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REVIEW

Tick-borne viruses in Europe

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Abstract The aim of this review is to present briefly background information on 27 tick-borne viruses ("tiboviruses") that have been detected in Europe, viz flaviviruses tick-borne encephalitis (TBEV), louping-ill (LIV), Tyuleniy (TYUV), and Meaban (MEAV); orthobunyaviruses Bahig (BAHV) and Matruh (MTRV); phleboviruses Grand Arbaud (GAV), Ponteves (PTVV), Uukuniemi (UUKV), Zaliv Terpeniya (ZTV), and St. Abb's Head (SAHV); nairoviruses Soldado (SOLV), Puffin Island (PIV), Avalon (AVAV), Clo Mor (CMV), Crimean-Congo hemorrhagic fever (CCHFV); bunyavirus Bhanja (BHAV); coltivirus Eyach (EYAV); orbiviruses Tribec (TRBV), Okhotskiy (OKHV), Cape Wrath (CWV), Mykines (MYKV), Tindholmur (TDMV), and Bauline (BAUV); two thogotoviruses (Thogoto THOV, Dhori DHOV); and one asfivirus (African swine fever virus ASFV). Emphasis is laid on the taxonomic status of these viruses, range of their ixodid or argasid vectors and vertebrate hosts, pathogenicity for vertebrates including humans, and relevance to public health. In general, three groups of tibovirus diseases can be recognized according to main clinical symptoms produced: (i) febrile illness—usually with a rapid onset, fever, sweating, headache, nausea, weakness, myalgia, arthralgia, sometimes polyarthritis and rash; (ii) the CNS affection—meningitis, meningoencephalitis or encephalomyelitis with pareses, paralysis and other sequelae; (iii) hemorrhagic disease. Several "European" tiboviruses cause very serious human (TBEV, CCHFV) or animal (LIV, ASFV) diseases. Other arboviruses play definite role in human or animal pathology though the disease is usually either less serious or infrequently reported (TYUV, BHAV, AVAV, EYAV, TRBV, DHOV, THOV). The other European arboviruses are "orphans" without a proven medical or veterinary significance (BAHV, MTRV, MEAV, GAV, PTVV, ZTV, SAHV, UUKV, SOLV, PIV, AVAV, CMV, OKHV, CWV, MYKV, TDMV, BAUV). However, certain arbovirus diseases of free-living vertebrates (but also those of domestic animals and even man) may often pass unnoticed or misdiagnosed and eventually, they might potentially appear as emerging diseases. Active search for new tiboviruses or for new, pathogenic variants of the known tiboviruses in Europe should therefore continue.

Abbreviations

CF(T)	Complement fixation (test)
CPE	Cytopathic effect
HA	Hemagglutinin
HI(T)	Hemagglutination-inhibition (test)
i.c.	Intracerebral
i.m.	Intramuscular
i.n.	Intranasal
IFA	Immunofluorescent antibody assay
i.p.	Intraperitoneal
i.v.	Intravenous
p.o.	Peroral
PRNT	Plaque-reduction neutralization test
s.c.	Subcutaneous
TOT	Transovarial transmission (in arthropods)
TST	Transstadial transmission (in arthropods)
VN(T)	Virus neutralization (test)

Introduction

Tick-borne viruses (acronym "tiboviruses" might be used, for short) belong to an ecological group of viruses characterized by their specific biological transmission via competent hematophagous hard (ixodid) or soft (argasid) ticks

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(*Ixodidae* and *Argasidae*, respectively) to endotherm (homeotherm, warm-blooded) vertebrates. Competent vectors are those arthropods that are able to imbibe the virus in the course of blood-feeding on an infected donor vertebrate host, to support the multiplication of the virus in their organism and to deliver a sufficiently large inoculum to the recipient, uninfected vertebrate host. Usually certain minimum level of viremia ("infection threshold") in a donor vertebrate host is necessary for an efficient infection of particular arthropod vectors. Therefore, only those vertebrate species that produce at least moderate viremia have been regarded as competent, "true" or "amplifying" hosts of particular arboviruses (Bárdoš 1979). However, co-feeding ixodid ticks on a viremia-free host can sometimes also contribute to infection of noninfected ticks (Jones et al. 1987; Alekseev and Chunikhin 1990; Labuda et al. 1993). Some tiboviruses are transmitted from larvae to nymphs and imagoes during metamorphosis (transstadial transmission, TST), from infected female to the offspring (transovarial transmission, TOT), and from male to female tick during copulation (venereal or horizontal transmission). These modes are extremely important ecologically: e.g., under conditions of TOT, the tick vector also plays the role of a long-term reservoir of the virus.

In addition to two "major" severe, occasionally re-emerging virus diseases transmitted by ixodid ticks in Europe, viz tick-borne encephalitis and Crimean-Congo hemorrhagic fever, there is a number of other, neglected tick-borne virus infections of vertebrates. They are usually infrequent, although some of them are probably underdiagnosed, and other of these tiboviruses are nonpathogenic, or of low pathogenicity, for vertebrates (Tables 1 and 2).

This review briefly summarizes present knowledge especially on the taxonomy, ecology, epidemiology and distribution of European tiboviruses; for related reviews and additional, more detailed data, see, e.g. Theiler and Downs (1973), Karabatsos (1985), Málková et al. (1986), Lvov et al. (1989), Hubálek and Halouzka (1996), Charrel et al. (2004), Labuda and Nuttall (2004), Gratz (2006), and Dobler (2010). The virus taxonomy and nomenclature has been adopted from King et al. (2012).

Family *Flaviviridae*

Flavivirus of tick-borne encephalitis (TBEV)

There are three recognized TBEV subtypes: (1) Western or European subtype (TBEV-W), also called Central European (CEEV—topotype strains are Hypr and Neudoerfl) or sometimes "ricinus" subtype (Clarke 1964; Votyakov et al. 1978; Rubin and Chumakov 1980; Calisher 1988; Calisher et al. 1989; Gritsun et al. 2003; Lindquist and Vapalahti 2008)—varieties of this subtype are Spanish sheep encephalitis (SSE), Turkish sheep encephalitis (TSE) and Greek goat encephalitis ("Vergina") viruses; these three varieties are antigenically more closely related to TBEV-W (CEEV) than to louping ill virus (Hubálek et al. 1995); (2) (Ural-)Siberian subtype (TBEV-S: the prototype strains are Aina and Vasilchenko), sometimes called "persulcatus" subtype, causing Russian spring–summer encephalitis (RSSEV:); (3) Far Eastern subtype (TBEV-FE with prototype strain Sofyin, isolated from human brain in Khabarovsk, 1937). However, all three subtypes occur in Europe—the TBEV-S and TBEV-FE subtypes were recently detected in the Baltic republics and eastern Finland (Golovljova et al. 2004; Jääskeläinen et al. 2010). A taxonomic and nomenclatural confusion around TBEV has repeatedly been emphasized (Clarke 1964; Calisher 1988; Holzmann et al. 1992). In addition, TBEV is very closely related to louping-ill virus which should be regarded in fact as the fourth (or, historically, the first) subtype of TBEV (see below).

History: in Europe, RSSEV subtype of TBEV was first isolated in the Russian Ural Mts. in 1938 (Chumakov and Zeitlenok 1939), and CEEV (strain "256") from *Ixodes ricinus* ticks collected near Minsk, Belarus in 1940 (Levkovich and Karpovich 1962; Votyakov et al. 1978). Further isolations of CEEV were reported in Czechland from human patients and *I. ricinus* ticks in 1948–1949 (Gallia et al. 1949; Krejčí 1949; Rampas and Gallia 1949).

Principal arthropod vectors are ticks of the genus *Ixodes*: for CEEV *I. ricinus* (TST, TOT: Benda 1958b; Řeháček 1962; the infection rate may attain 0.5 % to 3 % in valent natural foci: Grešíková 1972), and *Ixodes gibbosus* (a vicariant, marginal vector in the Mediterranean). Occasional vectors are other tick species such as *Ixodes hexagonus* (Křivanec et al. 1988), possibly *Ixodes arboricola* (successful experimental transmission: Lichard and Kožuch 1967), while only sporadically metastriate tick species *Haemaphysalis inermis*, *Haemaphysalis concinna* (Riedl et al. 1971; TOT), *Haemaphysalis punctata*, *Dermacentor marginatus*, *Dermacentor reticulatus* (Georgiev et al. 1971; Kožuch and Nosek 1971; Naumov et al. 1980; Nosek and Kožuch 1985), and *Hyalomma marginatum* (Crimea). Main vector for RSSEV is *Ixodes persulcatus* (infection prevalence rates can reach frequently >2 %; TST, TOT: Chunikhin 1990), less often *Ixodes ovatus*, but also *Dermacentor silvarum, D. reticulatus, D. marginatus, H. concinna* (TOT), *Haemaphysalis longicornis*, and *Haemaphysalis japonica* (Naumov et al. 1980).

Competent vertebrate hosts of TBEV are small forest mammals, especially rodents and insectivores (*Apodemus flavicollis*, *Apodemus sylvaticus*, *Myodes glareolus*, *Myodes rufocanus*, *Microtus agrestis*, *Sciurus vulgaris*, *Talpa europaea*, *Sorex araneus, Erinaceus concolor*); additional hosts

Table 1 Experimental pathogenicity of tiboviruses occurring in Europe (Karabatsos 1985; Hubálek and Halouzka 1996)

	SM i.c.	SM i.p.	M i.c.	M i.p.	H i.c.	H i.p.	GP i.c.	GP i.p.	C s.c.	CE y.s.	Other
TBEV	3–5	3–6	4–7	5–9	4–6	4–12	7–8	(−)	−	3–7	RM, lamb ic + sc−
LIV	3–4	3–5	7	10	+	(+)	9–12	−	−	(+)	Lamb and goat ic+ M(+), grouse sc+
TYUV	3–6	4–8	3–7	(−)	nd	nd	(+)	−	−	nd	R ip−, RM in(−)
MEAV	5	+	+	−	nd	nd	nd	nd	−	nd	
BAHV	3–4	+	(+)	−	nd	nd	nd	nd	nd	nd	
MTRV	3	10	6	−	nd	nd	nd	nd	nd	nd	
GAV	7	nd	−	−	nd	nd	nd	nd	nd	nd	
PTVV	6	nd	7–8	−	nd	nd	nd	nd	nd	nd	
UUKV	4–6	+	−	−	−	−	−	−	−	3–7	RM ic(−) ip−
ZTV	+	−	−	−	nd	nd	nd	nd	(+)	nd	
SAHV	(+)	−	−	−	nd	nd	nd	nd	nd	nd	
SOLV	4–7	(−)	5–9	−	−	nd	5–8	nd	+	4–5	R, pigeon ic−
PIV	+	nd	nd	nd	nd	nd	nd	nd	nd	nd	
AVAV	7–12	(+)	(+)	−	nd	−	nd	−	−	nd	Rat ic−
CMV	4–11	6–15	−	−	nd	−	nd	−	−	nd	
CCHFV	4–7	5–9	(+)	−	−	−	−	−	nd	nd	RM, sheep ic (+)
BHAV	3–5	5–6	5–8	−	−	−	5–6	−	nd	4–6	RM, lamb ic(+)
EYAV	6–8	(+)	−	−	nd	−	nd	nd	nd	nd	
TRBV	3	4–6	(−)	−	(−)	−	−	−	−	2–4	ic: SH + RM(+)
OKHV	3	−	−	−	nd	nd	nd	nd	nd	nd	
CWV	2–4	3–8	−	−	nd	nd	nd	−	−	nd	Chick ic−
MYKV	3	nd	nd	nd	nd	nd	nd	nd	nd	nd	
TDMV	4	nd	nd	nd	nd	nd	nd	nd	nd	nd	
BAUV	3–4	4–5	−	−	nd	nd	nd	nd	3–5	nd	Chick ic +
THOV	3	3–4	4–8	(+)	+	3	nd	−	nd	nd	Sheep iv fever
DHOV	2–5	3–7	3–6	5–8	+	+	nd	−	nd	−	Ad rat ip,sc−
ASFV	nd	nd	nd	nd	nd	nd	nd	nd	nd	6–7	Pig sc+

The figures show the average survival time (days) of laboratory animals inoculated with particular viruses established after several mouse passages; +, death; (+), irregular death; (−), irregular encephalitis or pareses, but survival; −, no death; nd, not done. Animals: *SM* suckling mouse, *M* adult mouse, *H* adult Syrian hamster, *GP* guinea pig, *C* chick (newly hatched), *CE* chick embryo (inoculated into yolk sac), *RM* rhesus monkey, *R* rabbit. Inoculation mode: *i.c.* intracerebrally, *i.p.* intraperitoneally, *s.c.* subcutaneously, *i.n.* intranasally

may be (due to viremia) goat, sheep, rarely cattle (Brummer-Korvenkontio et al. 1973; Kožuch et al. 1966, 1967a, b; Kiffner et al. 2011). The role of some forest passerines and other birds as hosts of TBEV has not yet been fully elucidated; the virus was isolated occasionally from *Turdus pilaris, Turdus iliacus*, other *Turdus* spp., *Corvus monedula*, *Corvus corone, Pica pica, Sturnus vulgaris*, *Lanius collurio*, *Fringilla montifringilla, Fringilla coelebs*, *Loxia curvirostra, Carduelis flammea*, *Anthus trivialis, Motacilla alba, Motacilla flava*, *Emberiza* spp., *Jynx torquilla, Bonasa bonasia, Crex crex, Scolopax rusticola, Clangula hyemalis, Melanitta fusca*, *Anas querquedula*, *Fulica atra* (Brummer-Korvenkontio et al. 1973; Ernek 1959; Ernek et al. 1977; Grešíková 1972; Grešíková et al. 1975; Hubálek 1994; Lvov and Ilyichev 1979; Saikku 1973; Soběslavský et al. 1960; van Tongeren 1962). A potential for TOT was demonstrated in some avian species (*T. iliacus, T. pilaris*, *Turdus ruficollis*, *Turdus pallidus*, *Lanius cristatus, Emberiza fucata, Troglodytes troglodytes, Accipiter gentilis*) in Asian Russia by isolation of TBEV from their eggs (Kraminskiy et al. 1972). Experimental viremia has been demonstrated in many mammalian, avian, amphibian, and reptilian species (Naumov and Gutova 1979; Naumov et al. 1983, 1984a, b; Gutova et al. 1985; Chunikhin 1990): *Micromys minutus, Microtus arvalis*, *Microtus subterraneus* (Radda et al. 1968), *Myodes rufocanus, Myodes rutilus*, *Glis glis* (Kožuch et al. 1963), *Myotis myotis, Plecotus auritus, Barbastella barbastellus* (Nosek et al. 1961), cat, *Mustela nivalis*, *Mustela erminea* (Radda et al. 1969), *Coturnix coturnix*, *Anas platyrhynchos* (van Tongeren 1983), *Lacerta viridis*,

Table 2 Susceptibility of cell cultures to tiboviruses occurring in Europe (David-West 1971, 1972; Karabatsos 1985; Hubálek and Halouzka 1996)

	CEC, DEC	BHK	VERO	CV-1	GMK	LLC-MK2	PS, SPEV	HeLa	XTC-2	Other
TBEV	p	(+)	(p)	+	+	p	+	(+)	m	
LIV	p	(+)	(p)	+	+	p	+	(+)	m	
TYUV	p	p	p	(+)	(+)	(+)	+	−	nd	
MEAV	−	nm	nm	nd	nd	p	−	nd	nd	
BAHV	+	nd	(+)	nd	nd	nd	nd	nd	nd	
MTRV	+	nd	p	nd	nd	p	nd	nd	nd	
GAV	nd	nd	nd	nd	nd	nd	nd	nd	nd	
PTVV	nd	p	nd	nd	nd	nd	nd	nd	nd	
UUKV	+	+	(+)	+	m	p	+	m	p	BSC-1(+)
ZTV	m	nd	nd	nd	nd	nd	nd	nd	nd	
SAHV	+	+	(+)	nd	nd	nd	nd	nd	+	
SOLV	nd	−	(+)	nd	nd	−	nd	nd	+	
PIV	−	−	−	nd	nd	nd	nd	nd	+	
AVAV	m	m	(+)	nd	nd	nd	m	+	−	
CMV	nd	nd	+	nd	nd	nd	nd	nd	+	
CCHFV	nm	m	nm	p	(p)	(+)	(p)	−	nd	Lamb kidney (p)
BHAV	m	+	+	+	+	m	+	(+)	−	BSC-1 (+)
EYAV	−	m	(p)	(p)	−	−	m	−	nd	
TRBV	(+)	+	+	nd	nd	+	+	+	nd	L, Hep-2, RU-1 +
OKHV	+	(+)	(+)	nd	nd	nd	+	−	nd	
CWV	+	+	p	nd	nd	nd	nd	nd	(+)	
MYKV	nd	nd	p	nd	nd	nd	nd	nd	nm	
TDMV	nd	nd	nd	nd	nd	nd	nd	nd	nd	
BAUV	nd	nd	+	nd	nd	nd	nd	nd	nd	
DHOV	p	+	+	−	nd	+	+	nd	nd	BSC-1−
THOV	p	+	+	nd	nd	p	nd	nd	nd	BSC-1m
ASFV	+	+	+	nd	nd	nd	+	nd	nd	Lamb testis +

Explanations: +, CPE and plaques produced; (+), faint CPE formed; p, plaques produced (under overlay) but no CPE; (p), indistinctive plaques produced, usually no CPE; −, neither CPE nor plaques produced (data on multiplication missing); *m*, multiplication without CPE/plaques production; *nm*, no multiplication; *nd*, not done

Lacerta agilis (Grešíková-Kohútová and Albrecht 1959) and some other vertebrate species (Chunikhin 1990; Gutova et al. 1985; Hubálek 1994; Naumov et al. 1983, 1984a, b; Naumov and Gutova 1979).

TBEV causes fatal disease in suckling and adult laboratory mouse at any route including i.n. and p.o., suckling rat (i.c.) but not adult rat (i.c., i.p.), newborn guinea pig (i.c.), suckling hamster (i.c., i.p.), rhesus monkey (i.c., but not all strains, and not at i.n., i.p., s.c. or i.v. routes: Ilyenko et al. 1974; Zlotnik et al. 1976; Pogodina et al. 1981, 1986), lamb and kid (i.c., i.n. but not s.c.). The diffuse meningoencephalitis is characterized by perivascular infiltration, neuronal degeneration and necrosis, and focal glial proliferation. On the other hand, no mortality is produced by TBEV in adult forest rodents *Apodemus* and *Myodes* spp. (i.p., s.c.), adult rabbit (i.c., i.p.). Encephalitis with ataxia, jumping, tremor, and convulsions can affect lambs, kids or, exceptionally, dogs (Tipold et al. 1993; Pfeffer and Dobler 2011). CEEV infection is usually subclinical in adult ruminants and pig; goats, sheep, and cows excrete virus in the milk (Smorodintsev et al. 1953; van Tongeren 1955; Benda 1958a; Grešíková 1958a, b). TBEV (especially TBE-S and TBE-FE virus subtypes) occasionally kills birds of some species, e.g., *C. flammea* (long-term viremia and the virus excretion in droppings up to 11 months was confirmed experimentally), *Passer domesticus*, and *F. atra* (van Tongeren 1962; Hubálek 1994), amphibians *Rana temporaria* and *Bufo bufo* (s.c.).

Natural foci of TBE have been classified (Rosický 1959) as "theriodic" (situated in deciduous and mixed forest ecosystems, often game preserves), "boskematic" (pastoral), mixed "theriodic-boskematic" or "mountain" (Rosický and Bárdoš 1966; Nosek et al. 1982). Urban foci of CEE have also been described in Europe (Málková et al. 1983).

There are two basic modes of human infection with TBEV—by the bite of an infective tick or by consumption of infected raw (unpasteurized) goat (less often sheep or cow) milk or dairy products (Smorodintsev et al. 1953; Grešíková 1972; Grešíková et al. 1975). Whereas the tick-transmitted cases are sporadic, the milk-borne infections usually affect whole families or population groups in outbreaks. For instance, a large milk-borne TBE epidemic occurred in Rožňava, East Slovakia in 1951, when 660 persons were infected and 274 of them hospitalized (Blaškovič 1954). As much as 76 % of human infections have been alimentary in Belarus (Ivanova 1984). The virus may resist in milk at 60°C for more than 10 min and partially even the pasteurization at 62°C for 20 min, and it is not inactivated at pH 2.8 within 24 h/4°C. In addition, many laboratory infections (usually by infectious aerosol) have been reported in unvaccinated personnel.

Human disease caused by TBEV is meningoencephalitis, usually with typical biphasic course: the first phase starts with sudden fever and flu-like symptoms (pronounced headache, general weakness, nausea, myalgia, arthralgia), sometimes conjunctivitis; the second phase appears after an interval of usually 4–7 days of an apparent recovery, with affection of the CNS (meningoencephalitis) accompanied with fever, retrobulbar pain, photophobia, stiff neck, sleep disorders, excessive sweating, drowsiness, tremors, nystagmus, meningeal signs, ataxia, pareses of cranial nerves and extremities, dizziness, confusion, psychic instability, excitability, anxiety, disorientation, memory loss, and sometimes personality changes. In the CNS, the virus produces diffuse degenerative changes of neurons, perivascular lymphocytic infiltration ("cuffing") and damage to Purkinje cells. Case fatality rate in humans ranges from *c*. 1 % (in TBEV-W), 7–8 % (in TBEV-S), up to 20–40 % (TBEV-FE); convalescence is prolonged, and neurological sequellae (residua) sometimes including pareses are quite common. Major sequelae such as atrophic paralysis of the neck and shoulder are rare in CEE (Ackermann and Rehse-Küpper 1979; Kunz 1981; Holmgren and Forsgren 1990), whereas they are relatively frequent and occasionally combined with a chronic and progressive course (e.g., Kozhevnikov's epilepsy, progressive neuritis of the shoulder plexus, dispersed sclerosis, progressive muscle atrophy) in RSSE (TBEV-S: Zlotnik et al. 1976; Asher 1979; Pogodina et al. 1986; Gritsun et al. 2003).

Several thousand cases of TBE are recorded in Europe each year, with considerable inter-annual variation (Korenberg and Kovalevski 1999; Gritsun et al. 2003; Petri et al. 2010). In some European countries, TBE is quite frequent: for instance, on average, 368 cases (140 to 744 in individual years) a year were reported in Czechland between 1970 and 1999, corresponding to the incidence of 4.2 (1.4–7.4) per 100,000 inhabitants, and it peaked at 1,029 patients (10.0 per 100,000) in the year 2006. In the years 2004–2007, only a few countries have had a higher incidence of TBE than Czech Republic (5.0–10.0): Slovenia 10.2–18.6, Estonia 10.4–13.5, Lithuania 6.5–13.5, Latvia 6.2–10.8, while the TBE incidence was as low as 0.6–1.2 in neighboring Austria, due to a much higher vaccination rate in that country (Mantke et al. 2008).

Diagnosis: serology (ELISA, HIT, CFT, VNT), detection of IgM in early phase or seroconversion in paired serum samples; rarely used is the isolation of the virus from the blood or CSF in cell cultures (e.g., PS pig embryo kidney cells) or in mice, and detection of the virus RNA by using RT-PCR.

Therapy: specific immunoglobulins can be applied to infected persons but they are only effective when inoculated immediately, i.e., within 1–2 days after infection, otherwise they could be even detrimental.

Prevention and control include mapping and surveillance of natural foci of TBE, pasteurization of milk (CEE virus may persist in some dairy products at +4°C for more than 60 days: Grešíková-Kohútová 1959), protection from tick exposure (clothing, repellents), vector tick control, and vaccination. "FSME-Immun" and "Encepur" vaccines (Loew-Baselli et al. 2011; Petri et al. 2010) consist of purified inactivated virus grown in chicken embryo cells produced by methods largely based on a study of Czech virologists (Daneš and Benda 1962). A mass vaccination campaign of Austrian population living in endemic foci led to a significant decline of TBE from 612 cases recorded in 1982 to 89 cases diagnosed in 1990 (C. Kunz, pers. comm.), and a similar 5-to-10 times decrease of TBE incidence has been reported in other European countries after frequent vaccination of population.

European distribution: Fig. 1 Outside Europe, TBEV occurs in the Asian part of Turkey, Asian Russia (Siberia, Far East), Kazakhstan, Kirghizia, Armenia, Azerbaijan, north-eastern China, Japan, and Korean peninsula.

Flavivirus louping ill (LIV)

Synonym: Negishi virus. Prototype strain of LIV is LI-31. Louping-ill virus is very closely related to TBEV, in fact indistinguishable from it by conventional serological and cross-protection tests (Clarke 1962, 1964; Calisher 1988; Calisher et al. 1989; Kopecký et al. 1991; Shiu et al. 1991; Holzmann et al. 1992; Venugopal et al. 1992; Hubálek et al. 1995) and with difficulties by nucleotide sequence homology of the E gene (Gao et al. 1993; Venugopal et al. 1994; Fig. 2 in Gould et al. 2003, Fig. 3 in Weaver 2006; Grard et al. 2007, Fig. 1 in Jääskeläinen et al. 2010). LIV is antigenically and genomically much closer to CEEV than CEEV is related to RSSEV; LIV should thus not be regarded as a separate virus, in that RSSEV and CEEV are considered subtypes of one virus (TBEV). Therefore, Hubálek et al. (1995) and Grard et al.

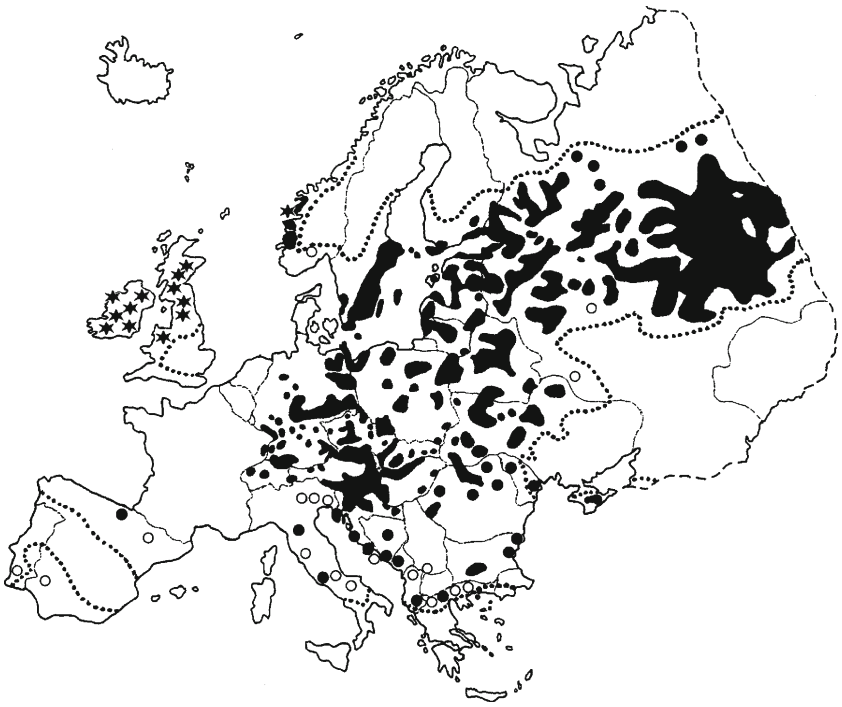

Fig. 1 European distribution of natural foci of tick-borne encephalitis (CEE and RSSE) and louping ill (*asterisks*). Explanation: *black dots* and *black areas*, TBE virus isolation or the virus disease. The *dotted line* shows the limits of the *Ixodes ricinus* plus *I. persulcatus* area

(2007) suggested arrangement of LIV as another subtype of TBEV, and not as a separate virus.

Louping-ill has long been recognized as a disease of sheep in Scotland. For instance, it was recorded in the 1795 Statistical Account or by Walter Scott in 1891 (Davidson et al. 1991). The virus was first isolated from sheep brain in Selkirkshire, Scotland in 1929 (prototype strain Moredun LI-31: Pool et al. 1930) and it is, in fact, the very first arthropod-borne virus isolated in Europe.

Principal vector of LIV is the tick *I. ricinus* (MacLeod and Gordon 1932); LI is also transmissible by the goat and sheep milk (Reid et al. 1984; Reid and Pow 1985), analogically as the other TBEV subtypes.

Vertebrate hosts are e.g., wood mouse (*A. sylvaticus*), common shrew (*S. araneus*), mountain hare (*Lepus timidus*), sheep, and red grouse (*Lagopus lagopus scoticus*: Reid 1990; Gilbert et al. 2000). LIV infection is fatal to suckling rat (i.c., i.p.), lamb (i.c., not s.c.), sometimes rhesus

Fig. 2 European distribution of Tyuleniy (*circles*) and Meaban (*squares*) flaviviruses. (*Slanted area*: antibodies to TYUV)

Fig. 3 European distribution of Uukuniemi (*circles*), Grand Arbaud (*square*), and Ponteves (*asterisk*) viruses. (*Slanted area*: antibodies to UUKV)

monkey (i.c., i.n.: Zlotnik et al. 1976). No symptoms are seen in adult *M. agrestis* (i.c., s.c.), *Cervus elaphus* (s.c.), and *Capreolus capreolus* (s.c.), although meningoencephalitis was demonstrated histologically in the deer (Reid et al. 1982), and LIV was isolated from a roe deer (Reid et al. 1976). LIV occasionally affects also cattle, pig (piglets), goat (kids), horse, dog, hare, and red grouse (with a mortality rate of 70–80 % especially in juvenile birds: Reid et al. 1978, 1980); interestingly, the grouse chicks die when they eat infected ticks. Typical course of LI in sheep is biphasic, with fever and weakness, followed by meningoencephalitis with cerebellar ataxia, generalized tremor, jumping (to "loup" means to leap in vernacular Scottish), vigorous kicking, salivation, champing of jaws, progressing to paralysis, coma and death (lethality 40–60 %). The histopathology shows (sheep, pig, rhesus monkey, or mouse) a diffuse meningoencephalitis with perivascular cuffing, neuronal degeneration, and destruction of Purkinje cells, similar to TBE (Reid 1990). Concurrent tick-borne fever (*Anaplasma phagocytophilum* infection) and external stress enhance the disease course (Reid 1990).

Natural foci of LI are "boskematic" (pastoral: Rosický 1959)—rough, poorly drained hill pastures, heather moorlands with bracken and moor-grass; principally a sheep-tick or sheep-tick-grouse cycle (Reid 1990; Smith and Varma 1981). Unfortunately, spring lambing on hilly pastures coincides with the period of peak seasonal activity of the vector in endemic foci.

The human illness is usually biphasic; the febrile phase, after a short period of improvement, is followed by high fever and symptoms of meningoencephalitis, headache, weakness, stiff neck, conjunctivitis, retrobulbar pain, photophobia, myalgia, arthralgia, dysarthria, excessive sweating, nausea, vomiting, insomnia, drowsiness, confusion, tremors, nystagmus, and ataxia. Additional symptoms are similar to that of TBE.

Nineteen naturally acquired human cases and 26 laboratory infections with LIV have been described in Great Britain between 1934 and 1990 (Davidson et al. 1991), including one fatal encephalitis in a butcher from northern Scotland (Williams and Thorburn 1962). LIV transmission to man is obviously infrequent in the U.K. because the vector ticks only occasionally bite people in endemic areas (similarly as with Lyme borreliosis). It is primarily an occupational disease, affecting shepherds, crofters, veterinary personnel, forestry workers, butchers and laboratory personnel. However, human cases of LI with a milder symptomatology might remain underreported.

Diagnosis: as for TBE.

TBE vaccine is also protective aginst LIV. Control of LI is mainly based on vaccination of sheep; the inactivated LI vaccine is commercially available and in general use. Tick control by dipping the sheep with residual acaricides is also practicized. The methods of environmental control of ticks such as pasture rotation, cutting or burning grass and bush vegetation, and drainage are effective but economically less feasible (Smith and Varma 1981).

European distribution: Norway is the only country of the continental Europe where a typical LIV strain was isolated (Gao et al. 1993) (Fig. 1). LIV does not occur outside Europe.

Flavivirus Tyuleniy (TYUV)

Flavivirus Tyuleniy (TYUV) is related to the Australian Saumarez Reef virus by CFT, VNT and nucleotide sequence of the envelope gene (Marin et al. 1995), while less similar to TBEV by CFT and HIT. TYUV is a member of the Seabird tick-borne virus subgroup of tick-borne flaviviruses.

The virus was first isolated from *Ixodes uriae* collected in nesting grounds of *Uria aalge* on Tyuleniy Island near Sakhalin, Sea of Okhotsk (Asian Russia) in 1969 (Lvov et al. 1971), and simultaneously off the western U.S. coast (Clifford et al. 1971). In Europe, the agent was revealed in fact even earlier—in 1967 as "Murman" virus under similar conditions on the Kola Peninsula, northern Russia (Bekleshova et al. 1970).

Principal vector is *I. uriae* (TST, TOT). Mosquitoes (*Aedes communis*, *Aedes punctor, Aedes excrucians)* may possibly act as secondary (or mechanical) vectors; successful experimental TYUV transmissions by *Aedes aegypti*, *Culex pipiens*, and *Hyalomma asiaticum* have been reported (Lvov and Ilyichev 1979; Lvov et al. 1971, 1973a, b, c, d).

Vertebrate hosts are seabirds *U. aalge*, *Eudyptula minor*, and the suslik *Citellus undulatus*. Antibodies are often present in additional seabirds *Uria lomvia, Lunda cirrhata*, *Fratercula arctica, Fulmarus glacialis, Phalacrocorax urile, Phalacrocorax aristotelis, Larus argentatus, Larus fuscus, Larus marinus, Larus ridibundus*, *Rissa tridactyla* (French coast: Chastel et al. 1985a, b), and in some mammals (*Callorhinus ursinus*, *Alopex lagopus, Lutreola lutreola*). Antibodies were detected in 22–33 % of cattle in the N.-European Russian taiga and tundra zones (Lvov et al. 1989).

Animal disease is unknown, but experimentally inoculated (i.c. or s.c.) birds show clinical symptoms: encephalitis with pareses and occasional death in *R. tridactyla, L. argentatus,* and *U. lomvia* (Berezina et al. 1974). The virus is not pathogenic to adult rabbit (i.p.). Febrile illness with adynamia and anorexia was observed in rhesus monkeys infected aerogenically.

Natural foci of TYUV are seabird colonies on steep rocks.

Three TYUV cases of febrile illness with malaise, laryngitis, lymphadenopathy, arthralgia, and skin petechiae were documented in biologists collecting samples in seabird colonies in the Murmansk region, 1972–78 (Voinov 1978).

European distribution: Fig. 2 Outside Europe TYUV occurs in Asian Russia (Far East–Sea of Okhotsk); coastal West USA (Oregon) and Canada. Migratory seabirds play a role in the exchange of TYUV complex flaviviruses between the northern and southern hemispheres (Lvov and Ilyichev 1979).

Flavivirus Meaban (MEAV)

MEAV is a member of the Seabird tick-borne virus subgroup of tick-borne flaviviruses, Tyuleniy antigenic complex (Calisher et al. 1989). Prototype: Brest/Ar/T707 (*Ornithodoros maritimus*, France, 1981). Closely related to the Australian Saumarez Reef virus by CFT, HIT and even VNT (Chastel et al. 1985a, b), while more distantly related to TYUV (unrelated by VNT), TBEV and other flaviviruses.

First isolated from argasid ticks collected in seagull colonies on Méaban and Penfred islands, Brittany (France) in 1981–82 (Chastel et al. 1985a, b).

Principal vector is the soft tick *O. maritimus* (TST).

Vertebrate hosts are unknown, but antibodies have been detected in gulls *L. argentatus* and *L. fuscus*. Meningoencephalitis in suckling mouse caused by MEAV is characterized by perivascular cuffing and diffuse neuronal necrosis (Chastel et al. 1985a, b).

Natural foci of MEAV occur in seabird colonies.

Animal and human disease caused by MEAV has not been reported, and no antibodies to MEAV were detected by HIT in 562 human sera collected in Brittany (Chastel et al. 1985a, b).

European distribution: Fig. 2 Long-distance migratory *Sterna paradisaea* and *Sterna hirundo* terns could have contributed to the dispersal of MEAV and Saumarez Reef viruses or their common progenitor between Australia and France (Chastel et al. 1985a, b).

Family *Bunyaviridae*

Orthobunyavirus Bahig (BAHV)

Tete antigenic group. Prototype: EgB-90 (*Oriolus oriolus* blood, Egypt, 1966). European topotype: ISS.U.45 (*F. montifringilla* blood, Italy, 1968). Related to Matruh virus by CFT and HIT (indistinguishable by CFT), less to Tete virus.

Originally isolated from the blood of *O. oriolus* caught at Bahig village near Alexandria, Egypt, in 1966 (Watson et al. 1972). In Europe, first reported from migrating birds in N. Italy (Balducci et al. 1973).

Arthropod vector is *H. marginatum* (TOT).

Vertebrate hosts are passerine birds of the genera *Oriolus, Muscicapa, Sylvia, Phylloscopus, Phoenicurus, Luscinia, Chloris,* and *Fringilla* (Balducci et al. 1973; Watson et al. 1972).

Human and animal disease caused by this virus has not been reported.

European distribution: central and northern Italy. Outside Europe: Egypt, Cyprus. BAHV was isolated from larval *H. marginatum rufipes* collected on a northward migrating *Oenanthe oenanthe* in Egypt (Converse et al. 1974) which indicates a possible means of dispersal.

Orthobunyavirus Matruh (MTRV)

Tete antigenic group. Prototype: EgAn 1047–61 (*Sylvia curruca* blood, Egypt, 1961). European topotype: ISS.U.60

(*F. coelebs* blood, Italy, 1968). Related to BAHV by CFT and HIT.

The virus was first isolated by J.R. Schmidt from migrating passerines in Burg el Arab, Matruh Governorate, Egypt, 1961 (Theiler and Downs 1973). In Europe, it was recovered from migrating birds in North Italy (Balducci et al. 1973).

Arthropod vector is probably *H. marginatum*.

Vertebrate hosts are passerine birds of the genera *Phylloscopus, Sylvia, Saxicola, Phoenicurus, Luscinia, Lanius*, *Serinus*, *Carduelis* and *Fringilla* (Italy: Balducci et al. 1973), and *C. coturnix*.

Human and animal disease caused by this virus has not been reported.

European distribution: northern Italy. Outside Europe: Egypt, Cyprus.

Phlebovirus Grand Arbaud (GAV), Phlebovirus Ponteves (PTVV)

Uukuniemi antigenic group. GAV prototype: Argas-2 (*Argas reflexus*, Camargue, France, 1966). PTVV prototype: Larves-6 (*A. reflexus*, France, 1966). Both viruses are related, producing one-way reaction in cross-CFT. Also related to UUKV by CFT.

The viruses were isolated only once from argasid ticks collected in a pigeon house in South France, 1966 (Hannoun et al. 1970).

Arthropod vector is *A. reflexus* (TST, TOT in PTVV).

Vertebrate host is probably pigeon.

Animal and human disease caused by either GAV or PTVV has not been reported.

European distribution: Fig. 3. Outside Europe: unknown.

Phlebovirus Uukuniemi (UUKV)

Uukuniemi antigenic group. Synonyms: Poteplí virus; Sumakh virus. Prototype: S-23 (*I. ricinus*, Finland, 1960). Topotypes: Poteplí PO-63 (*I. ricinus*, Bohemia, 1963), Sumakh (*Turdus merula* heart and lungs, Azerbaijan, 1968). Hemagglutinin is produced, but not readily in all strains.

The virus was originally isolated from *I. ricinus* collected from cattle at Uukuniemi, southeast Finland in 1959 (Oker-Blom et al. 1964), later (1963) in Central Bohemia as “Poteplí” virus (Kolman et al. 1966).

Arthropod vectors are the ticks *I. ricinus* (TST, TOT: Samoilova and Voinov 1980), less commonly *I. persulcatus*. The virus was also isolated occasionally from mosquitoes *Culex modestus, Aedes vexans*, *A. punctor*, *A. communis* and *Aedes cataphylla* (Lvov et al. 1987, 1989; Vinograd et al. 1971)—but mosquitoes are obviously only mechanical vectors.

Vertebrate hosts are forest rodents (*Myodes glareolus, A. flavicollis*: Kožuch et al. 1970a, b; Wróblewska-Mularczykowa et al. 1970; Vinograd et al. 1981) and birds, largely ground-feeding passerines (*T. merula, Turdus philomelos, T. iliacus, T. pilaris, Erithacus rubecula, Prunella modularis, Sylvia communis, O. oenanthe, S. vulgaris, C. corone, P. pica, F. coelebs, Coccothraustes coccothraustes, Emberiza citrinella, Streptopelia turtur,* and *Phasianus colchicus*: Gaidamovich et al. 1971; Hubálek 1994; Lvov and Ilyichev 1979; Saikku 1974; Saikku and Brummer-Korvenkontio 1973; Vasilenko et al. 1975a, b; Vinograd et al. 1971, 1975). Viremia and long-term persistence of the virus was demonstrated in experimentally infected birds of many species. Antibodies were also detected in cows and reptiles. Fatal meningoencephalitis with myositis occurs in suckling mouse but no symptoms are observed in adult mouse (any route incl. s.c., i.n.) or adult rat (i.c.); also pathogenic to suckling but not adult *M. arvalis, A. flavicollis* or *M. glareolus* (i.c., usually not i.p.: Kožuch et al. 1970a, b) and suckling rat (i.c., not i.p.), and non-pathogenic for rhesus monkey inoculated i.p. (but lymphocytic meningitis appeared when UUKV was given i.c.: Grešíková et al. 1970).

Animal and human disease caused by UUKV has not been reported. Antibodies were detected infrequently (≤5 % persons examined) in a few areas (Kolman et al. 1973; Málková et al. 1980; Molnár et al. 1976; Sekeyová et al. 1970; Vasilenko et al. 1975a, b) while only exceptionally at a higher frequency (e.g., 13–14 % in western Belarus and Hungary: Voinov 1978; Molnár et al. 1980), and much more often these serosurveys for UUKV were negative.

European distribution: Fig. 3. Outside Europe: Azerbaijan, Asian Russia. Antibodies in Tunisia. Migratory birds play a role in the widespread distribution of UUKV; e.g., several strains of the virus have been isolated from immature *I. ricinus* collected on migratory passerines (Traavik 1979).

Phlebovirus Zaliv Terpeniya (ZTV)

Uukuniemi antigenic group. Prototype: LEIV-21C. Distantly related to UUK virus by CFT.

Originally isolated from adult *I. uriae* collected in rocky breeding grounds of marine birds (*U. aalge* etc.) on Tyuleniy Island (Sakhalin region) and Commodore Islands (Kamchatka region), Russia in 1969 (Lvov et al. 1973a, b, c, d). In Europe, first isolated under similar conditions in the Murmansk region, North Russia in 1970 (Lvov et al. 1973a, b, c, d, 1989).

Arthropod vectors are *I. uriae* (TST, TOT), rarely *I. signatus*. Occasional isolations from *Ae. communis* mosquitoes in N.-European tundra (Lvov et al. 1987, 1989).

Vertebrate hosts are *U. lomvia*, *R. tridactyla*. Antibodies were also detected in *L. marinus* and *U. aalge*. Some

mortality (acute viral encephalitis) has been observed in chickens inoculated i.c. or s.c. (Chastel 1988).

Animal and human disease caused by ZTV has not been reported. Antibodies rarely occur in farmers who have lived near Cap Sizun (Chastel 1988).

European distribution: Fig. 4. Outside Europe: E. and N. Asian Russia (Sakhalin, Kamchatka, Taimyr), NW. Canada and USA.

Phlebovirus St. Abb's Head (SAHV)

Uukuniemi antigenic group. A non-registered virus (isolates GM710 and M349) that involves a number of closely related (SAHV-like) strains. Prototype: M-349 (*I. uriae*, North Scotland, 1979).

First isolated from adult *I. uriae* and the blood and organs of moribund juvenile kittiwakes (*R. tridactyla*) collected on breeding grounds off N. Scotland, 1979 (Nuttall et al. 1981) and NE. England (Eley and Nuttall 1984).

Arthropod vectors are *I. uriae* (TST) and *I. rothschildi* (Nuttall et al. 1984a).

Main vertebrate host is kittiwake *R. tridactyla*. An illness in juvenile kittiwakes has repeatedly been observed. Antibodies have also been detected in *U. aalge, Alca torda,* and other marine birds (Nuttall 1984; Nuttall et al. 1984a). A relatively low mortality of suckling mice was observed at i.c. inoculation (Nuttall et al. 1984b; Moss and Nuttall 1985).

Human disease caused by SAHV has not been reported.

European distribution: Fig. 4.

Labuda and Nuttall (2004) list a number of additional uukuvirus-like isolates from *I. uriae* ticks collected from European colonial seabird habitats, that may belong either to SAHV or ZTV, or some of them possibly to a novel virus: Arbroath ARB2, (Scotland), Ellidaey ELL-1,-2,-4 (Iceland), Flatholm (Iceland), Foula F89-1 (Shetland Islands), Great Saltee Island GS80-4,-10,-11 (SE. Ireland), Isle of May M320/79, M326/79, M34-81, M35-81 (Scotland), Marsden (England), Rost Islands NorV-697,-707,-820-868 (Norway), Runde Island Ru E82 (Norway), Soay (Scotland–St. Kilda).

Nairovirus Soldado (SOLV)

Hughes antigenic group. Prototype: TRVL-52214 (*Ornithodoros capensis/denmarki*, Trinidad, 1963). European topotypes: EgAr-3608 (*O. maritimus,* N. Wales, 1974) and Brest-Ar/T13 (*O. maritimus*, France, 1977). A remarkable antigenic heterogeneity of SOLV isolates has been found by CFT; in fact, some European (French, Irish) isolates differ from the prototype strain more than eightfold in reciprocal titres (Chastel et al. 1983). SOLV is distantly related to Zirqa and Punta Salinas viruses of the Hughes serogroup by CFT, VNT, and IFA (Converse et al. 1976; Yunker et al. 1977). The virus is very stable at pH 3.

SOLV was originally isolated from mixed nymphal *O. capensis* and *O. denmarki* ticks infesting *Anous stolidus* colonies on Soldado Rock near Trinidad, 1963 (Jonkers et al. 1973). In Europe, it was recovered from *O. maritimus* infesting *L. argentatus* nests on Puffin Island (N. Wales: Converse et al. 1976), Ireland (Keirans et al. 1976), England (Nuttall et al. 1986), and Cap Fréhel and Cap Sizun (Brittany, France: Chastel et al. 1979, 1981a, b, 1988a, b; Quillien et al. 1986).

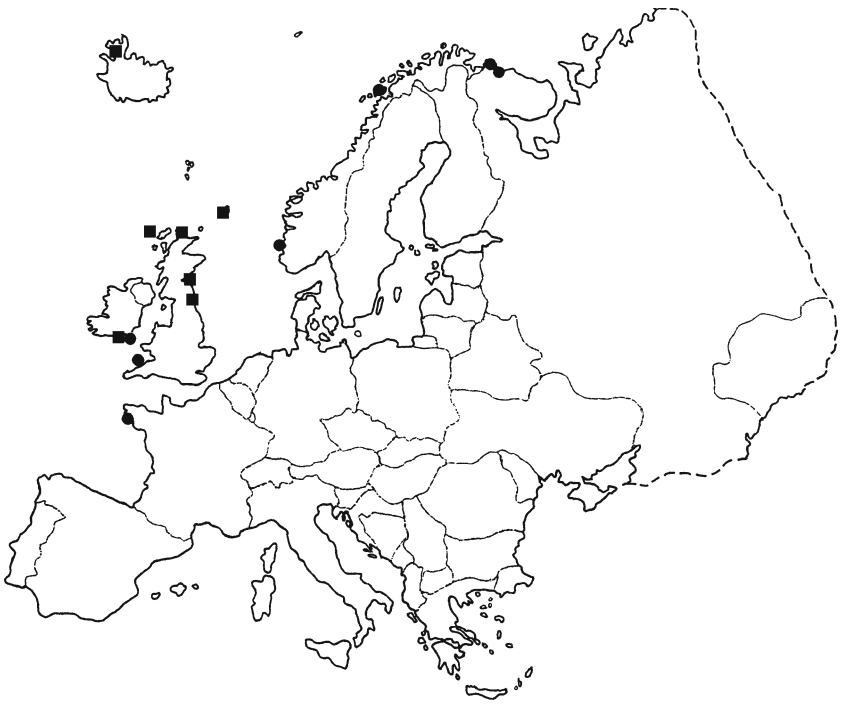

Fig. 4 European distribution of Zaliv Terpeniya (*circles*) and St. Abb's Head (*squares*) viruses

Arthropod vector is *O. maritimus* (TST; the mean infection rate of vector ticks can be as high as 20 %: Johnson et al. 1979) in Europe, while *O. capensis* elsewhere.

Vertebrate hosts are seabirds *Sterna fuscata*, *L. argentatus,* and *R. tridactyla* (Chastel et al. 1990). Antibodies were also detected in *Larus cachinnans*, *Larus cirrhocephalus*, *Phalacrocorax aristotelis,* and other species. Mortality due to SOLV was observed in young seabirds such as *S. fuscata* or *L. argentatus* (Converse et al. 1975; Chastel et al. 1990). Infected *O. capensis* have transmitted the virus to domestic chicks and caused their death on days 5 to 8 post-feeding (Converse et al. 1975).

Natural foci are seabird colonies (usually on rocky offshore islands).

Ornithologists bitten by *O. capensis* in the Seychelles experienced severe pruritus persisting for a few days (Converse et al. 1975); the etiology has remained unclear in that a possible cutaneous reaction to tick bites could not be excluded. A case of febrile illness with persistent rhinopharyngitis and pruritus due to SOLV was observed in a scientist who had been repeatedly bitten by *O. maritimus* in Morocco (Chastel et al. 1981a, b). However, antibodies rarely occur in farmers who live near Cap Sizun (Chastel 1988). The related Zirqa and Punta Salinas viruses may cause fever with headache, pruritus, and erythema in people in the Arabian Gulf and Peru, respectively (Converse et al. 1975, 1976).

European distribution: Fig. 5. Outside Europe: Trinidad, Ethiopia, Senegal, Seychelles, South Africa, Morocco, USA (Hawaii, Texas). Seabird migrations account for the widespread distribution of SOLV (Converse et al. 1975). A number of additional Hughes group SOLV-like isolates from *I. uriae* ticks collected from European colonial seabird habitats were reported (Labuda and Nuttall 2004): Ellidaey ELL81-3b (Iceland), Foule F80-1 (Shetland Islands), Great Saltee 59972, GS80-3 (Ireland), Grimsey G82-1b (Iceland), Inner Farne IF80-3,-4 (England), Isle of May (Scotland).

Nairovirus Puffin Island (PIV)

Hughes antigenic group. Prototype: 9617 (*O. maritimus*, Wales, 1974); other similar isolates are EgArt 608, 3615, 3616 (Wales), and Petticko Wick (Scotland: Labuda and Nuttall 2004). A non-registered virus composed of strains closely related to SOLV but distinguishable by IFA and VNT (Gould et al. 1983). The virus is very sensitive at pH 3.

PIV was first isolated from argasid ticks collected in *L. argentatus* nests on Puffin Island, N. Wales in 1974 and originally referred to as SOLV, but re-identified as a new virus later (Gould et al. 1983).

Arthropod vector is *O. maritimus*, but several Icelandic and British isolates have been recovered also from *I. uriae*.

Vertebrate hosts are *L. argentatus* and *F. arctica*. Antibodies were also detected in *U. aalge*, *A. torda,* and other seabirds.

Animal and human disease caused by PIV has not been reported.

European distribution: Fig. 5 In addition, antigenically closely related virus strains were isolated in Ireland (GS-80-3:

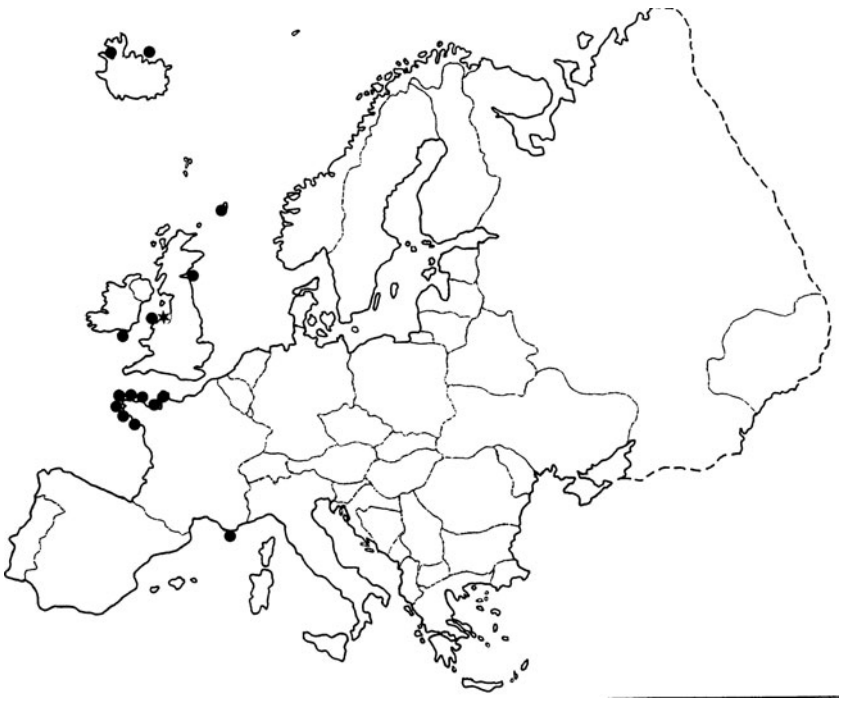

Fig. 5 European distribution of Soldado (*circles*) and Puffin Island (*asterisks*) nairoviruses

Nuttall et al. 1984a), Britain (Nuttall et al. 1986) and Iceland (GRIMS82-1b, ELL-3b: Moss et al. 1986).

Nairovirus Avalon (AVAV)

Sakhalin antigenic group. Synonym: Paramushir virus. Distantly related to Sakhalin virus (SAKV) by CFT (Main et al. 1976a, b). Prototype: CanAr-173 (*I. uriae*, Newfoundland, 1972). Topotype: LEIV-2268Ku ("Paramushir": *I. signatus*, Paramushir Island, Far East, 1969).

First isolated from engorged adult and nymphal *I. uriae* collected in a *L. argentatus* nest on Great Island, Newfoundland, Canada in 1972 (Main et al. 1976a, b). "Paramushir" virus was isolated from *I. uriae* and *I. signatus* collected from seabird colonies in the Far East in fact earlier, in 1969 (Lvov et al. 1976). In Europe, several strains of AVAV were isolated from *I. uriae* collected in Cap Sizun, Brittany, France in 1979 (Chastel et al. 1981a, b; Quillien et al. 1986).

The virus is stable at pH 3, but some strains might be acid labile (Quillien et al. 1986); heat sensitive (inactivated at 56°C within 30 m).

Arthropod vectors are *I. uriae* (TST) and *I. signatus.*

The vertebrate host is *L. argentatus* (Main et al. 1976a, b). Antibodies were also detected in *F. arctica*, *Oceanodroma leucorrhoa*, *Larus marinus*. Spontaneous animal disease is unknown. Although fatal to suckling mouse (i.c.), the survival is long and the titres in suckling mouse brain are rather low.

Natural foci are seabird colonies on cliffs.

Three human cases of cervical adenopathy were described in France (Chastel 1985). However, antibodies in humans occur rarely: only 1 % of farmers who had lived near Cap Sizun were seropositive (Quillien et al. 1986).

European distribution: Fig. 6. Outside Europe: Asian Russia (Far East), Canada.

Nairovirus Clo Mor (CMV)

Sakhalin antigenic group. Prototype: ScotAr-7 (*I. uriae,* Scotland, 1973). Closely related to SAKV (prototype LEIV-71c: *I. uriae,* Far East, 1970–Lvov et al. 1972), the difference in titres being only three to fourfold in cross-CFT (Main et al. 1976a, b). CMV may be regarded as a subtype of SAKV.

First isolated from engorged nymphal *I. uriae* collected in a *U. aalge* colony at Clo Mor, Cape Wrath, Scotland in 1973 (Main et al. 1976a, b).

The virus is very stable at pH 3 (>3 h at 4°C). HA is occasionally produced in suckling mouse brain.

Arthropod vector is *I. uriae* (TOT: Lvov et al. 1972).

Vertebrate hosts are unknown (possibly seabirds, but antibodies have not yet been detected in them). Fatal to suckling mouse (s.c.) but not to adult mouse (s.c.) or chicks (i.c.). Suckling mice are relatively insensitive for the isolation attempts (Nuttall et al. 1984b). Moreover, CMV is poorly immunogenic in mouse at i.p. or i.c. inoculation.

Human disease caused by CMV has not been reported; no antibodies have been detected in humans.

European distribution: Fig. 6. Outside Europe: Asian Russia (northern Far East). Two strains similar to CMV were reported (Labuda and Nuttall 2004) from *I. uriae* ticks in seabird colonies: Old Copper Mine (England–Lundy) and Shiant Islands M325 isolate (Scotland).

Nairovirus of Crimean-Congo hemorrhagic fever (CCHFV)

Synonyms: Crimean hemorrhagic fever (CHF) virus; Congo (CON) virus. Prototype: Khodzha (human blood from a fatal case, Uzbekistan, 1967). African topotype: V-3011 (human blood, Zaire, 1956–registered in 1969). European topotype: Drozdov (human blood, southern Russia, 1967).

The disease (hemorrhagic fever) was first mentioned by Tadjik physician Abu-Ibrahim Djurdjani in the 12th century (Shapiro and Barkaghan 1960). It has been extensively studied since the 1944/45 epidemic (more than 200 human cases, *c.* 10 % were fatal) in the Crimean peninsula and called "Crimean hemorrhagic fever". Mikhail P. Chumakov and co-workers demonstrated viral etiology of the disease by experimental infection of a volunteer with an ultrafiltrate of homogenized nymphal *H. marginatum* ticks collected from local hares in 1945 (Chumakov 1974). CHF virus was first isolated from patients in Astrakhan, Rostov and Uzbekistan in 1967 (Butenko et al. 1968; Chumakov et al. 1971), and from ticks in Crimea in 1972–73 (Chumakov 1974), while CON virus was recovered earlier by G. Courtois from a patient in Zaire (Congo) in 1956 (Simpson et al. 1967). It was recognized that CONV is identical to CHFV (Casals 1969), and Harry Hoogstraal proposed the combined name of the virus and disease–CCHF (Hoogstraal 1979).

Arthropod vectors (and also a reservoir of CCHFV) are metastriate ixodid ticks—*H. marginatum* (TST, TOT), *H. rufipes* (TOT, Africa), *H. turanicum* (Asia), *H. truncatum* (TST, TOT), *H. asiaticum, Hyalomma anatolicum, H. excavatum, H. detritum, H. nitidum, H. impeltatum, H. impressum, H. lusitanicum* (Spain), *H. punctata* (Europe), *Rhipicephalus bursa* (Europe), *R. sanguineus* (Europe), *R. rossicus* (South Russia, TOT: Kondratenko 1976), *R. pumilio, R. pulchellus, R. turanicus, D. marginatus* (Europe, TOT: Kondratenko 1976), *D. daghestanicus, Amblyomma variegatum*, *Boophilus annulatus* (syn. *B. calcaratus*: Bulgaria, Russia), *B. decoloratus* and *B. microplus* (Pakistan). Much less frequent vectors are prostriate ticks (subfamily *Ixodinae*): *I. ricinus* (few CCHFV isolations in Crimea, Moldavia, Bulgaria and Hungary). Occasional vectors outside Europe can be soft ticks *Argas persicus* (Uzbekistan) and *Ornithodoros (Alveonasus) lahorensis* (Iran).

Fig. 6 European distribution of Avalon (*circles*) and Clo Mor (*asterisks*) nairoviruses

Vertebrate hosts are leporids, hedgehog, other small mammals, cattle, horse, goat, sheep. There is inapparent course of the CCHF infection in mammals, and birds are refractory to experimental infection. Fatal to suckling rat (i.c. but not i.p.) and newborn cotton rat (i.c., i.p.). No mortality in adult rat (i.p., s.c.), rabbit (i.p., s.c.; some symptoms after i.c.), hare *Lepus europaeus* (i.v., s.c.), *Citellus pygmaeus* (i.c., s.c.), rhesus monkey i.p. (rash only), sheep (s.c., i.p.), calf (i.v.), donkey and horse (i.v., s.c.). Plaques (and/or indistinct CPE) produced in primary *Cercopithecus* kidney cells. Usually no multiplication in BSC-1, HEp-2, and primary mouse embryo (David-West 1971, 1972).

Natural foci of CCHF are typically xerothermic, mostly open habitats with shrub and dispersed or solitary trees.

CCHF is transmitted mostly by bite of an infective tick, at removal of feeding ticks, but also during shearing of sheep with attached infectious ticks, slaughtering of infected animals (livestock-to-human transmission), or by direct contact with a human patient, e.g., at nursing and care for patients (human-to-human transmission). CCHF is highly contagious, and many hospital, household and laboratory infections (including fatal) have been described. For instance, 6 % of the human CCHF cases recorded in Bulgaria were nosocomial. A much greater proportion of nosocomial and family infections occur in the Middle East, Central Asia, and Pakistan, usually with a high mortality rate (Hoogstraal 1979). CCHF may be an occupational disease in cattle breeders, butchers, livestock industry, health professionals (nosocomial spread), laboratory workers (aerosol).

Human disease: CCHF is characterized by an abrupt onset with fever (3–16 days, often biphasic), chills, general weakness, severe headache, myalgia, neckache, back pains, generalized arthralgia, hyperemia of the face, neck and chest, conjunctivitis, pharyngitis, abdominal and epigastric pains, nausea, anorexia, vomiting, stiffness, diarrhea, photophobia, lymphadenopathy, hepatomegaly, hepatitis, dizziness, psychotic signs (depression, sleepiness, lassitude), bradycardia, hemorrhagic manifestations (from petechial rash on the trunk to large hematomas on the mucous membranes and skin, bleeding from mucous membranes—gums, nose, intestine and lungs or kidney; sometimes bleeding into brain), liver failure, pulmonary failure, hemorrhagic shock. Laboratory findings include increased levels of transaminases, leukopenia, thrombocytopenia and coagulopathy. Long convalescence (common problems are asthenia, hair loss, rapid fatigability, sweating, headache, poor vision and hearing), but without residua. Fatality rate is 3–30 % (but in nosocomial infections up to 50 %).

In south-eastern Europe, several outbreaks of CCHF have been recorded since the 1950s: e.g., 1,568 cases were notified in Bulgaria from 1953 to 2008, with a mean fatality rate of 17 %. Since 1999 (but especially in 2006–07), a reactivation of natural foci and re-emergence of CCHF occurred in Kosovo (119 cases during 1995–2001), southern Russia (regions Stavropol, Astrakhan, Rostov, Volgograd, Kalmykia, Dagestan:—a total of >1,300 patients were diagnosed with CCHF from 1999 until 2007, the fatality rate being 3–5 %. Albania reported eight CCHF cases in 2001, additional cases in 2003–2006. A surprising, continuous epidemic process started in the Asian part of Turkey in 2002,

and until 2009, a total of 4,430 human cases were reported from 680 settlements mainly in the Tokat and Sivas provinces (but as many as 2,615 cases were notified solely in the last 2 years 2008 and 2009), with a mean overall fatality rate of 5 %; in addition, 16 % of healthy population have antibodies to CCHF virus in Turkey at present (most often farmers and village residents). This exceptional epidemiological upsurge of CCHF in Turkey (largely in north-east Anatolia in the Asian part of the country) has been associated ecologically with fragmentation and use of agricultural land and the formation, by this way, of optimal habitats for *H. marginatum* vector ticks (Maltezou and Papa 2010). Some other recent epidemics outside Europe: Iran 248 cases between 2000 and 2004; Mauretania 38 cases (11 fatal) in 2003. In 2009, human cases of CCHF were also reported from Georgia, Kazakhstan, Tajikistan, Iran, Pakistan, and Afghanistan.

Diagnosis: RT-PCR, detection of antibodies or antigen (ELISA, IFA), isolation of the virus (extreme risk).

Treatment: in acute phase (if diagnosed very early) ribavirin though its efficacy has not been unequivocally confirmed in clinical studies. Specific immunoglobulins can be used prophylactically or therapeutically, but only in the first days after infection (Vasilev et al. 1991).

Prevention: a vaccine of Bulgarian provenience (inactivated, suckling mouse brains; not commercial, a small scale production) has been successfully applied to several hundred persons in the Rostov region and Bulgaria (Vasilenko et al. 1975a, b).

European distribution: Fig. 7. Outside Europe: Asian part of Turkey, Armenia, Azerbaijan, Kirghizia, Kazakhstan, Turkmenia, Uzbekistan, Tadjikistan, Mongolia, China, Afghanistan, Pakistan, Iran, Iraq, Saudi Arabia, United Arab Emirates, Oman, Kuwait, Ethiopia, Somalia, Senegal, Guinea, Uganda, Zaire (Congo), Nigeria, Central Africa, Mauritania, Upper Volta, Kenya, Zimbabwe (Rhodesia), S. Africa, Madagascar. Antibodies have been detected in India, Egypt, and Tanzania. Livestock movements and migratory birds play an important role in the transport of infected vector ticks to other areas. For instance, CCHF virus was isolated from nymphal *H. marginatum* removed from *Corvus frugilegus*, *Passer montanus, Galerida cristata,* and *Tockus erythrorhynchus* in Rostov, Astrakhan, Kirghizia and Senegal, respectively (Hoogstraal 1979; Wood et al. 1978; Zeller et al. 1994a, b).

Bhanja Bunyavirus (BHAV)

This virus is, together with two other African tick-borne viruses Kismayo (Butenko et al. 1979) and Forécariah (Boiro et al. 1986), a member of Bhanja group that has not yet been assigned to a recognized genus of the family *Bunyaviridae*. Synonym or subtype: Palma virus (PoTi-4.92 strain, isolated from male *H. punctata* in Portugal, 1992: Filipe et al. 1994); the mean cross-PRNT titre differences among European, Indian and African strains of BHA have been found as great as four to tenfold (Hubálek and Halouzka 1985).

BHAV was isolated first from *Haemaphysalis intermedia* (syn. *H. parva*) ticks that had been collected from a paralyzed goat in Bhanjanagar (district Ganjam, Orissa State, India) in 1954 (prototype strain IG-690), but the record was

Fig. 7 European distribution of Crimean-Congo hemorrhagic fever nairovirus. The *dotted line* shows the northern limits of the *Hyalomma marginatum* area in Europe

published much later (Shah and Work 1969). In Europe, the first isolation was from adult *H. punctata* collected in Italy, 1967 (European topotype ISS.IR.205: Verani et al. 1970a, b), then in Croatia (Vesenjak-Hirjan et al. 1977) and Bulgaria (Pavlov et al. 1978).

The virus is transmitted by metastriate ixodid ticks of several species—in Europe *H. punctata, Haemaphysalis sulcata,* and *D. marginatus*; elsewhere *H. intermedia, Boophilus decoloratus, B. annulatus, B. geigyi, A. variegatum, H. marginatum, H. detritum, H. dromedarii, H. truncatum, R. bursa,* and *Rhipicephalus appendiculatus.* Experimental transmission including TOT was demonstrated in *H. asiaticum* (Gaidamovich et al. 1976).

Vertebrate hosts for BHAV are sheep, goat (Verani et al. 1971), cattle; in Africa, BHAV was also isolated from the four-toed hedgehog (*Atelerix albiventris*) and striped ground squirrel (*Xerus erythropus*). Antibodies were detected in dogs, *C. elaphus, C. capreolus,* and *Sus scrofa* (Punda et al. 1986). The virus does not usually cause apparent infection in adult animals but is pathogenic for young ruminants (lamb, kid, calf), causing fever and CNS affection (meningoencephalitis), or leucopenia in cattle (Theiler and Downs 1973; Hubálek 1987; Semashko et al. 1976; Camicas et al. 1981; Mádr et al. 1984). Experimental encephalitis was produced in rhesus monkey (Balducci et al. 1970; Verani et al. 1970b). Fatal to suckling mouse i.n. and adult mouse (i.c., i.n., but not s.c., i.v., p.o., or per conjunctivae). Encephalitis in lamb (i.c., but not s.c. or i.v.: Semashko et al. 1976; Mádr et al. 1984) and rhesus monkey (i.c.: Balducci et al. 1970). Not fatal to adult goat (s.c.), rabbit (i.c., i.n., s.c., i.v., i.m., p.o.; a low viremia), and several passerine birds. Faint CPE and plaques produced in BSC-1, RK-13, and primary mouse embryo (David-West 1971) cells, while multiplication without CPE in HEp-2 cells (David-West 1972).

Natural foci of BHAV are boskematic—pastoral steppe or forest-steppe ecosystems in xerothermic areas or in karst habitats at more northern latitudes. Based on a comparison of several known natural foci of BHAV infection, their common and typical features were extracted and bio-indicator species (plants, animals) were selected that can be used for prediction of potential presence of BHAV in other geographic areas within Europe (Hubálek 2009).

BHAV causes in human febrile illness with headache, conjunctivitis, or sometimes meningoencephalitis with photophobia, vomiting, and pareses. About ten natural and/or laboratory infections with BHAV have been described in humans, one of them serious—quadriparesis (Calisher and Goodpasture 1975; Punda et al. 1980; Vesenjak-Hirjan et al. 1980). There is some occupational risk for shepherds and veterinary personnel. Probably an underdiagnosed disease in the Mediterranean and Balkan countries.

European distribution: Fig. 8. Outside Europe: India, Kirghizia, Kazakhstan, Azerbaijan, Armenia, Senegal, Guinea, Nigeria, Cameroon, Central Africa, Kenya, Somalia. Antibodies were detected in Srí Lanka, Pakistan, Iran, Turkmenia, Uzbekistan, Tadjikistan, Uganda, Tanzania, Egypt, and Tunisia. Migratory birds might play a role in the transport of infected immature ticks to distant areas.

Family *Reoviridae*

Coltivirus Eyach (EYAV)

A member of Colorado tick fever (CTF) group. Serologically closely related to North-American CTFV by CFT and VNT; however, CTFV is not neutralized with anti-EYA serum.

First isolated from *I. ricinus* ticks collected at Eyach near Tübbingen, Germany, 1972 (prototype: Eyach-38: Rehse-Küpper et al. 1976), later (1981) from *I. ricinus* and *Ixodes ventalloi* collected on a wild rabbit in NW. France (Chastel et al. 1984). There is a hypothesis that this virus, a descendant of CTF agent, could have been imported from North America with U.S. Army dogs and their *Dermacentor* ticks to a military base situated in Germany after the 2nd WW, and evolved into Eyach virus under the selective pressure of European ecosystem (Hubálek and Rudolf 2011). Another hypothesis suggests that CTFV could have been introduced to Europe with cottontail rabbits, *Sylvilagus floridanus* (Attoui et al. 1998).

The dsRNA of EYAV consists of 12 segments, in contrast to the genus *Orbivirus* with ten segments. Very sensitive to trypsin, acid, and heat (60°C).

Arthropod vectors are ticks *I. ricinus* (TST) and *I. ventalloi*.

Vertebrate hosts are rodents (they reveal prolonged experimental viremias) and lagomorphs (*Oryctolagus cuniculus*). Animal infection has an inapparent course, but meningoencephalitis in suckling mouse (i.c.) has been demonstrated histologically.

Serological data indicate possible association (not yet reliably demonstrated) of EYAV with human neuropathies including five patients with meningoencephalitis (Málková et al. 1980; Fraňková 1981); additional investigation is necessary. The closely related CTF virus (principal vector is *Dermacentor andersoni*) causes acute febrile illness in the mountainous northwestern parts of North America, with a number of cases each year.

Diagnosis: serology (IgM ELISA, IFA, VNT; but not HIT); virus isolation.

European distribution: Fig. 9.

Orbivirus Tribeč (TRBV)

Synonyms (or subtypes): Lipovník (LIP-91, *I. ricinus*, East Slovakia, 1963), Koliba, Cvilín (Libíková et al. 1965,

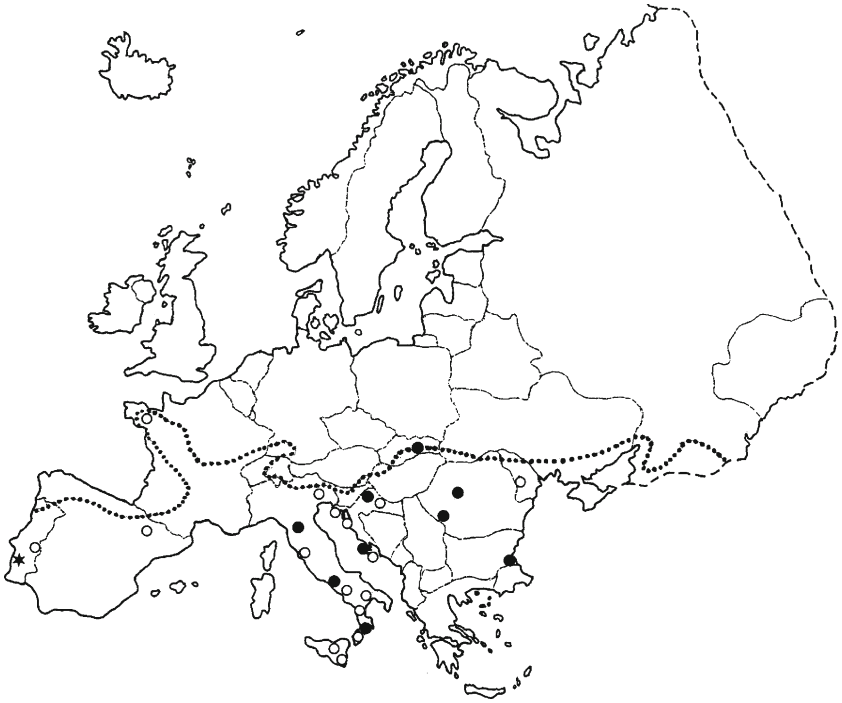

Fig. 8 European distribution of Bhanja virus. Explanation: *black dots*, the virus isolation; *asterisk*, Palma virus (a subtype of BHAV). The *dotted line* shows predicted northern limits of the Bhanja virus area in Europe, based on the presence of bio-indicators (Hubálek 2009) and largely compatible with the range of *Haemaphysalis punctata* and *Dermacentor marginatus* vector ticks

1977), Brezová (subtype: Hubálek et al. 1987a, b), Mircha (strain "634": Vinograd et al. 1977), Kharagysh (Skofertsa et al. 1972). Member of Kemerovo antigenic group, and the Kemerovo subgroup (Belhouchet et al. 2010). Contrary to coltiviruses, orbiviruses of the Kemerovo group have only 10 segments of dsRNA with a total size of 19 kbp. Prototype strain: Tribeč (*I. ricinus*, West Slovakia, 1963). Closely related to the Siberian Kemerovo virus by CFT but distinguishable by VNT (Libíková and Buckley 1971; Libíková and Casals 1971) or RNA-RNA hybridization (Brown et al. 1988). Gene pools of the Kemerovo group and other orbiviruses have a great reassortment potential (because of the segmented dsRNA) and resulting biological variability (Gorman et al. 1978, 1983; Gorman 1983; Brown et al. 1988, 1989). Interestingly, rabbit syncytium virus that occurs in *S. floridanus* rabbit in the USA is also closely related to TRBV.

First 28 strains of TRBV were isolated from *I. ricinus* in three regions of Slovakia in 1963; a few strains had been

Fig. 9 European distribution of Eyach coltivirus

isolated already in 1961 but lost thereafter (Libíková 1964; Libíková et al. 1964, 1965; Grešíková et al. 1965).

Nearly resistant to diethyl ether and sodium deoxycholate but very sensitive to acid (even pH 5–6), alkali (pH 10) and trypsin.

TRBV is transmitted by ticks *I. ricinus* (TST) and *I. persulcatus*, occasionally by *H. punctata* (Topciu et al. 1968).

Vertebrate hosts of TRBV are rodents, e.g., *M. glareolus* and *M. subterraneus* (Grešíková et al. 1965), hare *L. europaeus* (Dobler et al. 2006), goat (Grešíková et al. 1965), European starling *S. vulgaris* and chaffinch *F. coelebs* (Skofertsa et al. 1974, 1976). Antibodies are present very often in grazed ruminants in endemic areas (up to 45–88 % reactors: Hubálek et al. 1986). Animal disease is unknown (inapparent). However, TRBV is fatal to suckling mouse (also s.c.: meningoencephalitis—progressive neuronal and glial damage with perivascular infiltration), suckling rat, and suckling Syrian hamster (i.c., but not s.c.). Meningitis but survival or no symptoms at all in adult mouse inoculated i.c. (but local necrotizing encephalitis demonstrated histologically), while no symptoms in adult mouse given s.c., i.n. or p.o., adult rat (i.c.), rabbit (i.c.), and peripherally inoculated calf or foal. Fever and meningitis are present in rhesus monkey inoculated i.c. (Grešíková et al. 1966).

The virus causes an occasional febrile illness or aseptic meningitis in humans—e.g., at least 15 patients with the CNS infection (meningitis) revealed seroconversion against TRBV in Czechland (Fraňková 1981; Málková et al. 1986; Hubálek et al. 1987a, b). Antibodies occur in human population, interestingly at a higher frequency among patients with multiple sclerosis (Libíková et al. 1978). There is potential occupational risk for forestry workers. The disease caused by TRBV is probably underdiagnosed. Additional studies are necessary to evaluate the public health importance of TRBV.

Diagnosis: serology (CFT, VNT; but not HIT because these viruses do not produce hemagglutinin). Therefore, HIT (and ELISA) cannot be normally used in diagnostic serology.

European distribution: Fig. 10 Outside Europe TRBV was isolated exceptionally in northern Africa. Migratory birds have been implicated in the dispersal of Kemerovo serogroup viruses over vast distances. For instance, the Siberian Kemerovo virus was isolated from a southward migrating *Phoenicurus phoenicurus* in Egypt (Schmidt and Shope 1971; Brown et al. 1988).

Orbivirus Okhotskiy (OKHV)

Kemerovo antigenic group, the Great Island (GI) subgroup. Prototype: LEIV-70C (*I. uriae,* Tyuleniy Island—Far East, 1970). Antigenically and genetically closely related to other Kemerovo group and especially GI subgroup viruses; probably identical with CWV because it hybridizes to all ten OKHV genes. The GI complex viruses may represent a single viral gene pool, i.e., one species (Brown et al. 1989; Belhouchet et al. 2010).

OKHV was originally isolated from nymphal *I. uriae* collected in rocky breeding grounds of seabirds on Tyuleniy Island, Sea of Okhotsk (Russian Far East) in 1970 (Lvov et al. 1973a, b, c, d). In Europe, it was isolated under similar conditions in the Murmansk region, N. Russia, 1970 (Lvov et al. 1989).

The main arthropod vector is *I. uriae* (TST, TOT), occasionally *I. signatus.*

Vertebrate hosts are seabirds: *R. tridactyla*; antibodies were also detected in *F. glacialis, U. aalge,* and *Phalacrocorax pelagicus.* Avian disease is unknown.

Human disease has not been reported, although antibodies were detected in 12 % of inhabitants on the Commodore Islands.

European distribution: Fig. 11 Outside Europe: coastal Asian Russia (Far East), USA and Canada. Seabirds disperse the GI complex viruses transoceanically and introduce them to new areas and new hosts; the GI members therefore occur both in subarctic and subantarctic regions (Lvov and Ilyichev 1979).

Orbivirus Cape Wrath (CWV)

Kemerovo antigenic group, the GI subgroup. Prototype: ScotAr-20 (CW-20; *I. uriae*, Scotland, 1973). Antigenically and genetically closely related to GI, BAU, MYK, TDM, OKH, Nugget and Yaquina Head viruses; In fact, probably identical with (i.e., a synonym of) Okhotskiy virus because it hybridizes to all ten OKH genes (Brown et al. 1989). Very similar or identical non-registered viruses are Arbroath (ARB-1, Scotland: Moss and Nuttall 1985), Broadhaven (FT-363: Carey and Nuttall 1989; Jacobs et al. 1986; Nuttall et al. 1981, 1990a, b), Wexford (GS-80-9, SE. Ireland: Nuttall et al. 1984a; Carey and Nuttall 1989), Thormodseyjarklettur (Iceland), Scottish strains Mill Door/79, Above Maiden, Colony, Foula, Mill Door, North Clett, and Shiant Islands, Irish Great Saltee Island GS 80-4,-7,-8, Ellidaye ELL-3a and Grimsey (Iceland), English isolates Lundy, Inner Farne IF79-1,-2, and North End, Rost Islands NorV-808,-871,-962, and Vaeroy (Norway—Lofoten), and a number of other strains (Jacobs et al. 1986; Labuda and Nuttall 2004). Some of these viruses can be differentiated in PRNT (Carey and Nuttall 1989), but they reassort readily at a high frequency (Moss et al. 1988; Nuttall et al. 1990a, b; Nuttall and Moss 1989). Only minor variability has also been found in the induced protein profiles among different CWV and CWV-like isolates (Black et al. 1986; Spence et al. 1986). The gene reassortment potential of the isolates confirms the close taxonomic

Fig. 10 European distribution of Tribeč virus. Explanation: *black dots*, the virus isolation; *white circles*, specific antibodies detected

relationship of all the GI subgroup members which may, in fact, represent a single gene pool (Moss et al. 1988; Brown et al. 1989; Nuttall et al. 1990a) and therefore one virus species.

First isolated from engorged female *I. uriae* collected in a colony of the common murre *U. aalge* at Clo Mor on Cape Wrath, Scotland, June 1973 (Main et al. 1976a, b).

The virus is sensitive to trypsin and acid (pH 3) but resistant at pH 5.

Arthropod vector is *I. uriae.*

Vertebrate hosts are marine birds. Antibodies were detected in *U. aalge*, *A. torda,* and *O. leucorrhoa* (Main et al. 1976a, b; Nuttall et al. 1984a, b). However, avian disease is unknown. Suckling mouse is a rather insusceptible system for the CWV isolation attempts (Nuttall et al. 1984a, b).

Human disease has not been reported.

European distribution: Fig. 11. Outside Europe: Alaska.

Fig. 11 European distribution of the Great Island subgroup orbiviruses: Cape Wrath and CW-like (*circles*), Okhotskiy (*squares*), Mykines (*asterisk*), Tindholmur (*asterisk*) and Bauline (*diamond*) viruses

Orbivirus Mykines (MYKV) and Tindholmur (TDMV)

Kemerovo antigenic group, the GI subgroup. Prototype MYKV is DenAr-12 (*I. uriae*, Faeroe Islands, 1974), and TDMV DenAr-2 (*I. uriae*, Faeroe Islands, 1974). Both viruses are distinguishable by CFT, and antigenically related to CWV, GIV, BAUV, Yaquina Head, OKHV and other GI subgroup viruses (Brown et al. 1989).

First isolates originated from female *I. uriae* ticks collected in puffin (*F. arctica*) colonies at Mykines and Tindholmur, Faeroe Islands in 1974 (Main 1978).

Arthropod vectors: *I. uriae*.

Vertebrate hosts: probably *F. arctica*.

Animal and human disease has not been reported.

European distribution: Fig. 11.

Orbivirus Bauline (BAUV)

Kemerovo antigenic group, the GI subgroup. Prototype: CanAr-14 (*I. uriae*, Canada, 1971). European topotype: FI-873 (*I. uriae*, Norway, 1974). The Norwegian isolates FI-873 and FI-962 have been found identical with prototype BAUV by RNA–RNA hybridization (Brown et al. 1989). Antigenically closely related to other members of the GI or Kemerovo subgroups (Brown et al. 1989), and indistinguishable from GI virus (CanAr-41) by CFT; both viruses can be differentiated by VNT (Main et al. 1973). Some BAUV and GIV isolates from Newfoundland have exhibited a remarkable variation in all ten genome segments (Oprandy et al. 1988).

Originally isolated from engorged nymphal *I. uriae* ticks collected during July 1971 in a *F. arctica* colony on Great Island off the SE. coast of Newfoundland, Canada (Main et al. 1973). In Europe, it was isolated from *I. uriae* collected in a seabird colony on Rost Island, Lofoten (Norway) in 1974 (Brown et al. 1989; Saikku et al. 1980).

Vertebrate hosts are unknown; antibodies were detected in *F. arctica* and *O. leucorrhoa* birds.

Animal and human disease has not been reported.

European distribution: Fig. 11. Outside Europe: Canada (Newfoundland). Documented transoceanic flights of puffins from NW. Europe to Newfoundland and vice versa contribute to the dissemination of the GI subgroup viruses over wide geographical areas (Lvov and Ilyichev 1979; Main et al. 1973).

Family *Orthomyxoviridae*

Thogotovirus Thogoto (THOV)

Thogoto antigenic group. Prototype: Ken-IIA (mixed metastriate tick spp., Kenya, 1960). African topotype: IbAr-2012 (*Boophilus* spp., Nigeria, 1964); European topotype: SiAr-126 (*R. bursa*, Sicily, 1969). THOV shares only 15–20 % nucleotide homology with influenza orthomyxoviruses. Virions are spherical, 80–120 nm, enveloped, contain ss(−) RNA arranged in six segments with a total size of 10 kbp, and one surface glycoprotein. Some strains form HA in the liver and blood serum of SM or in Vero cells, whereas not in suckling mouse brain.

First isolated from a pool of *B. decoloratus* and *Rhipicephalus* spp. ticks collected on cattle in Thogoto Forest near Nairobi, Kenya in 1960 (Haig et al. 1965). In Europe, it was first isolated from ticks collected on ruminants in Sicily, 1969 (Albanese et al. 1971, 1972; Srihongse et al. 1974) and then in Portugal in 1978 (Filipe and Calisher 1984).

Arthropod vectors are metastriate ticks only—*B. decoloratus*, *B. annulatus, A. variegatum*, *R. appendiculatus, Rhipicephalus sanguineus* (Portugal), *R. bursa* (Sicily), *Rhipicephalus evertsi,* other *Rhipicephalus* spp., *Hyalomma truncatum,* and *H. anatolicum*.

Vertebrate hosts are cattle, camel, and man (isolations in Africa). Antibodies were also detected in sheep and goat. THOV causes leucopenia in cattle, and fever, and abortion in sheep (Davies et al. 1984). Fatal to, and highly hepatotropic or pantropic in, adult mouse (Filipe et al. 1986) and adult Syrian hamster (i.p.). No symptoms in suckling hamster and rabbit (i.p.). CPE is produced in primary mouse embryo and lamb testis cells; faint CPE in HEp-2 cells (David-West 1971, 1972).

Natural foci are boskematic—pastoral xerothermic ecosystems.

Human disease: two cases have been described, one with bilateral optic neuritis and another as a fatal meningoencephalitis with hepatitis although complicated by a sickle-cell disease (Theiler and Downs 1973; Moore et al. 1975). THOV is probably contagious from man to man. Antibodies occur rarely in human sera in Europe: e.g., only 1 % seropositive persons were detected in Portugal (Filipe et al. 1985).

European distribution: Fig. 12. Outside Europe THOV occurs in Nigeria, Kenya, Uganda, Ethiopia, Cameroon, Central Africa, Egypt, Iran. Tick-infested domestic animals (e.g., camels) and migratory birds could disseminate the virus over a wide geographic range (Calisher et al. 1987).

Thogotovirus Dhori (DHOV)

Prototype: IG-611313 (*Hyalomma dromedarii*, India, 1961). European topotype: PoTi-461 "Vidigueira" (male *H. marginatum*, Portugal, 1971). Synonyms: Astra (Butenko and Chumakov 1971), Batken (LEIV-306 K: *H. marginatum*, collected on sheep in Kirghizia, 1970: Lvov et al. 1974). Nucleotide sequence data suggest that DHOV is distantly related to influenza viruses but their envelope proteins (HA, neuraminidase) differ significantly. Virions are spherical,

Fig. 12 European distribution of Dhori (*circles*) and Thogoto (*squares*) viruses

80–120 nm, enveloped, contain ss(−)RNA arranged in 7 segments with a total size of 10 kbp, and one surface glycoprotein. HA is also produced in Vero cells, and HIT can use goose, sheep, monkey or human RBC.

DHOV was first isolated from *Hyalomma dromedarii* ticks collected on camels in Dhori, Gujarat State, India in 1961 (Anderson and Casals 1973). In Europe, it has been isolated several times from *Hyalomma marginatum* and twice from *Hyalomma scupense* collected at Astrakhan, South Russia since 1969 (as "Astra" virus: (Butenko and Chumakov 1971; Butenko et al. 1987; Bannova et al. 1974; Smirnova et al. 1988) and in Crimea (one strain —"Batken"); additional two strains were obtained from *H. scupense* near Astrakhan (Smirnova et al. 1988) and another one in southern Portugal, 1971 (Filipe and Casals 1979).

Arthropod vectors are metastriate ticks *H. dromedarii*, *H. marginatum* (Europe), *H. scupense* and *D. marginatus*. Occasional isolations of DHOV were reported from *Ornithodoros lahorensis* and mosquitoes (*Anopheles hyrcanus, Aedes caspius, Culex hortensis*).

Vertebrate hosts are camel, horse, bats (Kirghizia), but animal disease is unknown (asymptomatic). Antibodies have also been detected in goats, sheep and cattle (Filipe et al. 1985). DHOV is hepatotropic, and causing diffuse necrosis of neurons in mouse (Filipe et al. 1990). No symptoms were observed in inoculated adult or young rabbit (i.c., i.p., s.c.). No CPE or plaques (but multiplication) produced in BSC-1, L, human embryo kidney cells; CPE formed in monkey kidney 6619-1 cells (Smirnova et al. 1988).

Natural foci: boskematic (pastoral xerothermic and semi-desert ecosystems).

Human disease: acute illness with severe fever, headache, general weakness, retrobulbar pain, with encephalitis in *c.* 40 % of patients and a long, 2-month convalescence period. Five cases of severe laboratory infection (due to aerosol) have been described (Butenko et al. 1987). The virus could also be contagious from man to man.

European distribution: Fig. 12. Seroprevalence rate among humans is relatively high in Astrakhan (4–9 %) but low in Portugal (0.8 %: Filipe et al. 1985). Outside Europe DHOV occurs in India, Egypt, Armenia, Azerbaijan, Kirghizia, Uzbekistan, and antibodies were detected in Pakistan.

Family *Asfarviridae*

Asfivirus of African swine fever (ASFV)

The only DNA arbovirus occurring in Europe. There are several antigenic types, while no recognized prototype strain of ASFV. Hemadsorption-inhibiting antibodies are isolate specific, but HA is not produced. Interestingly, neutralizing antibodies do not appear in vertebrates. The virus is sensitive to dodecyl sulphate and heat (60°C) while less sensitive to putrefaction, formaldehyde and alkali.

History: originally isolated by R.E. Montgomery from the blood of a sick pig in Kenya, 1910, and in Europe ASFV was first isolated in 1957 (Karabatsos 1985).

Arthropod vectors are soft ticks *Ornithodoros moubata porcinus* (TST, TOT) in Africa, and *O. erraticus* in SW. Europe.

Vertebrate hosts are *S. scrofa* (domestic and wild swine), in Africa also common warthog *Phacochoerus africanus* (main reservoir), bushpig *Potamochoerus porcus,* giant forest hog *Hylochoerus meinertzhageni* (Jori and Bastos 2009). The wild suids are the reservoir of ASFV with usually inapparent infection (except for *S. scrofa*). ASF is a pantropic, highly contagious disease of pigs with fever, cough, anorexia, skin cyanosis, incoordination, diarrhea; destruction of lymphoreticular elements, vasculitis, widespread hemorrhages, thromboses, infarction, and abortion (Schlafer and Mebus 1984). Lethality is 100 % with virulent strains in naive commercial pig populations, while some strains may produce mild disease and carriership. Cattle, sheep, goat, dog and rabbit (s.c., i.v.) are insusceptible though the virus recovery has been sometimes reported in rabbit and goat. CPE is produced in primary porcine leucocyte, bone marrow and kidney cells.

European epizootics of ASF occurred in Portugal (1957 and 1960: Filipe 1980), SW. Spain (since 1957: Oleaga-Perez et al. 1990), Sardinia, Malta, recently in the Caucasus region (since 2007) including southern Russia (North Ossetia, Krasnodar territory, 2008–2011), and temporarily in France (1964), Italy (1967, 1983: Swaney et al. 1987), Belgium, and the Netherlands.

Natural foci: mainly tropical and subtropical pastoral ecosystems. Principally a wild hog/pig-*Ornithodoros* cycle. Moreover, circulation in pig pens in rural habitats.

Human disease has not been reported.

European distribution: Fig. 13. Occasionally introduced into southern Europe, Belgium, and the Netherlands. Outside Europe: many African countries; temporarily Brazil and some Caribbean islands (Cuba, Haiti).

Conclusions

Several "European" tiboviruses cause very serious human (CEEV, RSSEV, CCHFV) or animal (LIV, ASFV) diseases. Other arboviruses play definite role in human or animal pathology though the disease is usually either less serious or infrequently reported (TYUV, BHAV, AVAV, EYAV, TRBV, DHOV, THOV). In general, three groups of tibovirus diseases can be recognized according to main clinical symptoms produced: (i) febrile illness—usually with a rapid onset, fever, sweating, headache, nausea, weakness, myalgia, arthralgia, sometimes polyarthritis and rash; (ii) the CNS affection—meningitis, meningoencephalitis, or encephalomyelitis with pareses, paralysis, and other sequelae; (iii) hemorrhagic disease. The other European arboviruses are "orphans" without a proven medical or veterinary significance (BAHV, MTRV, MEAV, GAV, PTVV, ZTV, SAHV, UUKV, SOLV, PIV, AVAV, CMV, OKHV, CWV, MYKV, TDMV, BAUV). However, certain arbovirus diseases of free-living vertebrates (but also those of domestic animals and even man) may often pass unnoticed or misdiagnosed and eventually, they might potentially appear as emerging diseases. In addition, active search for new

Fig. 13 European distribution of African swine fever virus

tiboviruses or for new, pathogenic variants of the known tiboviruses in Europe should continue.

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