological results (Pernet et al. 2014). Therefore, there is still a lack of serological studies from different areas in Africa and different (animal) species to specifically detect antibodies against GhV, and to correlate the cross-reactivity of those sera to HeV or NiV-specific antigens, which would enable a better assessment of the variety and prevalence of different henipaviruses in Africa.

Conclusion and Recommendations

This review summarizes the current knowledge on the circulation of henipaviruses on the African continent, particularly in sub-Saharan Africa. Besides a number of studies in indigenous bat species, there is evidence for the exposure of livestock and humans to henipaviruses. In this light there is need for intensified national and regional surveillance and monitoring programs to provide adequate information on the epidemiology of henipaviruses in Africa. The programs should target wildlife, livestock, and companion animal species as well as human populations and their ecosystem in view of promoting the One Health concept. For a non-invasive sampling approach, molecular analysis is most promising from urine samples. However, if tissue samples like kidney, spleen, and brain are available for molecular analysis along with serology, the results might become much more rewarding.

There is also need for more serological and molecular studies in Africa using reliable and specific diagnostic tools that could discriminate the known species of henipaviruses to reveal the true prevalence of henipavirus infections in Africa. To complement that, a very important milestone would be to isolate the respective virus(es).

Livestock owners, farmers, hunters, traders, veterinarians, epidemiologists, foresters, health personnel, researchers, military personnel, and other stakeholders should be stringently trained on biosafety and biosecurity measures to be respected during sample collection in the field. Multi-ministerial and multidisciplinary teams should work in close collaboration with international organizations to effectively implement the correct biosafety and biosecurity measures. Hence, this integrated and collaborative approach will serve as an efficient tool in the detection and further characterization of henipaviruses that are circulating within the continent.

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the sampling and henipavirus screening studies in African countries that have been published so far.

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References

- AbuBakar S, Chang L-Y, Ali ARM, Sharifah SH, et al. Isolation and molecular identification of Nipah virus from pigs. *Emerg Infect Dis* 2004; 10:2228–2230.
- Afonso CL, Amarasinghe GK, Bányai K, Bào Y, et al. Taxonomy of the order Mononegavirales: Update 2016. *Arch Virol* 2016; 161:2351–2360.
- Ball MC, Dewberry TD, Freeman PG, Kemsley PD, et al. Clinical review of Hendra virus infection in 11 horses in New South Wales, Australia. *Aust Vet J* 2014; 92:213–218.
- Barr J, Smith C, Smith I, de Jong C, et al. Isolation of multiple novel paramyxoviruses from pteropid bat urine. *J Gen Virol* 2015; 96:24–29.
- Basler CF. Nipah and Hendra virus interactions with the innate immune system. *Curr Top Microbiol Immunol* 2012; 359: 123–152.
- Bellini WJ, Harcourt BH, Bowden N, Rota PA. Nipah virus: An emergent paramyxovirus causing severe encephalitis in humans. *J Neurovirol* 2005; 11:481–487.
- Bonaparte MI, Dimitrov AS, Bossart KN, Crameri G, et al. Ephrin-B2 ligand is a functional receptor for Hendra virus and Nipah virus. *Proc Natl Acad Sci U S A* 2005; 102:10652–10657.
- Breed AC, Meers J, Sendow I, Bossart KN, et al. The distribution of henipaviruses in Southeast Asia and Australasia: Is Wallace's line a barrier to Nipah virus? *PLoS One* 2013; 8: e61316.
- Breed AC, Yu M, Barr JA, Crameri G, et al. Prevalence of henipavirus and rubulavirus antibodies in pteropid bats, Papua New Guinea. *Emerg Infect Dis* 2010; 16:1997–1999.
- Centers for Disease Control and Prevention (CDC). Update: Outbreak of Nipah virus—Malaysia and Singapore, 1999. *MMWR Morb Mortal Wkly Rep* 1999; 48:335–337.
- Chakraborty A, Sazzad HM, Hossain MJ, Islam MS, et al. Evolving epidemiology of Nipah virus infection in Bangladesh: Evidence from outbreaks during 2010–2011. *Epidemiol Infect* 2016; 144:371–380.
- Chew MH, Arguin PM, Shay DK, Goh KT, et al. Risk factors for Nipah virus infection among abattoir workers in Singapore. *J Infect Dis* 2000; 181:1760–1763.
- Ching PKG, Reyes VCDL, Sualdito MN, Tayag E, et al. Outbreak of henipavirus infection, Philippines. *Emerg Infect Dis* 2015; 21:328–331.
- Chowdhury S, Khan SU, Crameri G, Epstein JH, et al. Serological evidence of henipavirus exposure in cattle, goats and pigs in Bangladesh. *PLoS One* 2014; 8:e3302.
- Chua KB. Nipah virus outbreak in Malaysia. *J Clin Virol* 2003; 26:265–275.
- Chua KB, Bellini WJ, Rota PA, Harcourt BH, et al. Nipah virus: A recently emergent deadly paramyxovirus. *Science* 2000; 288:1432–1435.
- Chua KB, Goh KJ, Wong KT, Kamarulzaman A, et al. Fatal encephalitis due to Nipah virus among pig-farmers in Malaysia. *Lancet* 1999; 354:1257–1259.
- Chua KB, Koh CL, Hooi PS, Wee KF, et al. Isolation of Nipah virus from Malaysian Island flying-foxes. *Microbes Infect* 2002; 4:145–151.
- Chua KB, Lam SK, Goh KJ, Hooi PS, et al. The presence of Nipah virus in respiratory secretions and urine of patients during an outbreak of Nipah virus encephalitis in Malaysia. *J Infect* 2001; 42:40–43.
- De Araujo J, Lo MK, Tamin A, Ometto TL, et al. Antibodies against henipa-like viruses in Brazilian bats. *Vector Borne Zoonotic Dis* 2017; 20:1–4.
- Diederich S, Moll M, Klenk HD, Maisner A. The Nipah virus fusion protein is cleaved within the endosomal compartment. *J Biol Chem* 2005; 280:29899–29903.
- Drexler JF, Corman VM, Muller MA, Maganga GD, et al. Bats host major mammalian paramyxoviruses. *Nat Commun* 2012; 3:796.
- Drexler JF, Drost C, Corman VM, Gloza-Rausch F, et al. Henipavirus RNA in African bats. *PLoS One* 2009; 4:e6367.
- Eaton BT, Broder CC, Middleton D, Wang LF. Hendra and Nipah viruses: Different and dangerous. *Nat Rev Microbiol* 2006. 4:23–35.
- Edson D, Field H, McMichael L, Vidgen M, et al. Routes of Hendra virus excretion in naturally-infected flying-foxes: Implications for viral transmission and spillover risk. *PLoS One* 2015; 10:e0140670.
- Enserink M. 2000. Emerging diseases. Malaysian researchers trace Nipah virus outbreak to bats. *Science* 2000; 289:518–519.
- Fahr J, Abedi-Lartey M, Esch T, Machwitz M, et al. Pronounced seasonal changes in the movement ecology of a highly gregarious central-place forager, the African straw-coloured fruit bat (*Eidolon helvum*). *PLoS One* 2015; 10:e0138985.
- Field H, de Jong C, Melville D, Smith C, et al. Hendra virus infection dynamics in Australian fruit bats. *PLoS One* 2011; 6:e28678.
- Field H, de Jong CE, Halpin K, Smith CS. Henipaviruses and fruit bats, Papua New Guinea. *Emerg Infect Dis* 2013; 19: 670–671.
- Field H, Young P, Yob JM, Mills J, et al. The natural history of Hendra and Nipah viruses. *Microbes Infect* 2001; 3:307–314.
- Fischer K, Diederich S, Smith G, Reiche S, et al. Indirect ELISA based on Hendra and Nipah virus proteins for the detection of henipavirus specific antibodies in pigs. *PLoS One* 2018; 13:e0194385.
- Giles JR, Eby P, Parry H, Peel AJ, et al. Environmental drivers of spatiotemporal foraging intensity in fruit bats and implications for Hendra virus ecology. *Sci Rep* 2018; 8:9555.
- Goyen KA, Wright JD, Cunneen A, Henning J. Playing with fire—What is influencing horse owners' decisions to not vaccinate their horses against deadly Hendra virus infection? *PLoS One* 2017; 12:e0180062.
- Gurley ES, Montgomery JM, Hossain MJ, Bell M, et al. Person-to-person transmission of Nipah virus in a Bangladeshi community. *Emerg Infect Dis* 2007; 13:1031–1037.
- Halim S, Polkinghorne B, Bell G, van den Berg D, et al. Outbreak-related Hendra virus infection in a NSW pet dog. *Public Health Res Pract* 2015; 25:e2541547.
- Halpin K, Hyatt AD, Fogarty R, Middleton D, et al. Pteropid bats are confirmed as the reservoir hosts of henipaviruses: A comprehensive experimental study of virus transmission. *Am J Trop Med Hyg* 2011; 85:946–951.
- Halpin K, Young PL, Field H, Mackenzie JS. Newly discovered viruses of flying foxes. *Vet Microbiol* 1999; 68:83–87.

- Harcourt BH, Tamin A, Ksiazek TG, Rollin PE, et al. Molecular characterization of Nipah virus, a newly emergent paramyxovirus. *Virology* 2000; 271:334–349.
- Harcourt BH, Lowe L, Tamin A, Liu X, et al. Genetic characterization of Nipah virus, Bangladesh, 2004. *Emerg Infect Dis* 2005; 11:1594–1597.
- Hasebe F, Thuy NTT, Inoue S, Yu F, et al. Serologic evidence of Nipah virus infection in bats, Vietnam. *Emerg Infect Dis* 2012; 18:536–537.
- Hayman DT, Suu-Ire R, Breed AC, McEachern JA, et al. Evidence of henipavirus infection in West African fruit bats. *PLoS One* 2008; 3:e2739.
- Hayman DT, Wang LF, Barr J, Baker KS, et al. Antibodies to henipavirus or henipa-like viruses in domestic pigs in Ghana, West Africa. *PLoS One* 2011; 6:e25256.
- ICTV 2011. ICTV 9th Report (2011). Mononegavirales. March 2019. Available at https://talk.ictvonline.org/ictv-reports/ictv_9th_report/negative-sense-rna-viruses_-2011/w/negrna_viruses/194/mononegavirales Accessed March 28, 2019.
- Iehlé C, Razafitrimo G, Razainirina J, Andriaholinirina N, et al. Henipavirus and Tioman virus antibodies in pteropodid bats, Madagascar. *Emerg Infect Dis* 2007; 13:159–161.
- Islam MS, Sazzad HMS, Satter SM, Sultana S, et al. Nipah virus transmission from bats to humans associated with drinking traditional liquor made from date palm sap, Bangladesh, 2011–2014. *Emerg Infect Dis* 2016; 22:664–670.
- Kessler MK, Becker DJ, Peel AJ, Justice NV, et al. Changing resource landscapes and spillover of henipaviruses. *Ann N Y Acad Sci* 2018; 1429:78–99.
- Kirkland PD, Gabor M, Poe I, Neale K, et al. Hendra virus infection in dog, Australia, 2013. *Emerg Infect Dis* 2015; 21:2182–2185.
- Kohl C, Tachedjian M, Todd S, Monaghan P, et al. Hervey virus: Study on co-circulation with Henipaviruses in Pteropodid bats within their distribution range from Australia to Africa. *PLoS One* 2018; 13:e0191933.
- Lee B, Pernet O, Ahmed AA, Zeltina A, et al. Molecular recognition of human ephrinB2 cell surface receptor by an emergent African henipavirus. *Proc Natl Acad Sci U S A* 2015; 112:e2156–e2165.
- Li Y, Wang J, Hickey AC, Zhang Y, et al. Antibodies to Nipah or Nipah-like viruses in bats, China. *Emerg Infect Dis* 2008; 14:1974–1975.
- Lloyd-Smith JO, George D, Pepin KM, Pitzer VE, et al. Epidemic dynamics at the human-animal interface. *Science* 2009; 326:1362–1367.
- Luby SP, Gurley ES, Hossain MJ. Transmission of human infection with Nipah virus. *Clin Infect Dis* 2009; 49:1743–1748.
- Luby SP, Rahman M, Hossain MJ, Blum LS, et al. Foodborne transmission of Nipah virus, Bangladesh. *Emerg Infect Dis* 2006; 12:1888–1894.
- Manyweathers J, Field H, Longnecker N, Agho K, et al. “Why won’t they just vaccinate?” Horse owner risk perception and uptake of the Hendra virus vaccine. *BMC Vet Res* 2017; 13:103.
- Marsh GA, de Jong C, Barr JA, Tachedjian M, et al. Cedar virus: A novel henipavirus isolated from Australian bats. *PLoS One* 2012; 8:e1002836.
- Marsh GA, Todd S, Foord A, Hansson E, et al. Genome sequence conservation of Hendra virus isolates during spillover to horses, Australia. *Emerg Infect Dis* 2010; 16:1767–1769.
- McCormack JG. Hendra and Nipah viruses: New zoonotically-acquired human pathogens. *Respir Care Clin N Am* 2005; 1:59–66.
- McNabb L, Barr J, Crameri G, Juzva S, et al. Henipavirus microsphere immunoassays for detection of antibodies against Hendra virus. *J Virol Methods* 2014; 200:22–28.
- Middleton D, Pallister J, Klein R, Feng YR, et al. Hendra virus vaccine, a one health approach to protecting horse, human, and environmental health. *Emerg Infect Dis*. 2014; 20:372–379.
- Mills JN, Alim AN, Bunning ML, Lee OB, et al. Nipah virus infection in dogs, Malaysia, 1999. *Emerg Infect Dis* 2009; 15:950–952.
- Muleya W, Sasaki M, Orba Y, Ishii A, et al. Molecular epidemiology of paramyxoviruses in frugivorous *Eidolon helvum* bats in Zambia. *J Vet Med Sci* 2013; 76:611–614.
- Murray K, Rogers R, Selvey L, Selleck P, et al. A novel morbillivirus pneumonia of horses and its transmission to humans. *Emerg Infect Dis* 1995a; 1:31–33.
- Murray K, Selleck P, Hooper P, Hyatt A, et al. A morbillivirus that caused fatal disease in horses and humans. *Science* 1995b; 268:94–97.
- Murray KA, Daszak P. Human ecology in pathogenic landscapes: Two hypotheses on how land use change drives viral emergence. *Curr Opin Virol* 2013; 3:79–83.
- Negrete OA, Levroney EL, Aguilar HC, Bertolotti-Ciarlet A, et al. EphrinB2 is the entry receptor for Nipah virus, an emergent deadly paramyxovirus. *Nature* 2005; 436:401–405.
- Nowak R. Cause of fatal outbreak in horses and humans traced. *Science* 1995; 268:32.
- Olson JG, Rupprecht C, Rollin PE, An US, et al. Antibodies to Nipah-like virus in bats (*Pteropus lylei*), Cambodia. *Emerg Infect Dis* 2002; 8:987–988.
- Olufemi OT, Umoh JU, Dzikwi AA, Olufemi YO. Serological evidence of henipavirus among horses and pigs in Zaria and environs in Kaduna state, Nigeria. *Adv Biol* 2015; 2015:7.
- Ossa G, Kramer-Schadt S, Peel AJ, Scharf AK, et al. The movement ecology of the straw-colored fruit bat, *Eidolon helvum*, in sub-Saharan Africa assessed by stable isotope ratios. *PLoS One* 2012; 7:e45729.
- Páez DJ, Restif O, Eby P, Plowright RK. Optimal foraging in seasonal environments: Implications for residency of Australian flying foxes in food-subsidized urban landscapes. *Philos Trans R Soc Lond B Biol Sci* 2018; 373:pii:20170097.
- Parashar UD, Sunn LM, Ong F, Mounts AW, et al. Case-control study of risk factors for human infection with a new zoonotic paramyxovirus, Nipah virus, during a 1998–1999 outbreak of severe encephalitis in Malaysia. *J Infect Dis* 2000; 181:1755–1759.
- Paul L. Nipah virus in Kerala: A deadly zoonosis. *Clin Microbiol Infect* 2018; 24:1113–1114.
- Peel AJ, Kate S, Baker KS, Crameri G, et al. Henipavirus neutralising antibodies in an isolated island population of African fruit bats. *PLoS One* 2012; 7:e30346.
- Peel AJ, Sargan DR, Baker KS, Hayman DTS, et al. Continent-wide panmixia of an African fruit bat facilitates transmission of potentially zoonotic viruses. *Nat Commun* 2013; 19:1–27.
- Pernet O, Lee B, Schneider BS, Beaty SM, et al. Evidence for henipavirus spillover into human populations in Africa. *Nat Commun* 2014; 5:5342.
- Plowright RK, Eby P, Hudson PJ, Smith IL, et al. Ecological dynamics of emerging bat virus spillover. *Proc Biol Sci* 2015; 282:20142124.

- Plowright RK, Parrish CR, McCallum H, Hudson PJ, et al. Pathways to zoonotic spillover. *Nat Rev Microbiol* 2017; 15: 502–510.
- PromED-mail. Hendra virus, equine—Australia (10): (Queensland, New South Wales) human exposure. Pro-med: International Society for Infectious Diseases; 2011. Available at www.promedmail.org/post/20110713.2110 Accessed March 29, 2019.
- Rahman M, Chakraborty A. Nipah virus outbreaks in Bangladesh: A deadly infectious disease. *WHO South East Asia J Public Health*. 2012; 1:208–212.
- Reynes JM, Counor D, Ong S, Faure C, et al. Nipah virus in Lyle's flying foxes, Cambodia. *Emerg Infect Dis* 2005; 11: 1042–1047.
- Richter HV, Cumming GS. First application of satellite telemetry to track African straw-coloured fruit bat migration. *J Zool* 2008; 275:172–176.
- Rissanen I, Ahmed AA, Azarm K, Beatty S, et al. Idiosyncratic Mòjiāng virus attachment glycoprotein directs a host-cell entry pathway distinct from genetically related henipaviruses. *Nat Commun* 2017; 8:16060.
- Rota PA, Lo Mk. Molecular virology of henipaviruses. *Curr Top Microbiol Immunol* 2012; 359:41–58.
- Sazzad HM, Hossain MJ, Gurley ES, Ameen KM, et al. Nipah virus infection outbreak with nosocomial and corpse-to-human transmission, Bangladesh. *Emerg Infect Dis* 2013; 19: 210–217.
- Selvey LA, Wells RM, McCormack JG, Ansford AJ. Infection of humans and horses by a newly described morbillivirus. *Med J Aust* 1995; 162:642–645.
- Sendow I, Field HE, Adjid A, Ratnawati A, et al. Screening for Nipah virus infection in West Kalimantan province, Indonesia. *Zoonoses Public Health* 2010; 57:499–503.
- Sendow I, Ratnawati A, Taylor T, Adjid RMA, et al. Nipah virus in the fruit bat *Pteropus vampyrus* in Sumatera, Indonesia. *PLoS One* 2013; 8:e69544.
- Smith I, Broos A, de Jong C, Zeddeman A, et al. Identifying hendra virus diversity in pteropid bats. *PLoS One* 2011; 6: e25275.
- Tamin A, Harcourt BH, Ksiazek TG, Rollin PE, et al. Functional properties of the fusion and attachment glycoproteins of Nipah virus. *Virology* 2002; 296:190–200.
- Thomas DW, Henry M. *Eidolon helvum* African straw-coloured fruit bat. In: Happold M, Happold DCD, eds. *Mammals of Africa, Vol IV: Hedgehogs, Shrews and Bats*. London: Bloomsbury, 2013:232–234.
- Tong S, Chern SW, Li Y, Pallansch MA, et al. Sensitive and broadly reactive reverse transcription-PCR assays to detect novel paramyxoviruses. *J Clin Microbiol* 2008; 46:2652–2658.
- Wacharapluesadee S, Lumlerdacha B, Boongird K, Wanghongsa S, et al. Bat Nipah virus, Thailand. *Emerg Infect Dis* 2005; 11:1949–1951.
- Wacharapluesadee S, Samseeneam P, Phermphool M, Kaewpom T, et al. Molecular characterization of Nipah virus from *Pteropus hypomelanus* in Southern Thailand. *Virol J* 2016. 13:1–7.
- Wang L, Harcourt BH, Yu M, Tamin A, et al. Molecular biology of Hendra and Nipah viruses. *Microbes Infect* 2001; 3: 279–287.
- Wang LF, Cramer G. Emerging zoonotic viral diseases. *Rev Sci Tech* 2014; 33:569–581.
- Wang LF, Yu M, Hansson E, Pritchard LI, et al. The exceptionally large genome of Hendra virus: Support for creation of a new genus within the family Paramyxoviridae. *J Virol* 2000; 74:9972–9999.
- Weiss RA, McMichael AJ. Social and environmental risk factors in the emergence of infectious diseases. *Nat Med* 2004; 10: 70–76.
- Weiss S, Nowak K, Fahr J, Wibbelt G, et al. Henipavirus-related sequences in fruit bat bushmeat, Republic of Congo. *Emerg Infect Dis* 2012; 18:1536–1537.
- Wolfe ND. Bushmeat hunting, deforestation, and prediction of zoonotic disease emergence. *Emerg Infect Dis* 2005; 11: 1822–1827.
- Wu Z, Yang F, Ren X, Dong JF. Novel henipavirus, Mojiang paramyxovirus in rats, China, 2012. *Emerg Infect Dis* 2014; 20:1064–1068.
- Xu K, Broder CC, Nikolov DB. Ephrin-B2 and ephrin-B3 as functional henipavirus receptors. *Semin Cell Dev Biol* 2012; 23:116–123.
- Yadav P, Sudeep A, Gokhale M, Pawar S, et al. Circulation of Nipah virus in *Pteropus giganteus* bats in northeast region of India, 2015. *Indian J Med Res* 2018; 147:318–320.
- Yadav PD, Raut CG, Shete AM, Mishra AC, et al. Short report: Detection of Nipah virus RNA in fruit bat (*Pteropus giganteus*) from India. *Am J Trop Med Hyg* 2012; 87:576–578.
- Yob JM, Field H, Rashdi AM, Morrissy C, et al. Nipah virus infection in bats (order Chiroptera) in peninsular Malaysia. *Emerg Infect Dis* 2001; 7:439–441.
- Yoneda M, Guillaume V, Sato H, Fujita K, et al. The non-structural proteins of Nipah virus play a key role in pathogenicity in experimentally infected animals. *PLoS One* 2010; 5:e12709.
- Young PL, Halpin K, Selleck PW, Field H, et al. Serologic evidence for the presence in *Pteropus* bats of a paramyxovirus related to equine morbillivirus. *Emerg Infect Dis* 1996; 2: 239–240.
- Zhu Z, Dimitrov AS, Bossart KN, Cramer G, et al. Potent neutralization of Hendra and Nipah viruses by human monoclonal antibodies. *J Virol* 2006; 80:891–899.

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