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## Review Article

## Do Bats Still Constitute Viral Public Health Threat to Man and Livestock? -

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## ABSTRACT

Different species of bats have been historically, incriminated of transmitting viral diseases to humans and livestock. However, in spite of the intensive studies conducted in this area of research, the outcome was not as people were expecting, in the sense that very few viruses were found to cause overt devastating clinical diseases in humans and domestic animals. Indeed, this topic is so inviting, and is of great interest, especially with the emergence of the three novel Coronaviruses (SARS-CoV-1, MERS-CoV, and SARS-CoV-2) that involved the human population, globally, during the last two decades (2005-2019). The present article up-dates knowledge regarding the role of bats in the maintenance and spread of significant human and livestock virus infections, globally.

**Keywords:** Bats; SARS coronavirus; MERS CoV; COVID-19; Virus infections

## INTRODUCTION

It is of interest, in this article, to understand some information about bats before discussing their role in the epidemiology of viral diseases of humans and livestock. This involves their nature, classification, habitat, their roosts, feeding behavior and any property that can aid in understanding their role in the epidemiology of the virus diseases they can transmit to humans and livestock.

The gathered Information about bats, so far, indicated that they are flying mammals of the order *Chiroptera*. They constitute 24% of the mammalian species. The number of described species is now over 1,400 [1].

Taxonomically, bats belong to two suborders known: as *Megachiroptera* (megabats) and *Microchiroptera* (microbats/echolocating bats). The largest bats are the flying foxes (*Acerodon jubatus*); with a wingspan of 1.7 meters and weighing 1.6 kg. The smallest bat is 150 mm across the wings, [1,2].

## HABITAT AND ROOSTS OF BATS

Bats are internationally ubiquitous, they can be found in almost every type of habitat and almost all parts of the world, except the poles. They prefer warm weather. In winter, bats either hibernate or migrate to warmer areas.

Bats live in different ecological and social conditions. Some bats live in colonies; others live solitary [3-5].

## FEEDING BEHAVIOUR OF BATS

According to their feeding behavior bats are classified into: Vampire bats, Insectivorous bats, Fruit-eater bats and Nectivorous bats.

### Vampire bats

Vampire bats feed, solely, on blood. They are also called leaf-nosed bats. They belong to three species, of the family *Phyllostomidae*, subfamily *Desmodontinae*. They are classified into three different genera: *Desmodus*, *Diphylla* and *Diaemus*. The known three species are the common vampire bat (*Desmodus rotundus*), the hairy-legged vampire bat (*Diphylla ecaudata*), and the white-winged vampire bat (*Diaemus youngi*). Vampire bats are found in Central and South America [6,7].

The feeding behavior of Vampire bats varies to their species. For instance the most common species, the common vampire (*Desmodus*) is not fastidious and will attack any warm-blooded animal (including

humans). The white-winged vampire bat (*Diaemus*) appears to have a special preference for birds and goats.

An interesting behavior of the *Desmodus* bat that before feeding on an animal with thick hair, it can use its canines and teeth to remove

away the hair [8,9]; and that, the bat's saliva, left in the victim's resulting bite wound, has anticoagulants and compounds that prevent vaso-constriction, so that blood continues flowing while the feeding process of the bat.

### Fruit-eater bats, flying foxes, (Frugivores)

Flying foxes of the genus *Pteropus* are known as Fruit-eating bats (fruit, flowers & pollen). They are classified under the suborder *Megachiroptera*, family *Pteropodidae* [10]. They are the largest bats in the world.

The geographical distribution and movement of members of the family *Pteropodidae* ranges from Africa, the eastern Mediterranean, Madagascar and the Indian Ocean islands in the west, across mainland southern Asia, throughout the islands of the west Pacific from the Ryukyu Archipelago and Ogasawara-shato in the north, to coastal eastern Australia, new Caledonia and the Loyalty Islands in the south, and east to Fiji, Tonga, Samoa and the Cook Islands. Many species are restricted to islands, while a number of them are widespread. Fruit bats are known to travel over considerable distances [11,12].

### Insect-eater bats (Insectivores)

Insectivorous bats predominantly belong to the microbats' group. As their name implies, they are predators, prying on insects such as flies, mosquitoes, beetles, moth, grasshoppers, termites, bees, wasps [1], etc. So, these insectivorous bats are useful in the environment, they also disperse seeds but can be destructive when eating bees.

Of these insectivorous bats [1] are the Mexican free-tailed bats, (*Tadarida brasiliensis*), the little brown bat (*Myotis lucifugus*), the brown long-eared bat (*Plecotus auritus*) and many horseshoe bat species.

### Bats feeding on vertebrates (Predators)

Bats of prey feed on birds, lizards, frogs, small mammals and fish. Greater bat (*Nyctalus lasiopterus*) uses its large teeth to catch birds. It was reported that the fringe-lipped bat (*Trachops cirrhosus*) for example, is skilled at catching frogs. These bats locate large groups of frogs by tracking their mating calls, then plucking them from the surface of the water with their sharp canine teeth.

Some species, like the greater bulldog bat (*Noctilio leporinus*)



hunt fish. They use echolocation to detect small ripples on the water's surface, swoop down and use specially enlarged claws on their hind feet to grab the fish, then take their prey to a feeding roost and consume it. Interestingly, two species of bat are known, so far, to feed on other bats: the spectral bat (*Vampyrum spectrum*), and the ghost bat (*Macroderma gigas*).

From our personal experience [13], we saw feather and remains of birds in roosts of bats in air-conditioners in human lodges.

## VIRUS DISEASES TRANSMITTED FROM BATS TO HUMANS AND LIVESTOCK

Historically, a large number of viruses, that are potentially infectious to man and domestic animals, have been isolated from bats [14]. Of these only very few were confirmed as causing devastating disease outbreaks in humans and domestic animals [15]. The main virus diseases confirmed to be contracted from bats and caused serious fatal outbreaks, are the henipaviruses, (Hendra virus (HeV) and Nipah virus (NiV)), the vampire bat rabies virus and to a lesser extent, the Australian Bat Lyssavirus (ABLV) infection [16], which can cause a fatal human illness indistinguishable from classic rabies.

Before and following emergence of the SARS-CoV-2, several related coronaviruses, were identified from bats. Zhou [17] gave a summary of most of these viruses. These included the RaTG13 and seven others, identified by ZHOU et al these were (RpYN06, RsYN04, RmYN05, and RmYN08 which were related to SARS-CoV-2, while the remaining three (RsYN03, RmYN07, and RsYN09) were closely related to SARS-CoV. Others were the BANAL 52; BANAL 103; BANAL 236, which are the closest to SARS-CoV-2; RmYN02, RacCS203 [18] the STT182 and STT200 [19]. Presence of these viruses and possibly others, in bats, indicate that bats are harboring coronaviruses that are closely-related to the SARS-CoV-2 over a wide range of localities in Asia. Such a situation can indeed, impose a future threat to human health.

## HENIPAVIRUSES

Taxonomically, the genus *Henipavirus* is a member of the family *Paramyxoviridae*, subfamily *Orthoparamyxovirinae* order *Mononegavirales* containing five species [20]. The present article deals with two virus species (hendra and Nipah) of the genus *henipavirus*. Characteristics of the genus *henipavirus* are typical of their family *orthomyxoviridae*. The virions are pleomorphic, ranging in size from 40 to 600 nm in diameter; their capsid is helical in structure and covered by a lipid membrane. The capsid core is tightly associated with the RNA to form the *nucleocapsid*. *Henipaviruses* are naturally harbored by *pteropid* fruit bats (flying foxes) and microbats of several species.

Beside Hendra virus and Nipah virus, two new *henipaviruses* were discovered in bats. These are the Cedar virus and the Ghanaian bat virus. Cedar virus was isolated from urine samples collected from a flying fox colony in Australia. There is no evidence that Cedar virus is pathogenic in humans [21]. Inclusion of the Ghanaian bat virus was based on detection of viral RNA rather than isolation of a novel virus [22,23].

A *henipavirus* RNA called Mojiang virus RNA was detected from rectal swabs from rats (*R. flavipectus*), from Mojiang locality in China. It was not detected in bats.

## GEOGRAPHICAL DISTRIBUTION OF MEMBERS OF THE GENUS HENIPAVIRUS

Published data on the geographical Distribution of members of the genus *Henipavirus* [24] indicated that they were recorded in Australia, Malaysia, Bangladesh, Cambodia, India, Thailand and Indonesia. HeV has been isolated from horses, humans, and flying foxes in Australia and NiV from humans, pigs, and flying foxes in Malaysia, Bangladesh, and Cambodia. NiV has also been isolated from fruit partially eaten by flying foxes in Malaysia, and NiV RNA has been detected in human patients and bats in India and Thailand, respectively. The geographic distribution of *Pteropus* species which ranges from the east coast of Africa, through the Indian subcontinent and Southeast Asia, north to Okinawa and south to Australia, suggests that *henipaviruses* may also be found in flying fox populations in geographically more diverse locations.

## TRANSMISSION OF HENIPAVIRUSES

Naturally, *henipaviruses* (Hendra & Nipah) are transmitted from bats to their definitive hosts (humans, horses & pigs), in an indirect manner; i.e. bats don't attack the susceptible hosts directly. Thus the sequence of events regarding infection with these two viruses takes two pathways. Initially, there is a sylvan cycle between the reservoir bats. Bat-to-bat transmission of Nipah and Hendra virus occurs through direct contact, with transmission being aided by the high density of bats in roosts and the use of urine in grooming. This is followed by an indirect transmission from bats to the definitive hosts.

Published data indicated that during infection of bats, Hendra & Nipah viruses are shed mainly in urine, but can also be detected in throat and rectal swabs. Vertical transmission has been shown to occur in pregnant bats.

It can be concluded that both hendra virus and nipah virus are circulated within fruit bats, horses, pigs and humans. The viruses are shed in urine of bats, and respiratory secretions in horses, pigs and humans. Regardless of the routes of shedding, close contact remains the main requirement to ensure transmission.

## HENDRA VIRUS DISEASE

Hendra virus disease was reported for the first time in a suburb of Brisbane, Australia, called Hendra, in 1994, as a small outbreak of a fatal respiratory disease in horses in a stable in that village. Shortly following the death of the horses, horse trainer who had been in close contact with the sick horses, developed an influenza-like illness, which progressed to fatal acute respiratory distress syndrome [25].

The disease was further reported during 1999 and 2004, also involving humans and horses, causing a high case fatality rate, [26]. Studies on the etiologic agent showed that it belongs to the family *Paramyxoviridae* genus *Henipavirus*, and that its natural hosts and reservoirs are the fruit bats ("flying foxes") of the family *Pteropodidae* genus *Pteropus*, including the black flying fox (*Pteropus alecto*), gray-headed flying fox (*P. poliocephalus*), little red flying fox (*P. scapulatus*), and spectacled flying fox (*P. conspicillatus*) (Table 1).

*Pteropus* is the largest genus in the family *Pteropodidae*, comprising about 65 species of flying foxes [1]. Members of this genus, are widespread, (Table 2) through the Indo-Pacific region westward to the islands off eastern Africa; mainly dwelling islands.

**Table 1:** The main bat-transmitted viruses, causing disease in humans and livestock.

Name of Virus	Date & Place of Discovery	Classification	Reservoirs	Hosts Affected	Disease	Case Fatality Rate (Cfr %)	Geographical Distribution
Hendra virus	Hendra village – Australia, 1996.	Family: <i>Paramyxoviridae</i> ; genus: <i>Henipavirus</i>	***Fruit-bats (flying foxes)	Humans & horses	Hendra	90% in horses & high case fatality rate in humans.	Australia & South East Asia
Nipah virus	Kampung Sungai - Nipah village – Malaysia, 1998.			Humans & pigs	Nipah	40-75% in humans. 40% in pigs.	Malaysia, Australia & South East Asia.
Vampire bat rabies virus	Brazil, 1911.	Family: <i>rhabdoviridae</i> ; Genus: <i>lyssavirus</i>	Vampire bats	Humans & hot-blooded animals	Vampire bat rabies Rabies –like disease	100%	South America & nearby geographical regions.
Australian Bat Lyssavirus (ABLV)	Australia,			Flying foxes (fruit bats) & the yellow-bellied sheath-tailed, microbat bat ( <i>Saccolaimus flaviventris</i> ).	Humans	Highly fatal.	Australia & Thailand

\*\*\* = *Pteropus alecto* (Black Flying Fox); *P. conspicillatus* (Spectaled Flying Fox); *P. poliocephalus* (Grey-Headed Flying Fox) *P. scapulatus* (Little Red Flying Fox).

**Table 2:** Fruit Bat (Flying Foxes) Species (Genus *Pteropus*): Reservoirs Of Hendra, Nipah & Australian Bat Lyssavirus.

Bat's Common Name	Fruit Bat (Flying Fox) Species	Viruses Disease Transmitted	Geographical Distribution
Black Flying Fox	<i>Pteropus alecto</i>	HENDRA & NIPAH (H&N)	Australia, Malaysia, Bangladesh, Cambodia, India, Thailand, Indonesia and East Coast of Africa.
Spectaled Flying Fox	<i>p. conspicillatus</i>	(H&N)	
Grey-Headed Flying Fox	<i>P. poliocephalus</i>	(H&N)	
Little Red Flying Fox	<i>P. scapulatus</i>	(H&N)	
Australian bat Lyssavirus (ABLV)	<i>Pteropus alecto</i> ; <i>p. conspicillatus</i> ; <i>P. poliocephalus</i> ; <i>P. scapulatus</i>	ABLV	Australia, Thailand.

## Epidemiology

Hendra virus causes fatal pneumonia and encephalitis in horses and humans [26].

This virus is maintained by enzootic, subclinical infection in certain species of fruit bats. The precise mechanism of virus transmission from bats to non-natural hosts such as horses and humans probably involves environmental contamination by secretions or excretions from the bats (saliva, feces, urine, placental fluids). The sporadic nature of the outbreaks is likely the result of changes in the feeding behavior of the bats due to changes in food supplies or habitat incursions that facilitate close interaction of horses and bats.

Kirkland, et al. [27], isolated hendra virus from a sick dog. However, the role of dogs in the epidemiology of hendra disease does not seem to be significant.

People at high risk of infection, include veterinarians and veterinary assistants, farriers, equine dentists, and feed delivery merchants, horse owners and stud workers. High exposure includes coming within five meters of an infected or suspect horse, or contact with blood, body fluids or faeces of infected or suspect horses or with contaminated surfaces.

The cycle of infection of the disease starts from the Fruit bat (flying fox), which appears to carry the virus without suffering any ill effects, excretes the virus in its urine. The horse ingests pasture or fruit contaminated with infected bat urine, droppings or saliva. The virus in the horse's body fluids (including blood, urine, saliva or nasal secretions) can then be transmitted to a person during close contact.

Although there is no evidence, so far, to suggest direct infection of humans from fruit bats, it is advisable to keep away from fruit bats to avoid any possibility of transmission of the infection.

## Hendra virus infection in humans

Fruit bats are the reservoir of infection. Disease transmission requires close contact with infected horses or bat excreta. There is no evidence of human-to-human infection by Hendra virus [28].

Hendra virus tends to attack either the respiratory system (lungs) or the nervous system (brain). The incubation period usually ranges from five to 21 days. The symptoms of infection in a person can include fever, tiredness, headache, and dry cough, sore throat, breathing difficulties, dizziness, confusion and insomnia.

Fatal complications have been recorded such as septic pneumonia – severe lung infection involving pus, abscesses and destruction of lung tissue. Meningitis, severe encephalitis that can lead to convulsions and coma and death were reported [29].

Hendra virus is classified as a Hazard Group 4 pathogen, which requires the highest level of biosecurity procedures.

## Treatment of hendra virus infection

As a virus infection, there is no treatment of Hendra clinical infection. So strategy of treatment is to ease symptoms and reduce the risk of complications until the person recovers. Hospitalization of the sick patients and close monitoring drugs and fluids given intravenously and life support if necessary – for example, mechanical ventilation are important in saving their lives [30].

## Control and prevention of hendra virus outbreaks

It is taken that a single confirmed case of Hendra virus in a person is considered an outbreak. If an infection occurs, neighboring states are expected to work as a team to locate and control the infection to reduce the risk of transmission.

As there are no vaccines currently in use; then, if a person comes in-contact with a sick horse, the best preventive measures have to be taken. The strategy is to follow, strictly, the general known hygienic personal measures. Beside this, special procedures are required. These include using of clean equipment between handling each horse, to void contact with the sick horse, to keep the sick horses isolated from other healthy horses and seek immediate veterinary advice. It is vital to avoid contact with secretions (including blood, urine, saliva or nasal secretions) even when the horse is dead – the virus may still be active. Refrain from kissing horses on surfaces such as the muzzle and side of the face.

Horse owners should minimize possible contact between horses and bat roosts.

## Vaccines for hendra virus infection in humans and animals

Since the discovery of the Hendra virus, in 1994, researchers have been working painstakingly to arrive at a potent vaccine to control this serious disease. Variable results were attained; however, no satisfactory vaccine was available to be used. In a recent study, Geisbert, et al. [31], reported that they have formulated a subunit vaccine from the attachment glycoprotein ectodomain. The vaccine, though in phase one clinical trials, gave promising results in a single dose in humans.

## Hendra virus infection in horses

In horses, Hendra infection usually takes a peracute form. The incubation period is 8 to 12 days. Generally, the clinical signs of Hendra virus in horses are similar to African Horse Sickness. Horses that are infected with virus develop severe and typically fatal respiratory disease that is characterized by fever, dyspnea, vasculitis, severe pulmonary edema, lethargy, anorexia, respiratory distress, ataxia, tachycardia, and frothy nasal discharge, when the horse is terminating. Encephalitic and marked subcutaneous edema may be observed in some cases. Infected horses excrete virus in their urine, saliva, and respiratory secretions. However, the virus is highly labile and can be destroyed by heat, lipid solvents, detergents, formaldehydes, and agents. The case-fatality rate in horses can reach 90%.

Natural and experimental data, indicated that the most likely route of transmission of Hendra virus between horses is through very close contact with infected horses in the late stage of the disease, i.e. when virus shedding is at its peak. On the other hand handling of sick horses without adequate measures to prevent cross-contamination could contribute to the spread of Hendra virus among horses also.

## NIPAH VIRUS DISEASE

The discovery of Nipah as a disease was made, for the first time, in 1998-1999, when a highly fatal disease affected pigs and adult humans in Kampung Sungai Nipah, Malaysia [32]. It was then reported in Singapore [33]. Later it was reported in India [34]. The disease was

characterized by respiratory and neurological symptoms in both pigs and humans. [35-37].

Humans were infected due to their contact with sick pigs. Outbreak in humans, resulted in a case fatality rate of 38.4%. Also in that occasion, more than million pigs were culled. The movement of pigs in that region, aided in the spread of the disease trans-territorially.

Virological investigations in the Nipah disease resulted in isolation of a virus from cerebrospinal fluid of a human fatal case. The virus was found to be closely related to the Hendra virus, it was named Nipah virus.

Outbreaks of the Nipah virus in pigs and other domestic animals such as horses, goats, sheep, cats and dogs were first reported during the initial Malaysian outbreak in 1999.

## Nipah virus infection in humans

Infection of Nipah virus in humans is characterized by an initial incubation period of 3-14 days after which the clinical signs are evident. The signs may be presented by variable degree of severity; including fever, headache, cough, sore throat, difficult of breathing, vomiting, disorientation, drowsiness, or confusion, seizures, coma, encephalitis leading to coma and death within 24-48 hours [38].

The symptoms can extend from 3-14 days. The case fatality rate is 40-75%.

Latent or dormant infections following exposure to Nipah infection have been reported. Sequelae due to Nipah virus infection were reported months or years following exposure; they are manifested as persistent convulsions and changes in the personality of the patients.

Like Hendra, Nipah virus is transmitted to the definitive hosts by the fruit bats (*Pteropus* spp.), [39,40].

It was observed that transmission of Nipah virus infection to human, in Malaysia and Philippines occurred through the definitive hosts, pigs and horses [41]. In Bangladesh, transmission to humans is thought to have occurred from bats to humans mainly through the consumption of raw palm sap contaminated with Nipah virus by fruit bats [42].

It was reported that in 2014, a limited outbreak of encephalitis in two villages in the Philippines was traced to the slaughtering and consumption of horses with neurological disease. Serologic evidence indicated that horses and humans were infected with Nipah virus.

Human-to-human transmission of Nipah virus has been reported to be so efficient [43] to the extent that 75% of the cases in India, Bangladesh and the Philippines were attributed to human-human transmission. Epidemiological studies have shown that close contact is required for human-to-human transmission of Nipah virus [44]. For instance, some social behavior of citizens in some countries can aid in spread of the disease. This was reported in Bangladesh where cultural practices require family members to care for their hospitalized relatives and friends. A situation that facilitated spread of Nipah virus infection. Nipah virus is shed, during the acute phase, from infected humans from urine, mouth and nose [45].

Nipah infection from dead persons was reported [46].

It is evident that nosocomial infection of hospital staff is significant [47-49].

### Nipah virus infection in pigs

Nipah infection in pigs ranges from non-symptomatic to severe acute form. The incubation period of Nipah in pigs is 4-14 days; during which pigs are infectious. The virus is highly contagious in pigs.

The acute disease is manifested as an acute febrile illness with respiratory signs such as nasal discharge, a barking cough and labored breathing, as well as neurological signs [50]. The severity of Nipah virus disease in naturally infected pigs depends on the age of the animals. The mortality rate in pigs in Malaysia was high (~40%) in suckling pigs, but low (1–5%) in pigs over 4 weeks of age [50].

Nipah virus should be suspected if pigs also have an unusual barking cough or if human cases of encephalitis are present.

Epidemiological data from the Nipah virus outbreak in Malaysia indicated that transmission of Nipah virus between pigs, in close contact, is rapid and efficient, through direct contact with nasal secretions.

### LABORATORY DIAGNOSTIC TESTS OF BOTH HENDRA & NIPAH VIRUSES

Four diagnostic tests for diagnosis of Nipah and Hendra viruses have been successfully developed [51-53] These are virus isolation, Electron Microscopy, immunohisto-chemistry, and Polymerase Chain Reaction (PCR) and sequencing. Two diagnostic tests for the detection of antiviral antibodies are Serum Neutralization Test (SNT) and Enzyme-Linked Immunosorbent Assay (ELISA) [54]. Because Hendra and Nipah viruses are classified internationally as Biosecurity Level 4 (BSL4) agents, tests necessarily involving live virus (i.e., virus isolation and SN tests) should only be carried out under physical containment level 4 (BSL4) conditions.

Both Hendra and Nipah viruses grow well in Vero cells from a range of tissue specimens, including brain, lung, kidney, and spleen. Cytopathic effect usually develops within 3 days, and virus isolates may be specifically identified by immunostaining, neutralization with specific antiserum, PCR, and EM [55].

### LYSSAVIRUSES FROM BATS CAUSING RABIES IN HUMANS & LIVESTOCK

Rabies virus is one of the most dangerous viruses known in nature. It causes almost 100% case fatality rate in untreated exposed humans or animals. Historically, classical terrestrial rabies in mammals is known to be circulated and maintained in nature in a sylvan cycle among wild canines. Domestic canines, like dogs, get infection when bitten by rabid wild canines, like foxes, skunks, and mongoose. Thus, in the urban societies rabies infection is maintained mainly, by pets and stray dogs.

Other way of maintenance of rabies virus in nature was discovered to be through bats.

Members of the genus *Lyssavirus* are known to cause classical rabies in mammals. The virus is transmitted between susceptible individuals directly by bites, scratches or contamination of abraded mucous membranes with infected saliva. Bats (order *Chiroptera*) and carnivores (order *Carnivora*), are the principal reservoir hosts for *lyssaviruses*. Viruses assigned to the genus *lyssavirus* are distributed world-widely.

Although many countries have remained free from classical terrestrial rabies from canines for an extended length of time; evidence indicated that human cases of bat-associated rabies have been identified in them during the last decades [56].

(Table 3), shows the world distribution of *lyssaviruses* that cause bat-associated rabies. In Europe, two *lyssaviruses* are reported [57]; the European Bat *Lyssavirus-1* (EBLV-1) and European Bat

**Table 3:** Virus members of the genus *lyssavirus* transmitted by bats.

<i>Lyssavirus</i> Species	Virus Abbreviation	Locality Of Isolation	Disease
1. Vampire bat <i>Lyssavirus</i>	VBLV	INITIALLY IN BRAZIL, THEN SOUTH AMERICA	VAMPIRE BAT RABIES.
2. Aravan Bat <i>Lyssavirus</i>	ARAV	KYRGHZYSTAN – 1. Central Asia	LIMITED RABIES-LIKE INFECTION (LRLI)
3. Australian bat <i>lyssavirus</i>	ABLV	AUSTRALIA	SEVERE RABIES-LIKE INFECTION
4. Bokeloh bat <i>lyssavirus</i>	BBLV	GERMANY	(LRLI)
5. Duvenhage bat <i>lyssavirus</i>	DBLV	South Africa	(LRLI)
6. European bat 1 <i>lyssavirus</i>	EBLV-1	Netherlands; Poland; Germany; Denmark; Spain; France.	(LRLI)
7. European bat 2 <i>lyssavirus</i>	EBLV-2	Britain; Netherlands; Germany; Finland; Switzerland.	(LRLI)
8. Gannoruwa bat <i>lyssavirus</i>	GBLV	India	(LRLI)
9. Irkut bat <i>lyssavirus</i>	IRKBV	Russia & China	(LRLI)
10. Lagos bat <i>lyssavirus</i>	LBV	Nigeria	(LRLI)
11. Lleida bat <i>lyssavirus</i>	LLEBV	Spain	(LRLI)
12. Shimoni bat <i>lyssavirus</i>	SHIBV	Kenya	(LRLI)
13. Taiwan bat <i>lyssavirus</i>	TWBLV	Taiwan	(LRLI)
14. West Caucasian bat <i>lyssavirus</i>	WCBV	Russia	(LRLI)
15. Kotalahti bat <i>lyssavirus</i>	KBLV	Finland	(LRLI)

*Lyssavirus-2* (EBLV-2). The EBLV-1, was frequently isolated in The Netherlands, Northern Germany, Denmark, Poland and also in parts of France and Spain [57]. Most EBLV-2 isolates originated from the United Kingdom (UK) and the Netherlands, Germany, Finland and Switzerland. The Bokeloh bat *lyssavirus* [58] was reported in Germany and France. A bat *lyssavirus* (Lleida) was identified in Spain [59].

A tentative novel member of the genus *Lyssavirus*, designated as Kotalahti bat *lyssavirus*, was detected in a Brandt's bat (*Myotis brandtii*) in Finland. Based on phylogenetic analysis, the virus differs from other known *lyssaviruses*, being closely related to Khujand virus, Aravan virus, Bokeloh bat *lyssavirus* and European bat *lyssavirus 2*.

In Asia, reports on identification of *lyssaviruses* or antibodies to *lyssaviruses* have been published. However, virus isolations were reported from various countries. A novel *lyssavirus* was isolated from brains of Indian flying foxes (*Pteropus medius*) in Sri Lanka. Phylogenetic analysis of complete virus genome sequences, and geographic location and host species, provides strong evidence that this virus is a putative new *lyssavirus* species, designated as Gannoruwa bat *lyssavirus*. In China there is serological evidence of *lyssaviruses* in bats; but the Irkut virus was isolated from a bat which fatally infected a woman [60]. The Aravan Bat *Lyssavirus*, the Aravan Bat *Lyssavirus* was isolated from Kyrgyzstan, Central Asia; the Taiwan bat *lyssavirus*, from Taiwan; the West Caucasian bat *lyssavirus* from West Caucasian, Russia.

Interestingly, in Latin America, more human rabies cases are now related to exposure to vampire bats than to carnivore bites [61]. Bovine paralysis caused by rabid vampire bat bites also has a major economic impact on cattle production in several South American countries [62]. In Africa, several *lyssaviruses* were reported to be associated with bat rabies. Examples are the *Duvenhage Lyssavirus* (DUVV) in South Africa and Kenya, Shimoni bat *lyssavirus* in Kenya and Lagos bat *lyssavirus* Nigeria [63].

In Australia: The first record of a bat transmitted bat *lyssavirus* in Australia was made in 1996, when a virus was isolated from tissues of a black flying fox (*Pteropus alecto*) with signs of encephalitis found near Ballina, New South Wales, Australia [64,65]. Few months later, a woman six months later, a bat handler from Rockhampton, Queensland, Australia, developed numbness and weakness in her arm and later died from encephalitis. She had been infected with what is now known as Australian Bat *Lyssavirus* (ABLV). In 1998, a woman from Mackay (Queensland, Australia) was diagnosed with ABLV infection at her death, 2 years after having been bitten by a sick bat [66].

In the present article two *lyssaviruses* will be discussed: the Vampire bat virus and the Australian Bat *Lyssavirus* (ABLV).

## VAMPIRE BAT-ASSOCIATED RABIES IN LIVESTOCK (DERRIENGUE)

There are three species of blood-feeding (hematophagous) bats found exclusively in Latin America. Only one of these, the common vampire bat *Desmodus rotundus*, is a well-known reservoir for rabies.

Evidence that bats are involved in rabies transmission was reported by Carini in 1911 in Brazil [67]. In 1931, the first isolation of the rabies virus was successfully made from a common vampire bat (*Desmodus rotundus*) of the family *Phyllostomidae*, [68]. From

1931, several publications had been reported indicating isolation of rabies virus from bats, e.g. Lima in Brazil [69] Pawan [70,71] who provided evidence connecting paralytic rabies with fruit eating bats in Trinidad.

Vampire bats are only found in Latin America, where they obtain their nutrition by blood-sucking (haematophagy) from animals and humans. Indeed, this haematophagy which has been associated with rabies transmission in cattle, have constituted a scourge to livestock industry [72].

Derriengue, a Spanish word for a fatal paralytic disease [73] is the common name of bovine rabies in Latin America. The clinical signs, exhibited by an infected animal are restlessness or excitement with sudden onset of hind limb paralysis which progresses to the fore limbs. There is difficulty in swallowing leading to excess salivation. The disease is fatal. Cattle and horses are the preferred prey for Vampire bats. Once a herd of cattle became known for a colony of bats, then they become a continuous target for the bats [74].

### Vampire bat-associated rabies in humans

Human deaths associated with vampire bat attacks were noted since the 16th century. However, the first documented outbreak of human rabies of vampire bat origin occurred in Trinidad in 1927, since then, these outbreaks have continued to occur and constituted a challenge to both the veterinary and human health settings. Historically, human mortality due to rabies transmitted by vampire bats has remained low because bats do not usually attack humans. However, in the absence of livestock, humans can become victims of vampire attacks, particularly if sleeping outdoors or in buildings to which bats can gain access [75]. Also, according to the same authors, the Pan-American Health Organization reported that, between 2010-2012, the Cases of human rabies in 10 countries in Latin America and the Caribbean, were 111, and that 63 (56.8%) of them were due to bat transmitted rabies.

The number of rabies cases transmitted by vampire bats, have increased and the patterns of occurrence of this disease are also changing [76]. This has been attributed to some causes: (i) association with increased reporting and diagnosis; (ii) changes in the vampire bats demography and distribution. Each of these, either individually or in combination, could have increased the reported number of human infections with rabies virus of vampire bat origin.

Vampire bat bites usually occur in exposed areas of the skin such as toes and the face. Blood-feeding by *Desmodus rotundus* bat, has been reported as the main cause of human bat rabies in Brazil [77].

Vampire bats have found roosting sites in close proximity to human dwellings as a result of the environmental changes that took place in many regions, such as deforestation, and land clearance for better conditions for implantations. This has indeed, reduced the numbers of natural prey species and brought vampire bats into contact with livestock and man.

Example of a Case History of Bat Rabies in a Human (Quoted by Johnson, et al. [78])

In this concept, it is felt that a report of a case history of bat rabies in a human in 2020, (ANON 78), is of high significance in describing vampire bat rabies in human. The patient in the study, developed fatigue with pain in his left hand and shoulder. Physical examination



revealed generalized areflexia and a drooping left upper eyelid. The patient developed fever with a temperature of 38.4 °C and he became generally less responsive. Following removal of the ventilator support, the patient died shortly after. Rabies virus was confirmed by detection of viral antigen in brain tissue taken at postmortem using the PCR and nucleic acid sequencing. Also Rabies virus-specific IgM and IgG were detected in the patient's CSF and serum. An interview with the patient's family, indicated that the patient had been bitten by a vampire bat while asleep; and that he didn't seek any medical advice and he was not vaccinated against rabies.

### Control of vampire bat rabies

Dissemination of vampire bat rabies has been found to be directly correlated to the spread of the Vampire bat reservoir. Realizing this, efforts to combat and control these reservoir bats has been continuing from early days. Several authors have discussed the different methods adopted for control of the vampire bat, e.g. Delpietro, et al. [79]. Various methods of control have been used in South American countries with variable results, as reported by Johnson et al Vampire bat control measures included a combination of different methods; which included repellents, physical barriers, and roost destruction and other lethal population reduction techniques.

From the 1970s and annually, the area inhabited by the common vampire bat, still shows bovine paralytic rabies at high prevalence and that the vampire bat rabies kills tens of thousands of livestock, dozens of humans and an indeterminate quantity of wildlife in South America [80].

Losses due to vampire bat rabies in livestock in South America are tremendous [81,82].

### THE AUSTRALIAN BAT LYSSAVIRUS (ABLV)

For decades, flying fox (e.g. *Pteropus alecto*) have been known to feed on fruits and plants; and were not incriminated of playing role in diseases transmitted from bats until in 1996, a *lyssavirus* virus was isolated for the first time, from tissues of a black flying fox (*Pteropus alecto*) showing signs of encephalitis found near Ballina, New South Wales, Australia, [83]. That virus was designated the Australian Bat *Lyssavirus* (ABLV). Through 1996, ABLV infection has been reported several times in Australia. Infected patients showed encephalitis and general nervous signs, like rabies, which led to death. The microbat (*Saccolaimus flaviventris*), has also been incriminated in transmission of the ABLV [84,85]. All the ABLV cases were associated with direct contact with fruit bats or their secretions e.g. saliva or through bat bites or scratches. ABLV infection does not require an intermediate host.

To avoid ABLV disease people should avoid handling of bats or come near bats as advised by the CDC [86]. Reported data indicated that most bat bites and scratches occur when people try to help sick or injured bats. If a person is bitten or scratched by a bat, the wound should be washed thoroughly well, apply antiseptic and seek immediate medical advice.

Rabies vaccine and immunoglobulin were found to be effective in prophylactic and therapeutic protection from ABLV infection [87].

### DISCUSSION

Before discussing the role of bats in the epidemiology of the viral

diseases they transmit to humans and livestock, it is worthwhile to understand the contacts between bats humans and livestock that can happen in nature. The contact can generally be direct or indirect, as summarized below:

- With the exception of the Vampire bats; bats do not attack humans or livestock; though they may roost nearby human lodges.
- When humans change the ecological conditions, where bats used to roost, such as by removing agricultural range and expand to build their lodges, then bats can come closer to these human lodges and can roost in their environment and attack people.
- As wild animals, bats can react, defensively, against any handling by humans. The reaction can be serious biting or scratching.
- When bats feed on fruits, they transmit some viruses to these fruits, so when humans consume those fruits, contaminated with the bat's saliva, they can be infected. A good example is the transmission of Nipah Virus by fruit bats.
- For research purposes, some researchers go to caves, to collect some research samples from the bats or their roosts. Some of those researchers got rabies infection by inhalation of rabies virus from the atmosphere of these caves [88]. This happens when the virus gets into the respiratory tract, where it may find abrasions through which it gains entry into the body of the individual. Laboratory workers handling bat rabies virus, or rabies virus in general, should be very careful. In this concept, it has been reported that, two cases of rabies have been attributed to airborne exposures in laboratories [89,90].

Since early days, bats have been hunted in some parts of the world, for reasons including food, perceived medical value, for hide or teeth, or for sport. At least 167 species of bats have been exposed to hunting globally. Bats are consumed for their meat in several regions, including Oceania, Australia, Southeast Asia, China, and West and Central Africa.

Bats have several characters that qualified them as efficient transmitter of viruses. These characters can be summarized in the following:

- a. As stated above, they constitute the second largest order (24%) in the mammalian kingdom, with 1400 species [83].
- b. They are the only flying mammals and that they are distributed all over the globe except the poles. Their capability to fly can enable them to transmit viral diseases during their search for forage, over a wide range of land. This indeed is also aided by their seasonal migration [91].
- c. The social life of bats indicated that they are one of the most social groups of mammals. They roost together in very large and dense colonies. Such dense clustering, gives a good chance of exchange of viruses within members of the group. Again the grooming between members with their urine and saliva, also helps in spreading of viruses within the group.
- d. Roosting of bats shows that they can inhabit a wide range of



ecological niches; such as caves and trees. The most important in the epidemiology of bat-transmitted diseases is the roosting of bats near human lodgings or agricultural areas.

- e. Under harsh conditions such as cold winter and lack of food, bats either migrate to warmer areas with more abundant food supply, or hibernate [92,93]. During hibernation bats adapt themselves to the surrounding conditions, such as the low freezing temperature. They also reduce their physiological functions e.g. reducing the heart rate, the respiratory rate and energy costs by about 98%. This condition allows the bat to survive for a long time without the need for food. Hibernation may extend to over six months in bats. Hibernating bats choose roosting niches (hibernacula) that are having ideal temperature and humidity. Such niches could be caves, mines, and rock crevices [93].

The viruses contained in the hibernating bats remain viable during the period of hibernation. So, it has been suggested by Beer & Richards, above, [92] that, long periods of hibernation lead to suppression of immunity, and the stress of arousal from hibernation reactivates the virus in bats with lower levels of anti-viral immunity.

- f. Some bats, e.g. the *Microchiroptera*, have the ability to echolocate to produce laryngeal vocalization for navigation purposes. This behavior was found to cause production of aerosols with virus particles in the nasal mucosa and saliva, enhancing transmission to other individuals [94].
- g. It has been reported that bats (*Chiroptera*) are the longest-living mammalian order [95]. By virtue of this character, bats as long-lived virus carriers would have more opportunities to transmit the infection within bats populations and to humans or livestock.

Calisher [96] reported that, since 1931 and hitherto, more than 100 viruses from 28 virus families have been either isolated from or otherwise detected in bats. These include viruses of families that were confirmed to cause significantly highly fatal disease outbreaks in humans and livestock, like *Hepadnaviridae*, *Rhabdoviridae*. Others are: *Adenoviridae*, *Arenaviridae*, *Astroviridae*, *Bornaviridae*, *Bunyaviridae*, *Caliciviridae*, *Circoviridae*, *Coronaviridae*, *Dicistroviridae*, *Filoviridae*, *Flaviviridae*, *Hepeviridae*, *Herpesviridae*, *Nodaviridae*, *Orthomyxoviridae*, *Papillomaviridae*, *Paramyxoviridae*, *Parvoviridae*, *Picobirnaviridae*, *Picornaviridae*, *Polyomaviridae*, *Poxviridae*, *Reoviridae*, *Retroviridae*, *Togaviridae*, and *Totiviridae*, as well as viruses that have not yet been placed in a taxon.

Many of these viruses were first recognized after they were associated with human or livestock illnesses and deaths but most were isolated coincidental to general virus surveys or during surveillance for specific viral pathogens. Calisher [96], also added that those genomes of hundreds more viruses will be found in bats and that bats will be shown to be reservoirs of many of them.

From the foregoing, it is evident that bats play a big role in the epidemiology of some serious and fatal viral diseases of human and livestock, e.g. rabies virus. They act as reservoir and vectors of these viruses. The main viruses that have been conclusively confirmed to be transmitted from bats and causing destructive outbreaks in both human and livestock, are the Vampire bat rabies, Hantavirus, Nipah virus, and to a low level of significance are some lyssaviruses

in Europe, Australia, Africa, Asia causing limited cases of nervous signs in humans [97]. Many other dangerous zoonotic viruses have been isolated from or otherwise detected in bats. For instance, Castro, [98], mentioned that bats host more than 60 human-infecting viruses. Leroy, et al, [99] found evidence of asymptomatic infection by Ebola virus in three species of *megabats* (Fruit bats), indicating that these animals may be acting as a reservoir for this deadly virus. Wong, et al [100], reported that bats are a continuing source of emerging infections in humans. Fenton, et al. [101], also linked bats to emerging diseases.

The WHO [102], in 2015, published a list of top emerging diseases likely to cause major epidemics.

Choi, et al [103] summarized various scientific publications indicating that bats long known as vectors for rabies, may also be the origin of some of the most deadly emerging viruses, including SARS, Ebola, Nipah, Hendra and Marburg. Tower, et al. [104] isolated genetically diverse Marburg viruses from Egyptian fruit bats. On the other hand, Joshua, et al. [105] reported that Retroviruses of Bats are a "Threat Waiting in the Wings?"

Some authors, have raised some question on the role of bats in the emergence of deadly viruses e.g. Moratelli, & Calisher [106] enquired that: "can we confidently link bats with emerging deadly viruses?" The CDC in a publication in 2020, [107] stated that: Scientists do not know where Ebola virus comes from. Olival, et al. in 2015, [108], also asked whether bats are really 'Special' as Viral Reservoirs. What We Know and Need to Know". Dobson [109], in 2005, asked: "What Links Bats to Emerging Infectious Diseases?"

In spite of the questions raised by some authors, above, e.g. [95,99,107]; the continuous evolution of viruses and other ecological changing conditions, emergence of any of the viruses detected in bats, which are not causing current epidemics of disease, may emerge at any specific time [109]. For instance, it was reported that bats act as reservoirs for over 200 viruses [110]. Some of which cause severe, life-threatening diseases in humans, livestock and wildlife; examples include rabies virus, ABLV, Hendra virus and Nipah virus. Other viruses are also reported in bats; examples are SARS and MERS coronaviruses and Ebola virus.

Realizing the concept of virus evolution from bats, then blocking of the cycle of emergence and transmission of such viruses to humans and livestock from bats has to be taken seriously.

In conclusion, it is felt that, the answer to the raised question that: 'can we confidently link bats with emerging viruses?' I think, from the foregoing that the answer to this question is 'yes'.

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