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Tick-borne viruses

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Summary. – Tick-borne viruses (TBVs) belong to the largest biological group known as arboviruses with unique mode of transmission by blood-feeding arthropods (ticks, mosquitoes, sand flies, biting midges, etc.) to a susceptible vertebrate host. Taxonomically, it is a heterogenous group of vertebrate viruses found in several viral families. With only one exception, African swine fever virus, all TBVs have a RNA genome. To date, at least 160 tick-borne viruses are known, some of them pose a significant threat to human and animal health worldwide. Recently, a number of established TBVs has re-emerged and spread to new geographic locations due to the influence of anthropogenic activities and few available vaccines. Moreover, new emerging tick-borne diseases are constantly being reported. Major advances in molecular biotechnologies have led to discoveries of new TBVs and further genetic characterization of unclassified viruses resulting in changes in TBVs classification created by the International Committee for the Taxonomy of Viruses. Although TBVs spend over 95% of their life cycle within tick vectors and the role of ticks as vectors has been known for over 100 years, our knowledge about TBVs and molecular processes involved in the virus-tick interactions is scarce.

Keywords: virus; tick; transmission

Contents:

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Abbreviations: ASFV = African swine fever virus; CCHFV = Crimean-Congo haemorrhagic fever virus; DHOV = Dhori virus; LIV = Louping ill virus; MHV-68 = Murid herpesvirus 4 strain 68; POWV = Powassan virus; SFTSV = Severe fever with thrombocytopenia syndrome virus; TBD = tick-borne diseases; TBVs = Tick-borne viruses; TBEV = Tick-borne encephalitis virus; THOV = Thogoto virus

1. Introduction

Ticks, obligate hematophagous ectoparasites of all classes of terrestrial vertebrates, are second only to mosquitoes as vectors of human pathogens, but are primary carriers of pathogens of veterinary importance (Mansfield *et al*., 2017). Ticks surpass all other blood-feeding arthropods in the variety of transmitted pathogenic agents, including viruses. Many unique features of ticks make them inevitably suitable to host and to carry different viruses as well as act as long-

term virus reservoirs. Some of the viruses have significant medical and veterinary impact by causing serious diseases in humans and animals (Nuttall, 2014; Brackney and Armstrong, 2016). Members of both families, *Argasidae* (soft ticks) and *Ixodidae* (hard ticks) are able to transmit viruses, but hard ticks are vectors of the majority of viruses of medical and veterinary importance (Labuda and Nuttall, 2004, 2008; Nuttall, 2014).

Tick-borne viruses (TBVs) belong to arboviruses (arthropod-borne viruses) representing the largest biological group of vertebrate viruses, and persist in nature through circulation between vector ticks and vertebrate hosts. To survive, TBVs have adapted to two entirely diverse inner environments in invertebrate and vertebrate hosts, and mastered to infect and multiply in both of them irrespective of whether they have a RNA genome double-stranded or single-stranded, segmented or non-segmented, or of positive or negative polarity (Nuttall, 2009). The long-lasting co-evolution of ticks with viruses led to their mutual tolerance and adaptation to the tick physiology (Mans, 2011). The inter-relationships among viruses, ticks and vertebrate hosts are very complex and dynamic and are influenced by the physiological and immunological status of vertebrate hosts and by hitherto unknown factors in ticks (Moshkin *et al.*, 2009; Nuttall 2014; Kazimírová *et al.*, 2017). Although it is estimated that TBVs spend over 95% of their life cycle within the tick vector (Nuttall *et al.*, 1994; Nuttall and Labuda, 2003; Turell, 2015; de la Fuente *et al.*, 2017), and the role of ticks as vectors has been known for over 100 years, our understanding of tick – virus – host interactions is still limited. Neither the molecular mechanisms that allow TBVs to switch between ticks and vertebrate hosts nor the mechanism of viral persistence in different environments are fully understood, but it is suggested that viral, tick as well as vertebrate host factors together with biotic and abiotic factors are involved in these complex processes (Nuttall *et al.*, 1994; Labuda and Nuttall, 2004; Robertson *et al.*, 2009; Mlera *et al.*, 2014; Nuttall, 2014). Major advances in molecular biotechnologies (PCR, qPCR, next-generation sequencing, proteomic analyses, RNA interference) together with tick cell lines, an important complementary tool to *in vivo* research of the tick – host – arbovirus relationships (Bell-Sakyi *et al.*, 2012) enhance the likelihood of elucidating tick – virus interaction and find the ways to control and prevent tick-borne diseases (TBD).

2. Taxonomy of tick-borne viruses

Viruses form a major group of pathogenic agents transmitted by ticks. TBVs (acronym "tiboviruses"; Hubálek and Rudolf, 2012) represent a diverse group of viruses characterized by their specific biological transmission among competent hard or soft ticks and vertebrate hosts and by their ability to infect and replicate in both, vertebrate as well as arthropod cells. The first described TBVs, Nairobi sheep disease virus (1910) and Louping ill virus (1929), triggered a sudden large amount of discoveries of around 530 arboviruses listed in the International Catalogue of Arboviruses Including Certain Other Viruses of Vertebrates (Karabatsos, 1985; Bichaud *et al.*, 2014). The catalogue (accessible online https://wwwn.cdc.gov/arbocat/) is a result of Rockefeller Foundation Virus Program established to investigate arthropod-borne viruses of vertebrates. During the two decades (c. 1960–1975) of its existence (the golden age of arbovirology), most of the current major arboviruses were discovered, characterized, studied and included in this catalogue. However, since the newly discovered potential arboviruses are recorded as genomic sequences in other databases, no registration has occurred for a long time. At least 160 named viruses are transmitted by ticks, of which about 50 are recognized or probable "virus species" (Nuttall, 2014). Taxonomically, it is a heterogenous group of viruses infecting vertebrates that are found in several viral families: *Asfarviridae, Flaviviridae, Reoviridae, Orthomyxoviridae, Rhabdoviridae,* the newly formed family *Nyamiviridae* (the order *Mononegavirales*), and the families *Nairoviridae, Phenuiviridae* and *Peribunyaviridae* in the new order, *Bunyavirales*. With only one exception (African swine fever virus) all TBVs are RNA viruses, with absolute majority of negative-sense RNA viruses.

Taxonomy of viruses is created by the International Committee on Taxonomy of Viruses (ICTV) established in 1966. According to the latest ICTV report (Adams *et al.*, 2017), virus taxonomy comprises 8 orders, 122 families, 35 subfamilies, 735 genera and 4404 species of viruses and viroids. Each virus family is characterized by a unique genome organization and replication strategy. This implies that TBVs lineages have evolved independently at least seven times (Nuttall, 2014). Almost 25% of TBVs are associated with diseases. Several TBVs cause very serious human or animal diseases, while others are either less serious or infrequently reported. Some TBVs had not proven medical or veterinary significance. However, certain viral diseases may often pass unnoticed or misdiagnosed and eventually, they may appear as emerging diseases (Dörrbecker *et al.*, 2010; Hubálek and Rudolf, 2012).

2.1 DNA viruses

2.1.1 African swine fever virus

The only established DNA tick-borne virus, African swine fever virus (ASFV), belongs to the *Asfarviridae* family with a single genus *Asfivirus* (Dixon *et al.*, 2011). The ASFV genome consists of a single molecule of linear, covalently close-ended, dsDNA varying in length from 170 to190 kbp. ASFV is the causative agent of African swine fever (ASF),

a highly contagious hemorrhagic disease of swine with mortality varying between 0 and 100% depending on the virus strain, the host, the dose and the route of exposure to the virus (Costard *et al.*, 2013). ASF was first described in Kenya in 1921, but in the middle of the 20th century it spread from Africa into Europe (Spain, Portugal) and South America. Although the infection was eradicated, in 2007 it re-emerged in Europe after introduction to the Caucasus (Costard *et al.*, 2013; Cisek *et al.*, 2016). In natural foci, ASFV circulates among warthogs and bushpigs (sylvatic cycle) without any apparent effects on their health. However, in domestic pigs (domestic cycle) it causes severe hemorrhagic disease with high mortality (Anderson *et al.*, 1998; Costard *et al.*, 2013). Several soft tick species of the genus *Ornithodoros,* such as *O. moubata* in Africa and *O. erraticus* in Southern Europe, are competent vectors and reservoirs for ASFV. The virus is maintained in natural tick populations through different routes (transovarial, transtadial and/or sexual transmission from tick to tick), and ticks can transmit the virus to the host via contaminated saliva or coxal fluid (Kleiboeker and Scoles, 2001). In the domestic cycle, pigs can aquire the ASFV directly by ingestion of infected meat, by fomites, or mechanically by biting flies (Mellor *et al.*, 1987). ASFV infection of the tick is remarkably variable, resulting either in a high-titer and persistent infection, depending upon the ASFV isolate and the tick species combination, or in high mortality of ticks (Kleiboeker and Scoles, 2001; Burrage, 2013).

Recent studies suggest that other DNA viruses may also be transmitted by ticks, Lmpy skin disease virus (LSDV) and Murid herpesvirus 4 (MuHV 4).

2.1.2. Lumpy skin disease virus

Lumpy skin disease virus (LSDV) belongs to the genus *Capripoxvirus*, member of the subfamily *Chordopoxvirinae* and the family *Poxviridae* that involve large enveloped viruses with linear double-stranded DNA (Skinner *et al.*, 2011). It causes lumpy skin diseases (LSD) of cattle in Africa and Middle-East. Currently, it is widely accepted that LSDV is associated with blood-feeding insects such as mosquitoes and stable flies (Carn and Kitching, 1995; Chihota *et al.*, 2001, 2003). During the outbreak of LSD in Sudan in 1971, affected animals were observed to be heavily infested with ticks, mainly *Amblyomma* spp. (Ali and Obeid, 1977). Fourty years later, recent transmission studies have demonstrated for the first time a role of the hard ticks *Amblyomma hebraeum* and *Rhipicephalus appendiculatus* in mechanical and transstadial transmission, and of *Rhipicephalus decoloratus* in transovarial transmission of LSDV (Tuppurainen *et al.*, 2011, 2013a,b; Lubinga *et al.*, 2014b,c, 2015). Detection of the virus in different organs (salivary glands, hemocytes, synganglion, midgut, ovaries, testes) of ticks fed on experimentally-infected cattle as well as in naturally infected ticks collected from the field indicates the potential for biological transmission of LSDV by ticks (Tuppurainen *et al.*, 2011, 2013a,b; Lubinga *et al.*, 2013, 2014a).

2.1.3 Murid herpesvirus 4

Another potentially tick-borne virus could be Murid herpesvirus 4 (MuHV 4) strain 68 (MHV-68, the genus *Rhadinovirus,* the subfamily *Gammaherpesvirinae,* the family *Herpesviridae,* the order *Herpesvirales*) (Hájnická *et al.*, 2017), a natural pathogen of rodents of the family Muridae that are hosts for immature tick stages as well. Transmission of the virus in rodent populations is direct and occurs mainly via the intranasal route and through body fluids, such as saliva, urine, tears, and breast milk. During acute respiratory infection, MHV-68 infects macrophages, B-lymphocytes, lung alveolar and endothelial cells. Similarly to other gammaherpesviruses, MHV-68 causes a life-long latent infection in host B-lymphocytes that may lead to lymphoproliferative disorders and tumor development (Rajčáni *et al.*, 1985; Rajčáni and Kúdelová, 2007). Thus, MHV-68 serves as an animal model for the study of human lymphotropic diseases, such as Burkitt lymphoma. In Slovakia, the first evidence of MHV-68 DNA in *Ixodes ricinus* feeding on green lizards and in questing *Haemaphysalis concinna* ticks was described by Ficová *et al.* (2011) and Vrbová *et al.* (2016), respectively. Presence of the viral DNA but also of live virus in organs of questing in *Dermacentor reticulatus* adult ticks from southwestern Slovakia may suggest that ticks could be natural reservoirs of the MHV-68 (Kúdelová *et al.* 2015, 2017).

2.2 RNA viruses

2.2.1 Flaviviridae, genus Flavivirus (ssRNA+)

The family *Flaviviridae* represents a diverse group of small enveloped viruses with single strand of positive-sense RNA genomes classified into four genera: *Flavivirus, Pestivirus, Hepacivirus* and *Pegivirus* (Simmonds *et al.*, 2017). Only one genus, *Flavivirus,* comprises arboviruses, of which about 50% are transmitted by mosquitoes, 28% are tick-borne and the remainder is without known vector. In a phylogenetic analysis, tick-borne flaviviruses formed three distinct groups, i.e., a group associated with sea-birds and mammals, respectively, and the Kadam virus that forms a third evolutionary lineage (Gaunt *et al.*, 2001; Grard *et al.*, 2007) (Table 1).

Tick-borne encephalitis virus (TBEV) causes tick-borne encephalitis (TBE), one of the most dangerous human neural infections in Europe and Asia (Gritsun *et al.*, 2003). At least 11,000 human cases of TBE have been reported annually in Russia and about 3,000 cases in the rest of Europe (Mansfield *et al.*, 2009; Dörrbecker *et al.*, 2010). There exist three TBEV subtypes, European (TBEV-Eu), Siberian (TBEV-Sib) and Far Eastern (TBEV-Fe), corresponding with different clinical outcome in infected humans. The principal vector for TBEV-Eu is *Ixodes ricinus*, whereas for two latter subtypes it is *I. persul-*

Table 1. *Flaviviridae* (ssRNA+)

Genus/Species	Vector	Geographic localization	Host
Flavivirus, tick-borne virus (TBV) group			
Mammalian TBV group			
Tick-borne encephalitis virus	*Ixodes* spp., many ixodid ticks	Europe, Asia	rodents
Louping ill virus	*I. ricinus, I. gibbosus*	Ireland, Spain, Scotland, Greece, Turkey	sheep, goats, cattle
Langat virus	*I. granulatus,*	Malaysia, Russia, Thailand	rats
	I. ricinus	England, Scotland, Wales, Norway	hare, sheep, red grouse
		Ireland	cattle, sheep
Powassan virus	*I. cookei, I. marxi, I. scapularis*	Canada, Russia, USA	white-footed mouse, squirrel, groundhog, woodchuck
Kyasanur Forest disease virus	*H. spinigera,* many other ixodid ticks	India	monkeys, rodents, shrews, bats
Omsk hemorrhagic fever virus	*D. reticulatus*	Russia	muskrat, narrow-headed vole
Gadgets Gully virus	*I. uriae*	Australia	penguins
Royal Farm virus	*Ar. hermanni*	Afghanistan	pigeons
West Nile virus	*C. maritimus, Ar. hermanni, Hy. marginatum*	Russia, Egypt	seabirds, wild birds
Related, Unclassified			
Karshi virus	*O. tholozani (papillipes), Hy. anatolicum*	Uzbekistan, Kazakhstan	gerbil
Seabird TBV group			
Tyuleniy virus	*I. uriae*	Russia, USA, Norway	seabirds
Meaban virus	*C. maritimus*	France	gulls
Saumarez Reef virus	*C. capensis, I. eudyptidis*	Australia	seabirds
Kadam TBV group			
Kadam virus	*Hy. dromedari, R. parvus*	Saudi Arabia, Uganda	camel, cattle

Based on Simmonds *et al.* (2011); King *et al.* (2011). *Ar. – Argas, C. – Carios, H. – Haemaphysalis, Hy – Hyalomma, I. – Ixodes, R. – Rhipicephalus.*

catus. Infection is usually initiated by a bite of an infected tick, but other infection routes, i.e. through consumption of raw, unpasteurized milk and dairy products or by aerosol, are also possible. Related viruses within the mammalian TBEV group, Louping ill virus (LIV), Langat virus (LGTV) and Powassan virus (POWV), also cause encephalitis in humans, whereas three other viruses, Omsk hemorrhagic fever virus (OHFV), Kyasanur Forest disease virus (KFDV) and Alkhurma virus (ALKV) cause fatal hemorrhagic fevers (Gritsun *et al.*, 2003; Mansfield *et al.*, 2009; Lani *et al.*, 2014). On the other hand, Gadgets Gully virus, Royal Farm virus and Karshi virus are flaviviruses with unknown pathogenicity to humans and animals (Dobler, 2010). Although little is known about effects of TBVs on their natural vertebrate hosts, three tick-borne flaviviruses – KFDV, LIV and OHFV – are known to be associated with diseases in free-living animals – monkeys, red grouses and muskrats, respectively (Nuttall, 2014). Significant antigenic and genetic similarity of LIV to TBEV suggests that LIV is another subtype of TBEV (Grard *et al.*, 2007; Dobler, 2010; Hubálek and Rudolf, 2012).

Viruses of the TBEV serocomplex are considered emerging and re-emerging pathogens due to the recent rise in the incidence of human infections, e.g. POWV in the USA (Hermance and Thangamani, 2017), the spread of TBEV into new geographic areas, and the emergence of new viruses such as ALKV, a subtype of KFDV (Charrel *et al.*, 2001), and Deer tick virus, a subtype of POWV (Ebel, 2010; Pesko *et al.*, 2010; Wormser and Pritt, 2015). In 2011, severe disease and mortality was reported in a herd of goats in Spain. Based on genome sequencing and phylogenetic analysis, the virus was significantly divergent from LIV and Spanish sheep encephalitis virus (SSEV) and was named as Spanish goat encephalitis virus (SGEV) (Mansfield *et al.*, 2015).

2.2.2 Reoviridae (dsRNA, segmented)

The *Reoviridae* represents the largest viral family of double-stranded RNA (dsRNA) non-enveloped viruses with genomes composed of multiple (9–12) segments of linear dsRNA. Currently it comprises a total 75 virus species in 15 recognized genera divided into two subfamilies (*Sedoreo-*

Table 2. *Reoviridae* (dsRNA)

Subfamily/Genus/Species	Vector	Geographic localization	Host
Spinareovirinae			
Coltivirus			
Colorado tick fever virus	*Dermacentor* spp., *H. leporis-palustris,*	USA	many mammalian species
Eyach virus	*I. ricinus, I. ventalloi*	France, Germany	rabbit
Sedoreovirinae			
Orbivirus			
Chenuda virus (7 serotypes)	*Argas* spp., *Hy. asiaticum, Carios* spp.	Egypt, South Africa, Azerbaijan, Uzbekistan, Morocco, USA	seabirds, pigeons, gulls
Chobar Gorge virus (2 serotypes)	*Ornithodoros* spp.	Nepal	cattle, sheep
Great Island virus (36 serotypes/ strains)	*I. uriae, Argas* spp., *Ornithodoros* spp.	Europe, USA, Russia, Canada, Australia	seabirds, rodents
Wad Medani virus (2 serotypes)	*Rhipicephalus* spp., *Hyalomma* spp., *Amblyomma* spp.	Malaysia, Singapore, Egypt, Sudan, India, Jamaica, Russia, Pakistan	sheep, camel, buffalo, pigs, rodents, carabao, cattle
St Croix River virus	*I. scapularis*	USA	unknown (probably a tick virus)
Unassigned			
Lake Clarendon virus	*Ar. robertsi*	Australia	egret
Matucare virus	*O. boliviensis*	Bolivia	bats

Based on Attoui *et al.* (2011); King *et al.* (2011). *Ar. – Argas, H. – Haemaphysalis, Hy. – Hyalomma, I. – Ixodes, O. – Ornithodoros.*

virinae, Spinareovirinae) based on the surface of intact virus particles or cores (Attoui *et al.*, 2011). TBVs belong to two genera – *Coltivirus* (*Spinareovirinae,* 12 segments of dsRNA) and *Orbivirus* (*Sedoreovirinae*, 10 segments of dsRNA) (Table 2). *Coltivirus* comprises two species, Colorado tick fever virus (CTFV) that causes acute febrile illness in humans, and Eyach virus (EYAV). Coltiviruses have been isolated from several mammalian species (including humans), as well as from ticks and mosquitoes.

CTFV, the causative agent of acute febrile illness primarily found in the Rocky Mountain region of the USA and south-western Canada, is transmitted mainly by adult and nymphal wood ticks *Dermacentor andersoni*. In addition, infections through contact with infected animal blood or tissues, and person-to-person transmission via blood transfusion have been reported (Cimolai *et al.*, 1988; Emmons, 1988). With 200–400 reported cases yearly, it is the second most important arboviral infection in the USA after West Nile (Meagher and Decker, 2012), and the prevalence of the disease is directly dependent on the seasonal activity and geographical distribution of the vector tick.

EYAV was originally isolated from *I. ricinus* in Germany in 1972 (Rehse-Küpper *et al.*, 1976) and later (1981) from *Ixodes ventalloi* and *I. ricinus* in France (Chastel *et al.*, 1984). In the former Czechoslovakia, EYAV was associated with meningoencephalitis and polyneuritis in humans based on detection of specific antibodies, but a causal relationship to the virus has not been found (Málková *et al.*, 1980). Vertebrate hosts are rodents and the European rabbit (Attoui *et al.*, 2002; Hubálek and Rudolf, 2012). Due to the lack of permissive mammalian cell lines for replication of EYAV, the virus can be isolated only from brains of suckling mice after intracranial injection. This virus is also able to multiply and persist in the blood of immunocompetent mice inoculated intraperitoneally and cause brain infections (Charrel *et al.*, 2004; Moutailler *et al.*, 2016).

Orbivirus currently comprises 22 distinct virus species and 10 probable members. Depending on the virus, they are primarily transmitted by different arthropod vectors (gnats, mosquitoes, phlebotomines or ticks). Orbivirus infection has little or no effect on arthropods, whereas infection in vertebrates can vary from inapparent to fatal, depending on both the virus and the host. Approximately 60 tick-borne orbiviruses have been identified and divided to five species (Table 2). At least 40 of them were isolated from the common seabird tick *Ixodes uriae* (Labuda and Nuttall, 2004, 2008). According to the last 9th ICTV report (Attoui *et al.*, 2011; King *et al.*, 2011), *Chenuda virus* includes seven different serotypes - Baku virus, Chenuda virus, Essaouira virus, Huacho virus, Kala Iris virus, Mono Lake virus, Sixgun city virus – isolated from soft ticks of the genera *Argas, Carios* and *Ornithodoros* parasitizing on birds. Chenuda virus was origi-

nally isolated from *Argas reflexus hermanni,* collected from a pigeon house in Egypt (Labuda and Nuttall, 2004, 2008). *Chobar George virus* has two serotypes, Chobar George virus and Fomede virus, associated with bats. The most diverse species, *Great Island virus*, transmitted by soft or hard ticks parasitizing on seabirds, rodents, and humans (Labuda and Nuttall, 2004, 2008), comprises 36 serotypes. *Vad Medani virus,* isolated from sheep and different ixodid ticks, includes 2 strains – Vad Medani virus and Seletar virus.

Interestingly, St. Croix River virus (SCRV) was isolated only from IDE2 tick cell lines derived from *Ixodes scapularis* ticks (Munderloh *et al*., 1994). The vertebrate host is unknown and SCRV can therefore be considered as a possible "tick-only virus" (Nuttall, 2009).

2.2.3 Buyavirales (ssRNA-, segmented)

Bunyaviridae, until recently the largest viral family comprising around 530 viruses infecting vertebrates, arthropods and plants, formerly divided into five genera, has been revised by the ICTV Bunyaviridae study group and has been elevated to the order *Bunyavirales* with 9 families (8 new families and one renamed, *Peribunyaviridae*) and 13 genera (Bries *et al*., 2016; Junglen, 2016; Kuhn *et al*. 2016a, b; Walker *et al*., 2016b). TBVs are included in three families – *Nairoviridae, Phenuiviridae* and *Peribunyaviridae*. The genome of all viruses consists of three single-stranded negative-sense or ambisense RNA segments – large, medium and small. The *Nairoviridae* comprises the genus *Orthonairovirus* with 12 species and several putative nairoviruses (Table 3) (Walker *et al*., 2015b, 2016b; Kuhn *et al*., 2016a,b). The most medically important member of the genus and the best studied representative is Crimean-Congo hemorrhagic fever virus (CCHFV), one of the most widely distributed medically important arbovirus associated with a series of outbreaks across Europe, Middle East, Asia and Africa (Hoogstraal, 1979; Papa *et al*., 2010; Tekin *et al*., 2010; Bente *et al*., 2013). The main vectors of CCHFV are hard ticks of the *Hyalomma* genus, which have very wide geographic distribution. The virus demonstrates very low vector specificity and has been isolated from 31 hard tick species and two soft tick species (Bente *et al*., 2013). CCHFV is non-pathogenic to its natural hosts, but highly pathogenic to humans; transmission to humans occurs through tick bite, crushing of infected engorged ticks, or by contact with infected animal blood (Whitehouse, 2004). The most significant nairovirus of veterinary importance is Nairobi sheep disease virus (NSDV) causing lethal hemorrhagic gastroenteritis in small ruminants in Africa and India.

Several newly discovered viruses belong to this family, e.g. *Huángpí tick virus* 1 (HTV-1), *Tǎchéng tick virus* 1 (TTV-1) and *Wēnzhōu tick virus* (WTV) (Li *et al*., 2015) of the new *Burana orthonairovirus* species, and Soft tick bunyavirus (STBV) isolated from *Argas vespertilionis* ticks (Oba *et al*., 2016) of the *Keterah orthonairovirus* species, later identified as an isolate of Keterah virus (Kuhn *et al*., 2016b).

The *Orthobunyavirus* genus (*Peribunyaviridae)* comprises 48 species, three of them are TBVs – Bakau, Estero Real and Tete. The third family *Phenuiviridae* with one genus *Phlebovirus,* contains two tick-borne species, *Uukuniemi phlebovirus* and the newly described *Severe fever with thrombocytopenia syndrome virus* (SFTSV), a causative agent of severe human infectious disease with high mortality rate, that was first reported in China (Xu *et al*., 2011; Yu *et al*., 2011; Zhang *et al*., 2011) and subsequently in Japan in 2011 (Takahashi *et al*., 2014) and in Republic of Korea in 2013 (Kim *et al*., 2013). The viral genomic RNA was detected mainly in *Haemaphysalis longicornis* and *Rhipicephalus (Boopilus) microplus* ticks. However, there is also evidence of direct transmission through infected blood. Recently, a new virus closely related to SFTSV named Heartland was isolated from two severely febrile patients in the USA (McMullan *et al*., 2012) and from field-collected *Amblyomma americanum* nymphs (Savage *et al*., 2013).

At least 40 bunyaviruses have not been assigned to genera or approved as species (Plyusnin *et al*., 2011), among them Bhanja virus (BHAV), Forecariah virus (FORV), and Kismayo virus (KISV). Based on serologic tests, they are antigenically related to each other and form a Bhanja serogroup together with Palma virus (PALV). Moreover, by phylogenetic and serological analyses, BHAV has been found to be closely related to both, SFTSV and Heartland virus (Dilcher *et al*., 2012; Matsuno *et al*., 2013). Virome studies of some tick species led to the discovery of several novel bunyaviruses in the genera *Orthonairovirus*, i.e. South Bay virus (SBV), and *Phlebovirus*, i.e. Blacklegged tick phlebovirus (BTPV) and the *D. variabilis*-associated American dog tick phlebovirus (ADTPV) (Tokarz *et al*., 2014b).

Phleboviruses have traditionally been classified into two groups consisting of sand fly/mosquito-borne viruses and TBVs (Nichol *et al*., 2005; Elliot and Brennan, 2014). At least three phylogenetic clusters of tick-borne phleboviruses have been identified, each comprised of several potential species: the Uukuniemi group, the Bhanja group, and the SFTSV group (Dilcher *et al*., 2012; McMullan *et al*., 2012; Palacios *et al*., 2013). Retrospective identification of several known but taxonomically unassigned phleboviruses (Lanja virus, Silverwater virus, Kaisodi virus) revealed a novel fourth cluster, the Kaisodi group, distinct from the other three mentioned above (Matsuno *et al*., 2015). Phylogenetic analysis revealed that BTPV does not cluster with any of these groups and forms a separate monophyletic clade outside all tick-borne and sand fly/mosquito-borne phleboviruses, similar to Gouleako and Cumuto mosquito-borne viruses. ADTPV is more similar to viruses within the Uukuniemi group but forms a distinct monophyletic clade outside this group (Tokarz *et al*., 2014b).

Table 3. *Bunyavirales,* (segmented ssRNA-)

Family/Genus/Species	Vector	Geographic localization	Host
Nairoviridae			
Orthonairovirus			
Burana orthonairovirus (3 strains)	*H. doenitzi, H. hystricis, D. marginatus*	China	unknown
Crimean-Congo hemorr. fever orthonairovirus	*Hy. marginatum,* many ixodid secies	Europe, Asia, Africa, Middle East	human, hare, camel
Dera Ghazi Khan orhonairovirus (4 strains)	*Argas* spp., *Hyalomma* spp.	Egypt, Iran, Pakistan, Taiwan, Australia, Java, South Africa, Thailand	pigeons, camel, turtle dove, cliff swallow
Dugbe orthonairovirus (2 strains)	*Amblyomma* spp., *R. pulchellus*	Africa	cattle, giant pouched rat
Hazara orthonairovirus (2 strains)	*I. redikorzevi*	West Pakistan	vole
Hughes orthonairovirus (8 strains)	*Carios* spp., *Ar. arboreus, Ar. cooleyi*	USA, Mexico, Cuba, Peru, Ireland, Wales, Trinidad, Uzbekistan, Azerbaijan	seabirds, gulls, terns, cormorant
Keterah orthonairovirus (4 strains)	*C. pusillus, C. vespertilionis*	Malaysia, Kyrgyzstan, Kazakhstan	bats,
Nairobi sheep disease orthonairovirus (2 strains)	*R. appendiculatus, H. intermedia, R. haemaphysaloides*	Ethiopia, Kenya, Rwanda, Tanzania, India, Sri Lanka	goats, sheep
Qalyub orthonairovirus (2 strains)	*Ornithodoros* spp., *I. uriae*	Senegal, Uzbekistan, Ethiopia, Egypt	rodents, rats
Sakhalin orthonairovirus (5 strains)	*I. uriae, I. signatus*	Russia, USA, Canada, Australia	seabirds
Putative Nairoviruses			
Artashat virus	*O. alactagalis, O. verrucosus*	Armenia, Azerbaijan	five-toed jerboa
Burana virus	*H. punctata, H. concinna*	Kyrgyzstan	cattle
Chim virus	*R. turanicus, Ornithodoros* spp.	Uzbekistan	gerbils
Ellidaey virus ELL 80-3b	*I. uriae*	Iceland	seabirds
Foula virus F 80-1	*I. uriae*	Scotland	seabirds
Geran virus	*O. verrucosus*	Azerbaijan	gerbils
Grimsey virus GRIMS82-1b	*I. uriae*	Iceland	seabirds
Inner Farne Island virus IF 80-3, IF 80-4	*I. uriae*	England	seabirds
Isle of May virus IM81	*I. uriae*	Scotland	seabirds
Kachemak Bay virus	*I. signatus*	USA	seabirds
Kao Shuan virus	*Ar. robertsi*	Taiwan, Australia, Java	night heron
Mykines virus M82-2	*I. uriae*	Denmark	seabirds
Pathum Thani virus	*Ar. robertsi*	Thailand	open-billed stork
Pretoria virus	*Ar. africolumbae*	South Africa	pigeons
Puffin Island virus	*C. maritimus*	Wales	seabirds
Nàyǔn tick virus	*Rhipicephalus* spp.	China	unknown
South Bay virus	*I. scapularis*	USA	unknown
Tamdy virus	*Hy. asiaticum, Hy. plumbeum*	Turkmenistan, Uzbekistan	sheep
Peribunyaviridae			
Orthobunyavirus			
Bakau orthobunyavirus	*Ar. abdussalami*	Pakistan	unknown
Estero Real orthobunyavirus	*O. tadaridae*	Cuba	unknown
Tete orthobunyavirus	*Hyalomma* spp.	Egypt, Cyprus, Italy	passerine birds
Phenuiviridae			
Phlebovirus			
Uukuniemi phlebovirus	*Argas* spp., *Ixodes* spp., *Rhipicephalus* spp.	USA, Africa, Europa, Russia, Pakistan, Australia,	pigeons, vultures, penguins, *Apodemus sylvaticus*, cattle, passerine birds, seabirds
SFTS phlebovirus	*H. longicornis, R. microplus*	China, USA, Japan, Korea	human

Table 3 (continued)

Family/Genus/Species	Vector	Geographic localization	Host
Unsigned/grouped			
Bhanja virus	*Haemaphysalis* spp., *A. variegatum, Rhipicephalus* spp., *Hyalomma* spp.	India, Italy, Nigeria, Senegal, Russia, Bulgaria, Central Asia,	sheep, goat, cattle, African hedgehog & ground squirrel
Forecariah virus	*Boophilus geigyi*	Guinea	cattle
Kismayo virus	*R. pulchellus*	Somalia	domestic animals, camel, jackal
Kaisodi virus	*H. spinigera,H. turturis*	India	passerine birds
Lanjan virus	*D. auratus, Haemaphysalis* spp., *I. granulatus*	Malaysia	rodents
Silverwater virus	*H. leporispalustris*	Canada, USA	snowshoe hare
Ungrouped			
Lone Star virus	*A. americanum*	USA	racoon
Razdan virus	*D. marginatus*	Armenia	unknown
Sunday Canyon virus	*Ar. cooleyi*	USA	cliff swallow
Wanowrie virus	*Hyalomma* spp.	India, Sri Lanka, Egypt, Iran	sheep

Based on Adams *et al.* (2016); King *et al.* (2011); Kuhn *et al.* (2016a,b). *A. – Amblyomma, Ar. – Argas, C. – Carios, D. – Dermacentor, H. – Haemaphysalis, Hy. – Hyalomma, I. – Ixodes, O. – Ornithodoros, R. – Rhipicephalus.*

Growth characteristics and genome sequencing analysis of Lone Star virus (LSV), an unclassified bunyavirus originally isolated from the lone star tick *A. americanum*, definitively identified LSV as a phlebovirus and by phylogenetic analysis it clustered with the Bhanja group viruses (Swei *et al.*, 2013).

Advances in molecular biotechnologies used in recent studies and analyses of different tick species revealed a wide range of novel phleboviruses worldwide – Malsoor virus isolated from bats (Mourya *et al.*, 2014), Hunter Island virus isolated from *Ixodes eudyptidis* collected from nests of shy albatross (Wang *et al.*, 2014), Shibuyunji virus from *Rhipicephalus* spp. ticks in Zambia (Matsuno *et al.*, 2015), Antigona virus and Lesvos virus identified in *Rhipicephalus sanguineus* and *Heamaphysalis parva* ticks, respectively, collected from sheep in Greece (Papa *et al.*, 2016, 2017), Odaw virus isolated from *Rhipicephalus* spp. ticks collected from domestic dogs and cattle in Ghana (Kobayashi *et al.*, 2017), RiPar virus, KarMa viral group and AnLuc viral group identified in questing as well in feeding hard ticks collected in Portugal (Pereira *et al.*, 2016). These findings demonstrate global distribution of a broad spectrum of divergent phleboviruses. However, for most of the newly described phleboviruses a clear association with human diseases has not yet been established.

2.2.4 Orthomyxoviridae (ssRNA-, segmented)

The family *Orthomyxoviridae*, in addition to three genera of Influenza viruses, includes the genus *Thogotovirus* with two species (Table 4) – Thogoto virus (THOV) and Dhori virus (DHOV) that are arboviruses transmitted biologically by *Rhipicephalus* spp. and *Hyalomma* spp. ticks, respectively (Davies *et al.*, 1986; Jones *et al.*, 1989). Virions are relatively large, enveloped, and depending on the genus, they contain different numbers of segments of linear, negative-sense single-stranded RNA (DHOV seven, THOV and Quaranjavirus six segments). One of them encodes a surface glycoprotein probably associated with the ability of THOV to infect ticks (Nuttall, 2009). THOV has been found to occur in the Central African Republic, Cameroon, Uganda, and Ethiopia as well as in southern Europe and has been isolated from *Rhipicephalus* sp. in Kenya and Sicily, from *Amblyomma variegatum* in Nigeria, and from *Hyalomma* sp. in Nigeria and Egypt. THOV is known to infect humans and animals (including cattle, sheep, donkeys, camels, buffaloes and rats). DHOV has different, but overlapping geographic distribution that includes India, eastern Russia, Egypt and southern Portugal. DHOV has been isolated from *Hyalomma* sp.

In 2012, the new genus *Quaranjavirus* was created in this virus family (Presti *et al.*, 2009; McCauley *et al.*, 2012). This genus comprises two species, *Quaranfil virus* and *Johnston Atoll virus*. Quaranfil virus was originally isolated from two children with febrile illness from the villages of Quaranfil and Sindbis in Egypt in 1953 (Taylor *et al.*, 1966). Subsequently several strains of the virus have been isolated from ticks and seabirds in a number of African and the Middle Eastern countries. Johnston Atoll virus is serologically related to Quaranfil virus. It was originally isolated from *Ornithodoros capensis* ticks collected in Noddy Tern bird nests (Sand Island, Johnston Atoll, central Pacific). Multiple strains have

Table 4. *Orthomyxoviridae* (segmented ssRNA-)

Genus/Species	Vector	Geographic localization	Host
Thogotovirus			
Thogoto virus	*A. variegatum, Hyalomma* spp., *Rhipicephalus* spp.	Cameroun, Egypt, Ethiopia, Iran, Kenya, Sicily, Uganda	cattle, camel, goat, sheep, rats,
Dhori virus	*D. marginatus, Hyalomma* spp.	Armenia, Azerbaijan, Egypt, India, Portugal, Russia, Saudi Arabia	sheep, waterfowl, camel, goats
Quaranjavirus			
Quaranfil virus	*Argas* spp.	Egypt, Nigeria, South Africa, Afghanistan, Iran	humans, egret, pigeons
Johnston Atoll virus	*C. capensis, C. denmarki*	Central Pacific Islands, Australia, New Zealand, southwest Africa, France, Germany	seabirds

Based on Adams *et al.* (2016); King *et al.* (2011). *A. – Amblyomma, C. – Carios, D. – Dermacentor.*

subsequently been isolated from ticks from eastern Australia, New Zealand, and Hawaii (Presti *et al.*, 2009).

In 2014, a new *Thogotovirus*, Bourbon virus, associated with febrile illness and death was described in the USA (Kosoy *et al.*, 2015).

2.2.5 Mononegavirales: Rhabdoviridae and Nyamiviridae (ssRNA-)

The order *Mononegavirales* was established in 1991 by ICTV to accommodate related viruses (assigned in three families, *Filoviridae, Paramyxoviridae*, and *Rhabdoviridae*) with non-segmented, linear, single-stranded negative-sense RNA genomes. Two families, *Bornaviridae* and *Nyamiviridae*, were added to the other three mononegaviral families in 1996 and 2014, respectively. In 2016, two new families, *Mymonaviridae* and *Sunviridae*, were included in the order *Mononegavirales* and the subfamily *Pneumovirinae* (*Paramyxoviridae*) was upgraded to family status *Pneumoviridae* (Afonso *et al.*, 2016).

By virome analysis of *I. scapularis*, Tokarz *et al.* (2014b) identified a new mononegavirales-like virus with the greatest similarity to the Nyamanini and Midway viruses (17% amino acid identity).

Members of the family *Rhabdoviridae* (Table 5) infect a wide range of vertebrates, invertebrates and plants. They can be transmitted by various arthropod vectors. A number of viruses of the genus *Vesiculovirus* are typical arboviruses, such as vesicular stomatitis virus (VSV). *Isfahan vesiculovirus* has been isolated from sandflies and also from *Hyalomma asiaticum* ticks in Turkmenia (Karabatsos, 1985). None of the recognised tick-borne rhabdoviruses is known to cause disease in humans. Within this family, a new *genus Ledantevirus* was created comprising 14 new species, four of which are TBVs – *Barur ledantevirus*, *Kern Canyon ledantevirus*, *Kolente ledantevirus* and *Yongjia ledantevirus* (Blasdell *et al.*, 2015; Walker *et al.*, 2015a, 2016a). Recently, a number of novel rhabdoviruses have been identified from various animal species, but so far only few tick-borne rhabdoviruses have been described. Ghedin *et al.* (2013) isolated Kolente virus from *A. variegatum* ticks and bats collected in Guinea, West Africa. However, little is known about its ecology, mode of transmission, host range or epidemiology. Another new probable TBV, Long Island tick rhabdovirus, was detected in *A. americanum* ticks (Tokarz *et al.*, 2014a). Dilcher *et al.* (2015) isolated a novel rhabdovirus named Zahedan virus (ZARV) from *Hyalomma anatolicum anatolicum* ticks in Iran, which is closely related to Moussa virus isolated from *Culex* mosquitoes from West Africa (Quan *et al.*, 2010) and Long Island tick rhabdovirus. Definitely, further studies are needed to confirm whether these viruses are tick-borne.

The new family *Nyamiviridae,* created in the order *Mononegavirales* in 2013 (Mihindukulasuriya *et al.*, 2009; Kuhn *et al.* 2013), comprises the genus *Nyavirus* including two TBVs, *Nyamanini nyavirus* (NYMV) and *Midway nyavirus* (MIDWV) (Table 5). NYMV was discovered in 1957 and repeatedly isolated from land birds and *Argas* spp. ticks. It is endemic to South Africa, Egypt, Thailand, Nigeria, Nepal, and Sri Lanka. MIDWV was discovered in 1966 and repeatedly isolated from sea birds and *Ornithodoros* spp. ticks. It is endemic to Hawaii, USA, and Japan. NYMV and MIDWV are serologically related, but clearly distinct from each other and not related serologically to any other virus tested (Kuhn *et al.*, 2013). *Sierra Nevada nyavirus* (SNVV), a new virus species in the family *Nyamiviridae*, was proposed in 2014 by Tesh *et al.* (2014). Based on its genomic structure and phylogeny, SNVV is closely related to NYMV and MIDWV, indicating that it is the third member of the *Nyavirus* genus (Rogers *et al.*, 2014). SNVV was originally isolated from Vero cell cultures inoculated with a homogenate of *O. coriaceus* ticks collected in northern California. The virus caused a viral cytopathic effect in both Vero and BHK cells within

Table 5. ***Mononegavirales*** **(ssRNA-),** ***Rhabdoviridae*** **and** ***Nyamiviridae***

Order/Family/ Genus/Species	Vector	Geographic localization	Host
Mononegavirales			
Rhabdoviridae			
Vesiculovirus			
Isfahan vesiculovirus	*Hy. asiaticum*	Russia, Iran	human, gerbils
Unassigned			
Kwatta	*H. spinigera, H. turturis*	Surinam	human, monkeys, rats
Ledantevirus			
Barur ledantevirus	*H. intermedia, R. pulchellus*	India, Kenya, Somalia	rats
Kern Canyon ledantevirus	*unknown*	USA	bats
Kolente ledantevirus	*A. variegatum*	Guinea	bats
Yongjia ledantevirus	*H. hystricis*	China	unknown
Connecticut virus	*I. dentatus*	USA	rabbit
New Minto virus	*H. leporispalustris*	USA	hare
Sawgras virus	*D. variabilis, H. leporispalustris*	USA	unknown
Nyamiviridae			
Nyavirus			
Nyamanini virus	*Argas* spp.	South Africa, Egypt, Thailand, Nigeria, Nepal, Sri Lanka	cattle egret
Midway nyavirus	*C.capensis, C. denmarki*	Hawaii, USA, Japan	seabirds, herons
Sierra Nevada nyavirus	*O. coriaceus*	USA	cattle

Based on Kuhn *et al.* (2013), Walker *et al.* (2016a), Adams *et al.* (2016), King *et al.* (2011). *C. – Carios, D. – Dermacentor*, *H. – Haemaphysalis*, *Hy. – Hyalomma*, *I.* – Ixodes, *O. – Ornithodoros, R. – Rhipicephalus*.

48 h after inoculation, and intracranial inoculation of newborne mice with SNVV lead to disease and death within 2–3 days (Tesh *et al.*, 2014).

3. Tick-virus interactions

3.1 Ticks as vectors of viruses

Ticks differ from other blood-feeding arthropods in several features (digestive process of blood within midgut cells, exceptional longevity, long feeding period, hematophagy in all postembryonic life stages, a wide array of vertebrate hosts) that greatly underline their remarkable success as vectors of viruses (Sonenshine *et al.*, 2002; Nuttall and Labuda, 2003; Nuttall, 2009). The survival strategy of ticks is very important for the survival of transmitted viruses. Because of their exceptional longevity, ticks can carry viruses for the duration of their lifespan and transmit them transstadially, thus ticks are also excellent reservoirs of TBVs.

Detection of a virus in a partially or fully engorged tick is not automatically a proof of tick vector competence. To determine tick vector competence, the following conditions must be fulfilled: (1) acquisition of the virus during blood-feeding on an infected host, and (2) transmission of the virus to a host by the tick after its moulting to the next development stage. In addition, during the "extrinsic incubation period" (i.e. between acquisition of the virus and its transmission) the tick is unable to transmit the virus (Nuttall, 2009).

The relationships between ticks and the transmitted viruses are highly specific. Only approximately 10% of the 900 known tick species have been proved to be vectors of TBVs (Labuda and Nuttall, 2008). However, the low percentage may be due to the fact that relatively few tick species, mainly members of the large tick genera, were screened for TBVs. For soft ticks these include *Ornithodoros, Carios* and *Argas*, and among hard ticks virus vectors have been found mostly in the genera *Ixodes, Haemaphysalis, Hyalomma, Amblyomma, Dermacentor* and *Rhipicephalus* (Labuda and Nuttall, 2004, 2008; Nuttall 2014). Majority of TBVs are transmitted either by hard ticks or by soft ticks, but rarely by both (Labuda and Nuttall, 2004). In addition, some tick species can be vectors of several (e.g. *I. ricinus, A. variegatum*) or many different TBVs species (e.g. *I. uriae* is the vector of at least 7 TBVs) (Labuda and Nuttall, 2008).

3.2 Transmission of viruses

Animal viruses can be transmitted by different modes – directly, mechanically and/or vertically. However, arboviruses undergo biological transmission through a competent arthropod vector and can be transmitted horizontally (from tick to tick = intrastadially, from tick to vertebrate host and vice versa) or vertically (transstadially and/or transovarially). A specific mode of TBVs persistence in the tick population is via transovarial transmission in which the virus from infected females is transmitted through eggs to their offspring. Although there is evidence of transovarial transmission from experimental studies for a number of TBVs, generally the levels of this mode of transmission in nature seem to be low (Nuttall *et al.*, 1994; Kuno and Chang, 2005).

The transmission cycle of TBVs can be presented as a triangle of parasitic interactions: (a) tick (vector) – virus, (b) virus – vertebrate host, and (c) tick (vector) – vertebrate host (Fig. 1). All three interfaces are essential for the survival of TBVs in nature. The direct interactions between TBVs and their vectors are initiated through infection of ticks during feeding on infected vertebrate hosts (Fig. 1a). The ability of TBVs to infect, replicate in and be carried by ticks is determined genetically and is also affected by extrinsic factors. Viruses taken up with the host blood as extracellular virions or within host cells enter the tick midgut (MG). They have to overcome several barriers (midgut infection barrier, midgut escape barriers, salivary gland infection barrier and salivary gland release barrier) to reach the salivary glands (SG) as well as to survive tissue histolysis and tissue replacement during molting (transstadial transmission) in order to be transmitted to the next host (Nuttall, 2014). In addition, viruses must evade tick innate immune responses in order to survive, persist, and be transmitted (Hynes, 2014). However, the mechanisms, by which TBVs disseminate in various tick tissues to reach the SG, where their replication is upregulated by feeding, are unknown and need to be further investigated (Nuttall, 2014; Slovák *et al.*, 2014).

Very important events determined by indirect interactions between vectors and viruses – "saliva assisted transmission" (SAT phenomenon), (Nuttall and Labuda, 2008) – occur in the vertebrate host skin at the site of the tick attachment (the tick – host interface, Fig. 1c), which is modified by the pharmacological properties of tick saliva and where TBVs are introduced via tick saliva. Tick saliva possesses a cocktail of pharmacologically active molecules with antihemostatic, vasodilatory, anti-inflammatory, antinociceptive and immunosuppressive activities (Kazimírová and Štibrániová, 2013; Štibrániová *et al.*, 2013; Wikel, 2013). Tick salivary molecules and their effects on host defense responses are exploited by TBVs for their transmission, replication and dissemination in the vertebrate hosts. Moreover, a novel mode of transmission, non-viremic transmission (NVT), is considered to be an indirect evidence of SAT. NVT represents a very efficient transmission between infected and uninfected ticks co-feeding in close proximity on the same host which may occur even in absence of viraemia. Since the first reports on SAT and NVT, indirect and direct evidence of SAT has been demonstrated for different TBVs (Nuttall and Labuda, 2008).

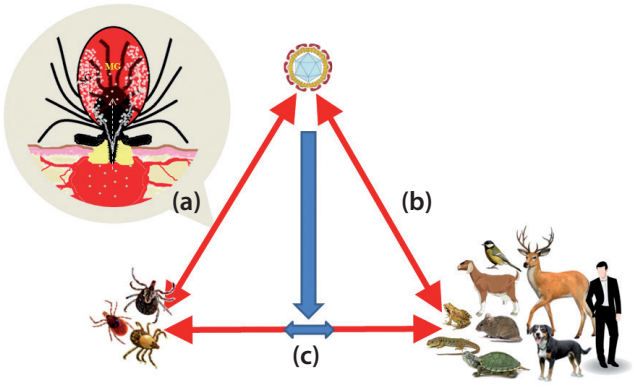

Fig. 1

Virus – tick – host interactions
The transmission cycle of tick-borne viruses is depicted as a triangle of parasitic interactions **(a)** virus – tick, **(b)** virus – vertebrate host, **(c)** tick – vertebrate host; MG – midgut, SG – salivary gland.

Virus – vector interaction is also affected by events in the vertebrate host skin (Fig. 1b). Once transmitted to a vertebrate host, TBVs face host immune responses, but the interactions of TBVs with vertebrate hosts and pathogenesis of viral infections will not be discussed in this review.

4. Conclusion

Current evidence suggests a global increase in the incidence of tick-borne diseases (TBD) causing a burden to human and animal health. In recent decades, a number of recognized TBVs have re-emerged and/or spread, and pose an increasing threat to human and animal health. Meanwhile, new TBVs are being discovered, and unclassified viruses are being allocated to genera or families thanks to improvements in molecular technologies. At present, more than 16 specific TBD of humans and 19 TBD of veterinary importance have been described (Nicholson *et al.*, 2009; Sonenshine and Roe, 2014). The latest emerging TBD, caused by Bourbon virus, was reported in Kansas in 2014 (Kosoy *et al.*, 2015). This trend of emerging TBD will likely continue.

Understanding the interactions between tick species and viruses represents a huge challenge and great opportunity to identify targets to control tick-borne viruses and to prevent the diseases they cause.

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References

Adams MJ, Lefkowitz EJ, King AMQ, Harrach B, Harrison RL, Knowles NJ, Kropinski AM, Krupovic M, Kuhn JH, Mushegian AR, Nibert M, Sabanadzovic S, Sanfacon H, Siddell SG, Simmonds P, Varsani A, Zerbini FM, Gorbalenya AE, Davison AJ, Arch. Virol. 161, 2921–2949, 2016. https://doi.org/10.1007/s00705-016-2977-6

Adams MJ, Lefkowitz EJ, King AMQ, Harrach B, Harrison RL, Knowles NJ, Kropinski AM, Krupovic M, Kuhn JH, Mushegian AR, Nibert M, Sabanadzovic S, Sanfaçon H, Siddell SG, Simmonds P, Varsani A, Zerbini FM, Gorbalenya AE, Davison AJ, Arch. Virol. 162, 2505–2538, 2017. https://doi.org/10.1007/s00705-017-3358-5

Afonso CL, Amarasinghe GK, Bányai K, Bao Y, Basler CF, Bavari S, Bejerman N, Blasdell KR, Briand FX, Briese T, Bukreyev A, Calisher CH, Dolnik O, Domier LL, Du R, Collins PL, Dietzgen RG, Freitas-Astu J, Dye JM, Easton AJ, Goodin MM, Formenty P, Hyndman TH, Hewson R, Lamb RA, Kobinger GP, Kurath G, Leroy EM, Lin X, Longdon B, Payne SL, Wang L, Zhang Y, Kuhn JH, Arch. Virol. 161, 2351–2360, 2016. https://doi.org/10.1007/s00705-016-2880-1

Ali BH, Obeid HM, Brit. Vet. J. 133, 184–189, 1977. https://doi.org/10.1016/S0007-1935(17)34140-4

Anderson EC, Hutchings GH, Mukarati N, Wilkinson PJ, Vet. Microbiol. 62 (1), 1–15, 1998. https://doi.org/10.1016/S0378-1135(98)00187-4

Attoui H, Mertens PPC, Becnel J, Belaganahalli S, Bergoin M, Brussaard CP, Chappell JD, Ciarlet M, del Vas M, Dermody TS, Dormitzer PR, Duncan R, Fang Q, Graham R, Guglielmi KM, Harding RM, Hillman B, Makkay A, Marzachì C, Matthijnssens J, Milne RG, Mohd Jaafar F, Mori H, Noordeloos AA, Omura T, Patton JT, Rao S, Maan M, Stoltz D, Suzuki N, Upadhyaya NM, Wei C, Zhou H, In: King AMQ, Adams MJ, Carstens EB, Lefkowitz EJ (Eds): Virus taxonomy: classification and nomenclature of viruses: Ninth Report of the International Committee on Taxonomy of Viruses. Elsevier Inc., 541–637, 2011.

Attoui H, Mohd Jaafar F, Biagini P, Cantaloube JF, De Micco P, Murphy FA, de Lamballerie X, Arch. Virol. 147, 533–561, 2002. https://doi.org/10.1007/s007050200005

Bell-Sakyi, L, Kohl A, Bente DA, Fazakerley JK, Vector-Borne Zoonotic Dis. 12, 769–81, 2012. https://doi.org/10.1089/vbz.2011.0766

Bente DA, Forrester NL, Watts DM, McAuley AJ, Whitehouse CA, Bray M, Antivir. Res. 100, 159–189, 2013. https://doi.org/10.1016/j.antiviral.2013.07.006

Bichaud L, de Lamballerie X, Alkan C, Izri A, Gould EA, Charrel RN, Microb. Pathog. 77, 136–141, 2014. https://doi.org/10.1016/j.micpath.2014.09.002

Blasdell K R, Guzman H, Widen SG, Firth C, Wood TG, Holmes EC et al., Am. J. Trop. Med. Hyg. 92, 405–410, 2015. https://doi.org/10.4269/ajtmh.14-0606

Brackney DE, Armstrong PM, Curr. Opin. Virol. 21, 67–74, 2016. https://doi.org/10.1016/j.coviro.2016.08.005

Briese T, Alkhovskiy SV, Beer M, Calisher CH, Charrel R, Ebihara H et al., Report number: ICTV [International Committee for Taxonomy of Viruses] Proposal (Taxoprop) No. 2016.030a-vM., 2016.

Burrage TG, Virus Res. 173, 131–139, 2013. https://doi.org/10.1016/j.virusres.2012.10.010

Carn VM, Kitching RP, Epidem. Inf. 114, 219-226, 1995. https://doi.org/10.1017/S0950268800052067

Charrel RN, Attoui H, Butenko AM, Clegg JC, Deubel V, Frolova TV, Gould EA, Gritsun TS, Heinz FX, Labuda M, Lashkevich VA, Loktev V, Lundkvist A, Lvov DV, Mandl CW, Niedrig M, Papa A, Petrov VS, Plyusnin A, Randolph S, Süss J, Zlobin VI, de Lamballerie X, Clin. Microbiol. Inf. 10, 1040–1055, 2004. https://doi.org/10.1111/j.1469-0691.2004.01022.x

Charrel RN, Zaki AM, Attoui H, Fakeeh M, Billoir F, Yousef AI, de Chesse R, De Micco P, Gould EA, de Lamballerie X, Biochem. Biophys. Res. Commun. 287, 455–461, 2001. https://doi.org/10.1006/bbrc.2001.5610

Chastel C, Main AJ, Couatarmanach A, Le Lay G, Knudson DL, Quillien MC, Beaucournu JC, Arch. Virol. 82, 161–171, 1984. https://doi.org/10.1007/BF01311160

Chihota CM, Rennie LF, Kitching RP, Mellor PS, Med. Vet. Entomol. 17, 294–300, 2003. https://doi.org/10.1046/j.1365-2915.2003.00445.x

Chihota CM, Rennie LF, Kitching RP, Mellor PS, Epidem. Inf. 126, 317–321, 2001. https://doi.org/10.1017/S0950268801005179

Cimolai N, Anand CM, Gish GJ, Calisher CH, Fishbein DB, Can. Med. Assoc. J. 139, 45–46, 1988.

Cisek AA, Dabrowska I, Gregorczyk KP, Wyzewski Z, Ann. Parasitol. 62, 161–167, 2016.

Costard S, Mur L, Lubroth J, Sanchez-Vizcaino JM, Pfeiffer DU, Virus Res. 173, 191–197, 2013. https://doi.org/10.1016/j.virusres.2012.10.030

Davies CR, Jones LD, Nuttall PA, Am. J. Trop. Med. Hyg. 35, 1256–1262, 1986. https://doi.org/10.4269/ajtmh.1986.35.1256

Dilcher M, Alves MJ, Finkeisen D, Hufert F, Weidmann M, Virus Genes 45, 311–315, 2012. https://doi.org/10.1007/s11262-012-0785-y

Dilcher M, Faye O, Faye O, Weber F, Koch A, Sadegh C, Weidmann M, Sall AA, Virol. J. 12, 183, 2015. https://doi.org/10.1186/s12985-015-0410-5

Dixon LK, Alonso C, Escribano JM, Martins C, Revilla Y, Salas ML,Takamatsu H, In King AMQ, Adams MJ, Carstens EB, Lefkowitz EJ (Eds): Virus taxonomy: classification and nomenclature of viruses: Ninth Report of the International Committee on Taxonomy of Viruses. Elsevier Inc. 153–162, 2011.

Dobler G, Vet. Microbiol. 140, 221–228, 2010. https://doi.org/10.1016/j.vetmic.2009.08.024

Dörrbecker B, Dobler G, Spiegel M, Hufert FT, Travel Med. Infect. Dis. 8, 213–222, 2010. https://doi.org/10.1016/j.tmaid.2010.05.010

Ebel GD, Annu Rev. Entomol. 55, 95–110, 2010, https://doi.org/10.1146/annurev-ento-112408-085446

Emmons RW, Annu. Rev. Microbiol. 42, 49–64, 1988. https://doi.org/10.1146/annurev.mi.42.100188.000405

Elliot RM, Brennan B, Curr. Opin. Virol. 5, 50–57, 2014. https://doi.org/10.1016/j.coviro.2014.01.011

de la Fuente J, Antunes S, Bonnet S, Cabezas-Cruz A, Domingos AG, Estrada-Pe-a A, Johnson N, Kocan KM, Mansfield KL, Nijhof AM, Papa A, Rudenko N, Villar M, Alberdi P, Torina A, Ayllón N, Vancova M, Golovchenko M, Grubhoffer L, Caracappa S, Fooks AR, Gortazar C, Rego ROM, Front. Cell. Infect. Microbiol. 7, 1–13, 2017. https://doi.org/10.3389/fcimb.2017.00114

Ficová M, Betáková T, Pančík P, Václav R, Prokop P, Halásová Z, Kúdelová M, Microb. Ecol. 62, 862–867, 2011. https://doi.org/10.1007/s00248-011-9907-7

Gaunt M, Sall AA, de Lamballerie X, Falconar AKI, Dzhivanian TI, Gould EA, J. Gen. Virol. 82, 1867–1876, 2001. https://doi.org/10.1099/0022-1317-82-8-1867

Ghedin E, Rogers MB, Widen SG, Guzman H, Travassos da Rosa APA, Wood TG, Fitch A, Popov V, Holmes EC, Walker PJ, Vasilakis N, Tesh RB, J. Gen. Virol. 94, 2609–2615, 2013. https://doi.org/10.1099/vir.0.055939-0

Grard G, Moureau G, Charrel RN, Lemasson JJ, Gonzalez JP, Gallian P, Gritsun TS, Holmes EC, Gould EA, de Lamballerie X, Virology 361, 80–92, 2007. https://doi.org/10.1016/j.virol.2006.09.015

Gritsun TS, Lashkevich VA, Gould EA, Antiviral Res. 57, 129–146, 2003. https://doi.org/10.1016/S0166-3542(02)00206-1

Hajnická V, Kúdelová M, Štibrániová I, Slovák M, Bartíková P, Halásová Z, Pančík P, Belvončíková P, Vrbová M, Holíková V, Hails RS, Nuttall PA, Front. Cell. Infect. Microbiol. 7, 458, 2017. https://doi.org/10.3389/fcimb.2017.00458

Hermance ME, Thangamani S, Vector-Borne Zoonotic Dis. 17(7), 453-462, 2017. https://doi.org/10.1089/vbz.2017.2110

Hoogstraal H, J. Med. Entomol. 15, 307–417, 1979. https://doi.org/10.1093/jmedent/15.4.307

Hubálek Z, Rudolf I, Parasitol. Res. 111, 9–36, 2012. https://doi.org/10.1007/s00436-012-2910-1

Hynes WL, In Sonnenshine D, Roe RM, (Eds): Biology of Ticks, Vol. 2, Oxford University Press, Oxford, New York, 129–146, 2014.

Jones LD, Hodgson E, Nuttall PA, J. Gen. Virol. 70, 1895-1898, 1989. https://doi.org/10.1099/0022-1317-70-7-1895

Junglen S, Curr. Opin. Insect Sci. 16, 81–86, 2016. https://doi.org/10.1016/j.cois.2016.05.017

Karabatsos N, International catalogue of arboviruses including certain other viruses of vertebrates. Karabatsos N (Ed) San Antonio, TX: American Society of Tropical Medicine and Hygiene; USA, 1985

Kazimírová M, Štibrániová I, Front. Cell. Infect. Microbiol. 3, 43, 2013. https://doi.org/10.3389/fcimb.2013.00043

Kazimírová M, Thangamani S, Bartíková P, Hermance M, Holíková V, Štibrániová I, Nuttall PA, Front. Cell. Infect. Microbiol. 7:339, 2017. https://doi.org/10.3389/fcimb.2017.00339

Kim KH, Yi J, Kim G, Choi SJ, Jun KI, Kim NH, Choe PG, Kim NJ, Lee JK, Oh MD, Emerg. Infect. Dis. 19, 1892–1894, 2013. https://doi.org/10.3201/eid1911.130792

King AMQ, Adams MJ, Carstens EB, Lefkowitz EJ, Virus taxonomy: classification and nomenclature of viruses: Ninth Report of the International Committee on Taxonomy of Viruses. Elsevier Inc., 2011.

Kleiboeker SB, Scoles GA, Anim. Health Res. Rev. 2, 121–128, 2001.

Kobayashi D, Ohashi M, Osei JHN, Agbosu E, Opoku M, Agbekudzi A, Joannides J, Fujita R, Sasaki T, Bonney JHK, Dadzie S, Isawa H, Sawabe K, Ohta N, Ticks Tick-Borne Dis. 8, 640–645, 2017. https://doi.org/10.1016/j.ttbdis.2017.04.010

Kosoy OI, Lambert AJ, Hawkinson DJ, Pastula DM, Goldsmith CS, Hunt DC, Staples JE, Emerg. Infect. Dis. 21, 760–764, 2015. https://doi.org/10.3201/eid2105.150150

Kúdelová M, Belvončíková P, Vrbová M, Kovaľová A, Štibrániová I, Kocáková P, Slovák M, Špitalská E, Lapuníková B, Matúšková R, Šupolíková M, Microb. Ecol. 70, 785–794, 2015. https://doi.org/10.1007/s00248-015-0622-7

Kudelova M, Janosova M, Vrbova M, Matuskova R, Slovak M, Belvoncíkova P, J. Infect. Dis. Ther. 5, 4, 1–4, 2017.

Kuhn JH, Alkhovskiy SV, Bào Y, Palacios G, Tesh RB, Vasilakis N et al., Technical Report. Report number: ICTV [International Committee for Taxonomy of Viruses] Proposal (Taxoprop) No. 2016.026a,bM. 2016a.

Kuhn JH, Bekal S, Caì Y, Clawson AN, Domier LL, Herrel M, Jahrling PB, Kondo H, Lambert KN, Mihindukulasuriya KA et al., Arch. Virol. 158, 2209–2226, 2013. https://doi.org/10.1007/s00705-013-1674-y

Kuhn JH, Wiley MR, Rodriguez SE, Bao Y, Prieto K, Travassos da Rosa APA, Guzman H, Savji N, Ladner JT, Tesh RB, Wada J, Jahrling PB, Bente DA, Palacios G, Viruses 8, 164, 1–27, 2016b.

Kuno G, Chang GJJ, Clin. Microbiol. Rev. 18, 608–637, 2005. https://doi.org/10.1128/CMR.18.4.608-637.2005

Labuda M, Nuttall PA, Parasitology 129 (Suppl.), S221–S245, 2004.

Labuda M, Nuttall PA, In Ticks Biology, Disease and Control, Bowman AS, Nuttall PA (Eds), Cambridges Univ. Press 253–280, 2008.

Lani R, Moghaddam E, Haghani A, Chang LY, AbuBakar S, Zandi K, Ticks Tick-Borne Dis. 5, 457–465, 2014. https://doi.org/10.1016/j.ttbdis.2014.04.001

Li CX, Shi M, Tian JH, Lin XD, Kang YJ, Chen LJ, Qin XC, Xu J, Holmes EC, Zhang YZ, Elife 4, 1–26, 2015.

Lubinga JC, Clift SJ, Tuppurainen ESM, Stoltsz WH, Babiuk S, Coetzer JAW, Venter EH, Ticks Tick-Borne Dis. 5, 113–120, 2014a. https://doi.org/10.1016/j.ttbdis.2013.09.010

Lubinga JC, Tuppurainen ESM, Coetzer JAW, Stoltsz WH, Venter EH, Exp. Appl. Acarol. 62, 77–90, 2014b. https://doi.org/10.1007/s10493-013-9721-7

Lubinga JC, Tuppurainen ESM, Coetzer JAW, Stoltsz WH, Venter EH, Exp. Appl. Acarol. 62, 67–75, 2014c. https://doi.org/10.1007/s10493-013-9722-6

Lubinga JC, Tuppurainen ESM, Mahlare R, Coetzer JAW, Stoltsz WH, Venter EH, Transbound. Emerg. Dis. 62, 174–182, 2015. https://doi.org/10.1111/tbed.12102

Lubinga JC, Tuppurainen ESM, Stoltsz WH, Ebersohn K, Coetzer JAW, Venter EH, Exp. Appl. Acarol. 61, 129–138, 2013. https://doi.org/10.1007/s10493-013-9679-5

Málková D, Holubová J, Kolman JM, Marhoul Z, Hanzal F, Kulková H, Markvart K, Simková L, Acta Virol. 24, 298, 1980.

Mans BJ, J. Innate. Immun. 3, 41–51, 2011. 10.1159/000321599 https://doi.org/10.1159/000321599

Mansfield KL, Jizhou L, Phipps LP, Johnson N, Front. Cell. Infect. Microbiol. 7, 298, 2017. https://doi.org/10.3389/fcimb.2017.00298

Mansfield KL, Johnson N, Phipps LP, Stephenson JR, Fooks AR, Solomon T, J. Gen. Virol. 90, 1781–1794, 2009. https://doi.org/10.1099/vir.0.011437-0

Mansfield KL, Morales AB, Johnson N, Ayllón N, Höfle U, Alberdi P, Fernández de Mera IG, Marín JFG, Gortázar C, de la Fuente J, Fooks AR, J. Gen. Virol. 96, 1676–1681, 2015. https://doi.org/10.1099/vir.0.000096

Matsuno K, Weisend C, Kajihara M, Matysiak C, Williamson BN, Simuunza M, Mweene AS, Takada A, Tesh RB, Ebihara H, J. Virol. 89, 594–604, 2015. https://doi.org/10.1128/JVI.02704-14

Matsuno K, Weisend C, Travassos da Rosa APA, Anzick SL, Dahlstrom E, Porcella SF, Dorward DW, Yu XJ, Tesh RB, Ebihara H, J. Virol. 87, 3719–3728, 2013. https://doi.org/10.1128/JVI.02845-12

McCauley JW, Hongo S, Kaverin NV, Kochs G, Lamb RA, Matrosovich M, Palese P, Perez D, Presti RM, Rimstad E, Smith G, Int. Comm. Taxon Viruses, 2011.012a-dV 1–7, 2012.

McMullan LK, Folk SM, Kelly AJ, MacNeil A, Goldsmith CS, Metcalfe MG, Batten BC, Albari-o CG, Zaki SR, Rollin PE, Nicholson WL, Nichol ST, N. Engl. J. Med. 367, 834–841, 2012. https://doi.org/10.1056/NEJMoa1203378

Meagher KE, Decker CF, Dis. Mon. 58, 370–376, 2012. https://doi.org/10.1016/j.disamonth.2012.03.010

Mellor PS, Kitchina RP, Wilkinson PJ, Res. Vet. Sci. 43, 109–112, 1987

Mihindukulasuriya KA, Nguyen NL, Wu G, Huang HV, Travassos APA, Popov VL, Tesh RB, Wang D, J. Virol. 83, 5109–5116, 2009. https://doi.org/10.1128/JVI.02667-08

Mlera L, Melik W, Bloom ME, Pathog. Dis. 71, 135–161, 2014. https://doi.org/10.1111/2049-632X.12178

Moshkin MP, Novikov EA, Tkachev SE, Vlasov VV, Bioessays 31, 620-628, 2009. https://doi.org/10.1002/bies.200800196

Mourya DT, Yadav PD, Basu A, Shete A, Patil DY, Zawar D, Majumdar TD, Kokate P, Sarkale P, Raut CG, Jadhav SM, J. Virol. 88, 3605–3609, 2014. https://doi.org/10.1128/JVI.02617-13

Moutailler S, Popovici I, Devillers E, Vayssier-Taussat M, Eloit M, New Microbes New Infect. 11, 71–81, 2016. https://doi.org/10.1016/j.nmni.2016.02.012

Mulenga A, Kim T, Ibelli AMG, Insect Mol. Biol. 22, 306–319, 2013. https://doi.org/10.1111/imb.12024

Munderloh UG, Liu YJ, Wang M, Chen CT, Kurtti J, J. Parasitol. 80, 533–543, 1994. https://doi.org/10.2307/3283188

Nichol ST, Beaty BJ, Elliot RM, Goldbach R. Plyusin A, Schmaljohn CS, Tesh R, In Fauquet CM, Mayo MA, Maniloff J, Desselberger U, Ball LA (Eds): Virus Taxonomy. Eighth Report of the International Committee on Taxonomy of Viruses. Elsevier Academic Press, London, United Kingdom. 695–716, 2005.

Nicholson WL, Sonenshine DE, Lane RS and Uilenberg G, In Mullen GR, Durden LA (Eds), Medical and Veterinary Entomology, 2nd edn., Academic Press, San Diego, CA. 493–541, 2009

Nuttall PA, In Sonenshine DE, Roe RM (Eds): Biology of Ticks, vol. 2. Oxford University Press, New York, USA, 180–210, 2014.

Nuttall PA, Labuda M, In Bowman SA, Nuttall PA (Eds): Ticks: Biology, Disease and Control. Cambridges University Press Disease, 205–219, 2008.

Nuttall PA, Labuda M, Adv. Virus Res. 60, 233–272, 2003. https://doi.org/10.1016/S0065-3527(03)60007-2

Nuttall PA, Front. Biosci. 14, 2466–2483, 2009. https://doi.org/10.2741/3390

Nuttall PA, Jones LD, Labuda M, Kaufman WR, J. Med. Entomol. 31, 1–9, 1994. https://doi.org/10.1093/jmedent/31.1.1

Oba M, Omatsu T, Takano A, Fujita H, Sato K, Nakamoto A, Takahashi M, Takada N, Kawabata H, Ando S, Mizutani T, J. Vet. Med. Sci. 78, 443–445, 2016. https://doi.org/10.1292/jvms.15-0536

Palacios G, Savji N, Travassos da Rosa A, Guzman H, Yu X, Desai A, Rosen GE, Hutchison S, Lipkin WI, Tesh R, J. Virol. 87, 3187-3195, 2013. https://doi.org/10.1128/JVI.02719-12

Papa A, Dalla V, Papadimitriou E, Kartalis GN, Antoniadis A, Clin. Microbiol. Inf. 16, 843–847, 2010. https://doi.org/10.1111/j.1469-0691.2009.02996.x

Papa A, Kontana A, Tsioka K, Chaligiannis I, Sotiraki S, Ticks Tick-Borne Dis. 7, 690–693, 2016. https://doi.org/10.1016/j.ttbdis.2016.02.017

Papa A, Kontana A, Tsioka K, Saratsis A, Sotiraki S, Ticks Tick-Borne Dis. 8, 157–160, 2017. https://doi.org/10.1016/j.ttbdis.2016.10.012

Pereira A, Figueira L, Nunes M, Esteves A, Cotão AJ, Vieira ML, Maia C, Campino L, Parreira R, Ticks Tick-Borne Dis. 8, 45–52, 2016. https://doi.org/10.1016/j.ttbdis.2016.09.015

Pesko KN, Torres-Perez F, Hjelle BL, Ebel GD, J. Gen. Virol. 91, 2698–705, 2010. http://dx.doi.org/10.1099/vir.0.024232-0 https://doi.org/10.1099/vir.0.024232-0

Plyusnin A, Beaty BJ, Elliott RM, Goldbach R, Kormelink R, Lundkvist Å, Schmaljohn CS, Tesh RB, In King AMQ, Adams MJ, Carstens EB, Lefkowitz EJ (Eds): Virus taxonomy: classification and nomenclature of viruses: Ninth Report of the International Committee on Taxonomy of Viruses. Elsevier Inc., 725–741, 2011.

Presti RM, Zhao G, Beatty WL, Mihindukulasuriya KA, Travassos da Rosa APA. Popov VL, Tesh RB, Virgin HW, Wang D, J. Virol. 83, 11599–11606, 2009. https://doi.org/10.1128/JVI.00677-09

Quan PL, Junglen S, Tashmukhamedova A, Conlan S, Hutchison SK, Kurth A, Ellerbrok H, Egholm M, Briese T, Leendertz FH, Lipkin WI, Virus Res. 147, 17–24, 2010. https://doi.org/10.1016/j.virusres.2009.09.013

Rajčáni J, Blaškovič D, Svobodová J, Čiampor F, Hučková D, Staneková D, Acta Virol. 29, 51–60, 1985.

Rajčáni J, Kúdelová M, In Minarovits J, Gonczol E, Valyi-Nagy T (Eds): Latency strategies of herpesviruses.

Chapt V. Springer, Berlin, 102–136, 2007. https://doi.org/10.1007/978-0-387-34127-9_5

Rehse-Küpper B, Casals J, Rehse E, Ackermann R, Acta Virol. 20, 339–342, 1976.

Robertson SJ, Mitzel DN, Taylor RT, Best SM, Bloom ME, Immunol Res. 43, 172–186, 2009. https://doi.org/10.1007/s12026-008-8065-6

Rogers MB, Cui L, Fitch A, Popov V, Travassos da Rosa APA, Vasilakis N, Tesh RB, Ghedin E, Am. J. Trop. Med. Hyg. 91, 159–164, 2014. https://doi.org/10.4269/ajtmh.14-0076

Savage HM, Godsey MS, Amy L, Panella NA, Burkhalter KL, Harmon JR, Lash RR, Ashley DC, Nicholson WL, Am. J. Trop. Med. Hyg. 89, 445–452, 2013. https://doi.org/10.4269/ajtmh.13-0209

Simmonds P, Becher P, Bukh J, Gould EA, Meyers G, Monath T, Muerhoff S, Pletnev A, Rico-Hesse R, Smith DB, Stapleton JT, Consortium IR, J. Gen. Virol. 98, 2–3, 2017. https://doi.org/10.1099/jgv.0.000672

Skinner MA, Buller RM, Damon IK, Lefkowitz EJ, McFadden G, McInnes CJ, Mercer AA, Moyer RW, Upton C, In King AMQ, Adams MJ, Carstens EB, Lefkowitz EJ (Eds): Virus taxonomy: classification and nomenclature of viruses: Ninth Report of the International Committee on Taxonomy of Viruses. Elsevier Inc., 291–307, 2011.

Slovák M, Kazimírová M, Siebenstichová M, Ustaníková K, Klempa B, Gritsun T, Gould EA, Nuttall PA, Ticks Tick-Borne Dis. 5, 962–969, 2014. https://doi.org/10.1016/j.ttbdis.2014.07.019

Sonenshine D, Lane R, Nicholson W, Med. Vet. Entomol. 517–558, 2002.

Sonenshine DE, Roe RM, Biology of Ticks Sonenshine DE, Roe RM (Eds), vol. 1, 2. Oxford University Press, New York, USA, 2014.

Swei A, Russell BJ, Naccache SN, Kabre B, Veeraraghavan N, Pilgard MA, Johnson BJB, Chiu CY, PLoS One 8, 2013.

Štibrániová I, Lahová M, Bartíková P, Acta Virol. 57, 200–216, 2013. https://doi.org/10.4149/av_2013_02_200

Takahashi T, Maeda K, Suzuki T, Ishido A, Shigeoka T, Tominaga T, Kamei T et al., J. Inf. Dis. 209, 816–827, 2014. https://doi.org/10.1093/infdis/jit603

Taylor RM, Hurlbut HS, Work TH, Kingston JR, Hoogstraal H, Am. J. Trop. Med. Hyg. 15, 76–86, 1966. https://doi.org/10.4269/ajtmh.1966.15.76

Tekin S, Barut S, Bursali A, Gul Aydogan G, Yuce O, Demir F, Yildirim B, S Afric. J. Microbiol. Res. 4, 214–217, 2010.

Tesh RB, Ghedin E, Vasilakis N, Rogers MB, Cui L, Fitch A, Popov V, Pravassos da Rosa, APA, ICTV taxonomic proposal 2014.007aV.A.v2. http://www. ictvonline.org/proposals-14/2014.007aV.A.v2.Nyavirus_sp.pdf 2014.

Tokarz R, Sameroff S, Leon MS, Jain K, Lipkin WI, Virol. J. 11, 1–5, 2014a. https://doi.org/10.1186/1743-422X-11-26

Tokarz R, Williams SH, Sameroff S, Sanchez Leon M, Jain K, Lipkin WI, J. Virol. 88, 11480–11492, 2014b. https://doi.org/10.1128/JVI.01858-14

Tuppurainen ESM, Lubinga JC, Stoltsz WH, Troskie M, Carpenter ST, Coetzer JAW, Venter EH, Oura CAL, Ticks Tick-Borne Dis. 4, 329–333, 2013a. https://doi.org/10.1016/j.ttbdis.2013.01.006

Tuppurainen ESM, Lubinga JC, Stoltsz WH, Troskie M, Carpenter ST, Coetzer JAW, Venter EH, Oura CAL, Epidemiol. Infect. 141, 425–430, 2013b. https://doi.org/10.1017/S0950268812000805

Tuppurainen ESM, Stoltsz WH, Troskie M, Wallace DB, Oura CAL, Mellor PS, Coetzer JAW, Venter EH, Transbound. Emerg. Dis. 58, 93–104, 2011. https://doi.org/10.1111/j.1865-1682.2010.01184.x

Turell MJ, PLoS Negl. Trop. Dis. 9, 1–8, 2015. https://doi.org/10.1371/journal.pntd.0004012

Vrbová M, Belvončíková P, Kovaľová A, Matúšková R, Slovák M, Kúdelová M, Acta Virol. 60, 426–428, 2016. https://doi.org/10.4149/av_2016_04_426

Walker PJ, Blasdell KR, Vasilakis N, Tesh RB, Calisher CH, Dietzgen RG, et al., ICTV 2016.006a-dM.A.v2.Ledantevirus. https://talk.ictvonline.org/ICTV/proposals/2016.006a-dM. A.v2.Ledantevirus.pdf 2016a.

Walker PJ, Firth C, Widen SG, Blasdell KR, Guzman H, Wood TG, Paradkar PN, Holmes EC, Tesh RB, Vasilakis N, PLoS Pathog. 11, e1004664, 2015a. https://doi.org/10.1371/journal.ppat.1004664

Walker PJ, Widen SG, Firth C, Blasdell KR, Wood TG, Travassos da Rosa APA, et al., Am. J. Trop. Med. Hyg. 93, 1041–1051, 2015. https://doi.org/10.4269/ajtmh.15-0344

Walker PJ, Widen SG, Wood TG, Guzman H, Tesh RB, Vasilakis N, Am. J. Trop. Med. Hyg. 94, 1107–1122, 2016b. https://doi.org/10.4269/ajtmh.15-0917

Wang J, Selleck P, Yu M, Ha W, Rootes C, Gales R, Wise T, Crameri S, et al., Emerg. Infect. Dis. 20, 1040–1043, 2014. https://doi.org/10.3201/eid2006.140003

Whitehouse CA, Antiviral Res. 64, 145–160, 2004. https://doi.org/10.1016/S0166-3542(04)00163-9

Wikel S, Front. Microbiol. 4, 1–10, 2013. https://doi.org/10.3389/fmicb.2013.00337

Wormser GP, Pritt B, Infect. Dis. Clin. North Am. 29, 371–381, 2015. 10.1016/j.idc.2015.02.009 https://doi.org/10.1016/j.idc.2015.02.009

Xu B, Liu L, Huang X, Ma H, Zhang Y, et al., PLoS Pathog. 7, e1002369, 2011. https://doi.org/10.1371/journal.ppat.1002369

Yu XJ, Liang MF, Zhang SY, Liu Y, Li JD, et al., N. Engl. J. Med. 364, 1523–1532, 2011. https://doi.org/10.1056/NEJMoa1010095

Zhang YZ, Zhou DJ, Xiong Y, Chen XP, He YW, Sun Q et al., Zhonghua Liu Xing Bing Xue Za Zhi 32, 209–220, 2011.