FORUM

Adaptations of Arboviruses to Ticks

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ABSTRACT Arboviruses differ from other viruses in their need to replicate in both vertebrate and invertebrate hosts. The invertebrate is a blood-sucking arthropod that is competent to transmit the virus between susceptible animals. Arboviruses transmitted by ticks must adapt to the peculiar physiological and behavioral characteristics of ticks, particularly with regard to blood feeding, bloodmeal digestion, and molting. Virus imbibed with the blood meal first infects cells of the midgut wall. During this phase the virus must contend with the heterophagic bloodmeal digestion of ticks (an intracellular process occurring within midgut cells) and overcome the as yet undefined "gut barrier" to infection. Genetic and molecular data for a number of tick-borne viruses indicate ways in which such viruses may have adapted to infecting ticks, but far more information is needed. After infection of midgut cells, tick-borne viruses pass to the salivary glands for transmission during the next blood-feeding episode. To do this, the virus must survive molting by establishing an infection in at least one cell type that does not undergo histolysis. Different tick-borne viruses have different strategies for surviving the molting period, targeting a variety of tick tissues. The infection can then persist for the life span of the tick with little evidence of any detrimental effects on the tick. Transmission to a vertebrate host during feeding most probably occurs via saliva that contains virus secreted from infected salivary gland cells. The virus then enters the skin site of feeding, which has been profoundly modified by the pharmacological effects of tick saliva. At least three tick-borne viruses exploit such tick-induced host changes. This phenomenon (saliva-activated transmission) is believed to underlie "nonviremic transmission," whereby a virus is transmitted from an infected to an uninfected cofeeding tick through a host that has an undetectable or very low viremia. Thus tick-borne viruses that have adapted to the feeding characteristics of their tick vectors may not need to induce a virulent infection (with high viremia) in their natural vertebrate hosts. Efficient transmission of tick-borne viruses between cofeeding ticks may be a means of amplifying virus infection prevalence in F_1 generations infected by transovarial transmission.

KEY WORDS ticks, arboviruses, arbovirus transmission

ARTHROPOD-BORNE VIRUSES (arboviruses) constitute the largest biological group of vertebrate viruses. Their considerable number (>530) suggests that transmission via an arthropod vector offers distinct benefits for viruses. However, there remain many questions as to how arboviruses are adapted to a mode of transmission dependent on blood-feeding arthropods.

By definition, arboviruses replicate in their arthropod vector. After a period of extrinsic incubation, they are transmitted as the infected vector imbibes a blood meal (horizontal transmission). Some viruses pass to the succeeding vector generation (vertical transmission). The horizontally transmitted virus replicates in a susceptible vertebrate, during which time it may be transmitted to uninfected vectors feeding on tha same animal. Thus arboviruses are distinct fron other viruses in their need to replicate in both vertebrate and invertebrate cells.

Approximately 50% of the viruses isolate from field-collected arthropods and listed in th International Catalogue of Arboviruses (Karabat sos 1985) are from mosquitoes, and 25% are fron ticks. The rest are mostly from sand flies an biting midges (gnats). Tick-borne viruses associ ated with diseases of vertebrates are transmitte mainly by ixodid species (Table 1). Most studie on the interactions between arboviruses an their vectors have focused on mosquito-born viruses. However, ticks differ considerably fror mosquitoes in their physiology and behavio Such differences probably explain why tick borne viruses are not readily transmitted by ir sects and, to a lesser degree, why insect-born viruses are not usually transmitted by ticks (Nu tall et al. 1991). A notable exception is the mo

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Table 1. Tick-borne viruses associated with disease in vertebrates

Virus	Primary tick vector species	Susceptible vertebrate host	Distribution
African swine fever	*Ornithodoros moubata* Walton, *O. erraticus*	Pigs	Africa, Europe
Colorado tick fever	*Dermacentor andersoni**	Humans	North America
Crimean-Congo hemorrhagic fever	*Hyalomma* spp.* and many others	Humans	Asia, Africa, Europe
Dhori	*Hyalomma dromedarii**, Koch *H. marginatum** Koch	Humans	Asia, Africa, Europe
Dugbe	*Amblyomma variegatum**	Humans	Africa
Issyk-Kul	*Argas vespertilionis* (Latreille)	Humans	Asia
Kemerovo	*Ixodes persulcatus** Schulze	Humans	Europe
Kyasanur Forest disease	*Haemaphysalis spinigera**, Neumann *H. turturis** Nuttall & Warburton	Humans, monkeys	Asia (India)
Lipovnik	*Ixodes ricinus**	Humans	Europe
Louping ill	*Ixodes ricinus**	Sheep, grouse, humans	Europe (Britain, Ireland)
Nairobi sheep disease	*Rhipicephalus appendiculatus** (Fabricius)	Sheep, humans	Africa
Omsk hemorrhagic fever	*Dermacentor reticulatus**, *Ixodes apronophorus** Schulze	Humans, muskrats	Asia (western Siberia)
Powassan	*Ixodes cookei**, Packard *I. persulcatus**	Humans	North America, Asia
Quaranfil	*Argas* spp.	Humans	Africa, Asia
Thogoto	*Rhipicephalus appendiculatus**	Sheep	Africa, Asia, Europe
Tick-borne encephalitis	*Ixodes persulcatus**, *I. ricinus**	Humans	Asia, Europe
Wanowrie	*Hyalomma* spp.*	Humans	Asia, Africa

Adapted from Karabatsos (1985).
* Ticks of the family Ixodidae.

quito-borne flavivirus, West Nile, which has several tick vectors that are believed to play a role in virus dissemination and overwintering (Hayes 1988).

Three biological features of ticks can be singled out for their potential influence on arbovirus infection, replication, persistence, and transmission: (1) blood feeding, (2) bloodmeal digestion, and (3) molting. In this paper, we consider how some viruses are adapted to these and other characteristics of ticks to ensure successful transmission.

Arbovirus Infection of Ticks

Ticks feeding on an infected host take up virus with their blood meal. The virus enters the tick gut lumen as extracellular virus particles (virions), infected host cells, or both. A general finding from several studies is that the higher the blood titer of virus, the greater the proportion of ticks that becomes infected (Singh & Anderson 1968, Davies et al. 1990).

Virus replication commences after entry of virions into cells of the midgut wall. For example, 24 h after capillary feeding of *Amblyomma variegatum* Fabricius with Dugbe virus, ≈10% of the gut digestive cells were infected (Booth et al. 1991). Similar studies with Powassan virus in *Dermacentor andersoni* Stiles (Chernesky & McLean 1969) and with Qalyub virus in *Ornithodoros erraticus* (Lucas) (Miller et al. 1985) demonstrated that cells of the midgut epithelium are the first site of virus infection.

Tick gut cells are also the site of genetic interactions between viruses. For Thogoto virus, which has a segmented genome, this involves swapping of genomic segments (reassortment) between replicating virions, giving rise to new viral genotypes (reassortants). Reassortment of Thogoto virus in its natural tick vector, *Rhipicephalus appendiculatus* Neumann, was demonstrated following superinfection of larvae or nymphs using an interrupted feeding technique (Davies et al. 1987). During the first partial blood meal, the ticks were infected with a temperature-sensitive (*ts*) mutant of Thogoto virus, and then they completed engorgement on a blood meal containing a second, genetically compatible *ts* mutant. Reassortant Thogoto virus (i.e., having a wild-type, ts^+ phenotype) was isolated 12 to 15 d later from the fed ticks. The ts^+ virus was transmitted to susceptible laboratory animals when the molted ticks took their next blood meal. Interference studies indicated that the primary site of reassortment was the tick gut (Davies et al. 1989, Jones et al. 1989b).

Experiments comparing different methods of infecting ticks have demonstrated the presence of a "gut barrier" to virus infection. For example, Dhori and Dugbe viruses replicated in *R. appendiculatus* after inoculation into the tick hemocoel, a route of infection bypassing the gut. However, neither virus established an infection when

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whereas others have few (e.g., Nairo
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differ markedly for ticks and insects
the principal reason tick-borne virus
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If the method of bloodmeal diges
exerts a strong selective pressure on
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viruses is likely to differ considerab

Susceptible vertebrate host	Distribution
gs	Africa, Europe
ımans	North America
ımans	Asia, Africa, Europe
umans	Asia, Africa, Europe
umans	Africa
umans	Asia
umans	Europe
umans, monkeys	Asia (India)
umans	Europe
ıeep, grouse, humans	Europe (Britain, Ireland)
ıeep, humans	Africa
umans, muskrats	Asia (western Siberia)
umans	North America, Asia
umans	Africa, Asia
heep	Africa, Asia, Europe
umans	Asia, Europe
umans	Asia, Africa

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The susceptibility of arthropod midgut cells to virus infection is one of the most important determinants of vector competence, "the combined effect of all the physiological and ecological factors of vector, host, pathogen, and environment that determine the vector status of members of a given arthropod population" (McKelvey et al. 1981). Understanding the determinants of vector competence is important in explaining why certain tick-borne viruses have many tick vectors (e.g., Crimean-Congo hemorrhagic fever virus) whereas others have few (e.g., Nairobi sheep disease virus).

The initial stages of virus infection are likely to differ markedly for ticks and insects and may be the principal reason tick-borne viruses are rarely, if ever, transmitted by insects. Thus, viruses entering the tick midgut are exposed to different environmental conditions compared with those existing in, for example, the mosquito midgut. This is because ticks are heterophagous (i.e., bloodmeal digestion is primarily an intracellular process [occurring within midgut cells; Sonenshine 1991]). In contrast, the blood meal of insect vectors is digested extracellularly (within the midgut lumen). Studies with mosquitoes and La Crosse virus (Bunyaviridae, *Bunyavirus*) indicate that cleavage of a protein exposed on the surface of virions is necessary to initiate infection (Ludwig et al. 1989). The necessary proteolytic conditions apparently occur in the midgut of mosquitoes, but such conditions may not be present in the midgut of heterophagic ticks.

If the method of bloodmeal digestion in ticks exerts a strong selective pressure on arboviruses, the structure of the outer surface of tick-borne viruses is likely to differ considerably from that of related insect-borne viruses (given that virion cell surface interactions are the first phase o infection). Currently, this hypothesis cannot be tested because there are insufficient data, for ar boviruses, on the three-dimensional structure o virions and the nature of virus receptors. How ever, comparative sequence data have revealec considerable differences in the virion surface proteins of gnat-transmitted orbiviruses (e.g. bluetongue viruses) and the tick-transmitted Ke merovo serogroup orbiviruses (Iwata et al. 1992 Moss et al. 1992) and in the surface envelope protein of tick-borne flaviviruses (e.g., tick-borne encephalitis virus), which contains a unique re gion of six contiguous amino acids not found ir the envelope protein of mosquito-borne flavivi ruses (e.g., yellow fever virus) (Shiu et al. 1991) It remains to be determined whether such differ ences are related to the specific adaptations o arboviruses to either tick or insect vectors.

A remarkable example of an apparent viral ad aptation to ticks is shown by Thogoto and Dhor viruses. They have no known insect-transmitted relatives and are classified with the influenza viruses in the family Orthomyxoviridae (Nuttal et al. 1993). The single glycoprotein of tick-borne orthomyxoviruses is unrelated to influenza vira proteins but instead shows significant amino acic sequence homology with the glycoprotein (gp 64/67) of baculoviruses (Morse et al. 1992). Apar from this glycoprotein, tick-borne orthomyxovi ruses and baculoviruses (which infect only inver tebrates) are totally unrelated. Tick glycopro teins, in common with glycoproteins of othe arthropods, do not seem to contain sialic acic (Del Pino et al. 1989). Thus, although the evolu tionary origin of the tick-borne orthomyxovira glycoprotein is obscure, it seems likely that thi protein represents a specific adaptation o Thogoto and Dhori viruses that facilitates infec tion of ticks.

Arbovirus Replication and Persistence in Ticks

As a result of the feeding behavior of ticks viruses must persist from one instar to the next t be transmitted to a vertebrate host. This mean that the "extrinsic incubation period," which i so important in determining the transmission dy namics of insect-borne viruses (Turell 1988), i not significant for virus transmission by ixodic ticks because it is unlikely to exceed the compar atively long molting period. However, the extrin sic incubation period is important in terms o virus survival (and in the rare cases of inter rupted feeding by ticks).

The histolytic enzymes and tissue replace ment associated with molting provide a poten tially hostile environment for infecting viruse (Balashov 1972). Several authors have suggested that the dynamics of viral replication within th tick reflect these events: a fall in virus titer, fol

Table 2. Virus localization in the tick vector

Virus	Tick	Localization	Reference
Powassan	*Dermacentor andersoni*	Midgut, salivary glands, Gené's organ	Chernesky & McLean (1969)
African swine fever	*Ornithodoros moubata*	Midgut, hemocytes	Greig (1972)
Qalyub	*Ornithodoros erraticus*	Midgut	Miller et al. (1985)
Thogoto	*Rhipicephalus appendiculatus*	Synganglion	Booth et al. (1989)
Dugbe	*Amblyomma variegatum*	Hemocytes	Booth et al. (1991)

lowed by an increase in titer as the virus infects and replicates in replacement tick tissues (Reháček 1965, Burgdorfer & Varma 1967, Chernesky & McLean 1969, Miller et al. 1985). However, the replication of some viruses (e.g., Thogoto virus in *R. appendiculatus*, Langat virus in *Ixodes ricinus* [Linnaeus]) is not obviously correlated with any particular stage of the molting period (Varma & Smith 1972, Davies et al. 1986). These conflicting observations can be explained by the variety of infection strategies adopted by tick-borne viruses (Table 2). The apparent targeting of specific cell types, tissues, or organs may reflect mechanisms by which different tick-borne viruses have adapted to survive the molting period, namely by establishing an infection in at least one cell type that does not undergo histolysis.

An additional feature that distinguishes tick-borne from insect-borne viruses is the comparative longevity of their vectors. The life cycle of ticks is usually measured in years rather than in weeks or months, and individual stages can survive several years without a blood meal (Sonenshine 1991). Experimental data indicate that virus infections persist in ticks for the duration of the ticks' life span (Reháček 1965, Miller et al. 1985, Davies et al. 1986). Ecological and epidemiological data also support the observation that tick-borne virus survival is greatly dependent on persistent infections in tick populations (Lewis 1946, Blaškovič & Nosek 1972, World Health Organization 1986).

If viruses rely on ticks for their long-term survival, selection must favor infections that have no detrimental effect on the tick. This appears to be the case, although few studies have been published. For example, differences were not detected in the reproductive output, molting success, and survival of uninfected *R. appendiculatus*, compared with ticks of the same population that were infected with Thogoto virus at the larval stage (L.D.J., unpublished observation). Furthermore, the physiology of adult female *A. variegatum*, as measured by the rate and volume of their saliva secretion, appeared to be the same for uninfected and Thogoto virus–infected ticks (W.R.K., unpublished observation). In contrast to these observations, African swine fever virus was reported to cause mortality in *Ornithodoros* sp. ticks, under laboratory conditions (Endris et al. 1992). However, there are far more reports that insect-borne viruses can adversely affect their vectors (Turell 1988).

One method of arbovirus persistence in the vector population is via vertical transmission, in which virus from the infected parent, usually the female, is transmitted via the egg to the succeeding generation. Although evidence of vertical transmission has been recorded for numerous tick-borne viruses (Table 3), the levels of vertical transmission and filial infection in nature generally seem to be low. Certainly, the high levels of vertical transmission of certain insect-borne viruses associated with stabilized infections of their vectors (Turell 1988) have not been recorded for any tick-borne viruses. However, vertical transmission of insect-borne viruses can have adverse effects on the vector population (Turell 1988). If, as discussed above, tick-borne viruses rely on their vectors for persistence, then any deleterious effects of vertical transmission on ticks may outweigh the advantages to the virus. The balancing of costs and benefits of vertical transmission, together with the gains from cofeeding and nonviremic transmission (see next section), may explain why vertical transmission is common among tick-borne viruses but occurs at a low level.

Transmission of Arboviruses by Ticks

The main route of virus transmission by infected ticks is via saliva secreted during feeding. Nevertheless, there are only a few studies reporting virus detection in tick saliva (Chernesky & McLean 1969, Plowright 1977), including Thogoto virus in the saliva of naturally infected *A. variegatum* (S. Lowell & L.D.J., unpublished data). Most of the evidence of a salivary gland route of transmission is based on observations of infection of vertebrate hosts on which infected ticks have engorged.

The salivary glands of ticks undergo resorption and regeneration during molting, hence virus infection of the salivary glands is likely to be a relatively late event in the infection cycle within ticks. A few reports describe virus in the salivary glands, but the timing of infection varies. Tick-borne encephalitis (TBE) and Powassan viruses infect the salivary glands before feeding; presumably they can be transmitted to the vertebrate host as soon as feeding is initiated (Reháček 1965, Chernesky & McLean 1969). In

Table 3. Tick-borne viruses transmitted

Virus family	Virus
Flaviviridae	Kyasanur Forest disease
	Louping ill
	Omsk hemorrhagic fever
	Tick-borne encephalitis (Far Eastern subtype)
	Tick-borne encephalitis (European subtype)
Bunyaviridae	Bahig
	Crimean-Congo hemorrhagic fever
	Dugbe
	Kaisodi
	Nairobi sheep disease
	Ponteves
	Sakhalin
	Tamdy
	Uukuniemi
Reoviridae	Colorado tick fever
(Poxviridae)	African swine fever

contrast, Thogoto and Dugbe viruses in the salivary glands after feeding (Booth et al. 1989, 1991).

It is not known what mechanism c release of virus into the saliva, or wh is secreted throughout the compara feeding period and at what rate. On traces of Thogoto virus were detecte liva of *A. variegatum* females stimu cially with dopamine immediately aft been inoculated parenterally with doses (W.R.K., unpublished observa suggests that virus that is secreted in ably originates from infected salivary rather than by dissemination to th glands from the hemocoel. Tick-bo may target secretory cells within th salivary glands of ticks to maximize t of transmission during feeding. In *variegatum* female ticks, Dugbe vir tected within discrete cells of type gland acini (Booth et al. 1991). The s of these observations requires invest cause knowledge of the timing and

ion	Reference
ls, Gené's organ	Chernesky & McLean (1969) Greig (1972) Miller et al. (1985) Booth et al. (1989) Booth et al. (1991)

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Table 3. Tick-borne viruses transmitted vertically

Virus family	Virus	Tick species	Reference
Flaviviridae	Kyasanur Forest disease	*Ixodes petauristae* Warburton	Singh et al. (1968)
		Argas persicus (Oken)	Singh et al. (1971)
		Ornithodoros tholozani (Laboulbène & Mégnin)	Bhat & Goverdhan (1973)
	Louping ill	*I. ricinus*	Stockman (1918)
	Omsk hemorrhagic fever	*Dermacentor reticulatus*	Avakian & Lebedev (1955)
	Tick-borne encephalitis (Far Eastern subtype)	*I. persulcatus*	Chumakov (1944)
		I. ricinus, D. nuttalli, Olenev *Hyalomma dromedarii, Hy. asiaticum* Schulze & Schlottke	Chumakov et al. (1945)
		Haemaphysalis concinna Koch	Pavlovsky & Soloviev (1963)
	Tick-borne encephalitis (European subtype)	*I. ricinus*	Benda (1958), Reháček (1962)
		I. hexagonus Leach	Streissle (1960)
Bunyaviridae	Bahig	*Hy. marginatum*	Converse et al. (1974)
	Crimean-Congo hemorrhagic fever	*Hy. marginatum, Hy. rufipes, D. marginatus* (Sulzer), *Rhipicephalus rossicus* Yakimov & Kohl-Yakomova	Reviewed by Hoogstraal (1979)
		Hy. truncatum Koch	Wilson et al. (1991)
	Dugbe	*Amblyomma variegatum*	Huard et al. (1978)
	Kaisodi	*Ha. spinigera*	Karabatsos (1985)
	Nairobi sheep disease	*R. appendiculatus*	Montgomery (1917), Daubney & Hudson (1931)
		R. pulchellus (Gerstaecker)	Pellegrini (1950)
	Ponteves	*Argas reflexus* (Fabricius)	Hannoun et al. (1970)
	Sakhalin	*I. uriae* White	L'vov et al. (1972)
	Tamdy	*Hy. asciaticum*	L'vov et al. (1984)
	Uukuniemi	*I. ricinus*	Samoilova & Danilova (1974)
Reoviridae	Colorado tick fever	*D. andersoni*	Florio et al. (1950)
(Poxviridae)	African swine fever	*O. moubata*	Plowright et al. (1970)

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It is not known what mechanism controls the release of virus into the saliva, or whether virus is secreted throughout the comparatively long feeding period and at what rate. Only irregular traces of Thogoto virus were detected in the saliva of *A. variegatum* females stimulated artificially with dopamine immediately after they had been inoculated parenterally with high viral doses (W.R.K., unpublished observation). This suggests that virus that is secreted in saliva probably originates from infected salivary gland cells rather than by dissemination to the salivary glands from the hemocoel. Tick-borne viruses may target secretory cells within the complex salivary glands of ticks to maximize the chances of transmission during feeding. In infected *A. variegatum* female ticks, Dugbe virus was detected within discrete cells of type III salivary gland acini (Booth et al. 1991). The significance of these observations requires investigation because knowledge of the timing and duration of virus secretion by ticks is important in developing control strategies for tick-borne virus diseases.

The introduction of salivary gland secretions into the feeding lesion is a potent mediator of host reactions (Kaufman 1989). To counteract these reactions, tick saliva possesses pharmacologically active substances that have antihemostatic, vasodilatory, anti-inflammatory, and immunosuppressive activities. Thus, a virus transmitted by a tick during feeding enters a skin site that is profoundly altered by the effects of tick saliva (Titus & Ribeiro 1990). What effects do these changes have on virus transmission?

Comparison of different methods of infecting ticks with viruses demonstrates clearly that co-feeding uninfected ticks with infected ticks is the most efficient means of virus transmission. For example, nearly all the uninfected *R. appendiculatus* nymphs, placed on an uninfected guinea pig, became infected when they fed together with (though physically separated from) infected *R. appendiculatus* adult ticks (Jones et al. 1987). In contrast, <10% of the nymphs be

came infected when fed on guinea pigs inoculated with the virus by needle and syringe; however, when salivary gland extract was included in the virus inoculum, an average of 60% of ticks were infected (Jones et al. 1989c). Similar observations have been made for TBE virus (Alekseev & Chunikhin 1990; Alekseev et al. 1991; Labuda et al. 1993b,c,d) and Dhori virus (L.D.J., unpublished information). The phenomenon has been termed saliva-activated transmission (SAT) because a protein(s) secreted in tick saliva potentiates virus transmission (Jones et al. 1992a,b). The SAT factor modulates the skin site of tick attachment, presumably to facilitate feeding, and this modulation is exploited by the virus. However, the mode of action of the SAT factor is unknown, but, at least for Thogoto virus, lymphoid tissues may be involved (Jones et al. 1992b).

What effect does SAT have on the adaptation of arboviruses to ticks? SAT is believed to be the mechanism underlying "nonviremic transmission," the transmission of arboviruses between infected and uninfected ticks cofeeding on a vertebrate host that has no detectable (or very low levels of) viremia (Nuttall & Jones 1991). If such is the case, SAT has considerable implications for virus transmissibility and virus virulence in the vertebrate host. A study of TBE virus transmission provides a graphic illustration of this (Labuda et al. 1993d). Uninfected and infected *I. ricinus,* the primary vector species of TBE virus in Europe, were allowed to feed together on different uninfected wild-caught vertebrate species. Pine voles (*Pitymys subterraneus*) developed a highly virulent infection but yielded few infected ticks. In contrast, field mice (*Apodemus flavicollis* and *A. agrarius*) had low or undetectable viremias, low titers of virus in target organs (spleen and lymph node), and no clinical signs of infection; however, they gave rise to the highest numbers of infected ticks. Based on the results of these studies, three hypotheses were proposed: (1) low viremia (synonymous with low virulence) ensures that the host remains alive for at least the duration of the relatively long tick feeding period; (2) nonviremic transmission is not delayed by the time taken for a viremia to develop and, consequently, nonviremic transmission maximizes the chances of transmission between cofeeding ticks; and, most important, (3) nonviremic transmission promotes the survival of tick-borne viruses in nature. Thus, by adapting to and exploiting the saliva-induced changes that occur in the skin site of tick feeding, tick-borne viruses possess a novel means of increasing their chances of survival in natural ecosystems.

Nonviremic transmission also has important implications for vertical transmission. As discussed in the preceding section, vertical transmission is common among tick-borne viruses but occurs at an apparently low level. This has led several authors to claim that vertical transmission is not a significant factor in the ecology and epidemiology of tick-borne viruses (Reháček 1965, Burgdorfer & Varma 1967). A recent study demonstrated that a low level of TBE virus infection in a population of larval ticks (detectable only by polymerase chain reaction) can be amplified by nonviremic cofeeding to yield a significant number of infected nymphal ticks (Labuda et al. 1993a). Similar results have been reported for Crimean-Congo hemorrhagic fever virus (Gordon et al. 1993). Because larvae quest in clusters, there are many opportunities for amplification of vertically acquired tick-borne virus infections in the vector population through nonviremic transmission between cofeeding larvae. As a result of such amplification, vertical transmission might be the difference between survival and extinction of certain tick-borne virus infections in nature.

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