

Rift Valley fever - a threat for Europe?

V Chevalier (veronique.chevalier@cirad.fr)¹, M Pépin², L Plée³, R Lancelot⁴

1. Centre International de Recherche Agronomique pour le Développement (CIRAD, International Centre of Agricultural Research for Development), Unit for animal and integrated risk management (UR AGIRs), Montpellier, France
2. Agence française pour la sécurité sanitaire des aliments (AFSSA, French Agency for Food Safety), Lyon, France
3. Agence française pour la sécurité sanitaire des aliments (AFSSA, French Agency for Food Safety), Unit for the evaluation of risks associated with food and animal health, Maisons-Alfort, France
4. Centre International de Recherche Agronomique pour le Développement (CIRAD, International Centre of Agricultural Research for Development), Unit for the control of exotic and emerging animal diseases (UMR CMAEE), Montpellier, France

Citation style for this article:

Citation style for this article: Chevalier V, Pépin M, Plée L, Lancelot R. Rift Valley fever - a threat for Europe?. *Euro Surveill.* 2010;15(10):pii=19506. Available online: <http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19506>

This article has been published on 11 March 2010

Rift Valley fever (RVF) is a severe mosquito-borne disease affecting humans and domestic ruminants, caused by a *Phlebovirus* (*Bunyaviridae*). It is widespread in Africa and has recently spread to Yemen and Saudi Arabia. RVF epidemics are more and more frequent in Africa and the Middle East, probably in relation with climatic changes (episodes of heavy rainfall in eastern and southern Africa), as well as intensified livestock trade. The probability of introduction and large-scale spread of RVF in Europe is very low, but localised RVF outbreaks may occur in humid areas with a large population of ruminants. Should this happen, human cases would probably occur in exposed individuals: farmers, veterinarians, slaughterhouse employees etc. Surveillance and diagnostic methods are available, but control tools are limited: vector control is difficult to implement, and vaccines are only available for ruminants, with either a limited efficacy (inactivated vaccines) or a residual pathogenic effect. The best strategy to protect Europe and the rest of the world against RVF is to develop more efficient surveillance and control tools and to implement coordinated regional monitoring and control programmes.

Relevance of Rift Valley fever to public health in the European Union

Rift Valley fever (RVF) is a zoonotic disease of domestic ruminants and humans caused by an arbovirus belonging to the *Phlebovirus* genus (family *Bunyaviridae*). It causes high mortality rates in newborn ruminants, especially sheep and goats, and abortion in pregnant animals. Human infection by the RVF virus (RVFV) may result from mosquito bites, exposure to body fluids of livestock or to carcasses and organs during necropsy, slaughtering, and butchering [1].

The public health impact of RVF can be severe. In Egypt in 1976, 200,000 people were infected and 600 fatal cases officially reported, among others in the River Nile delta [2]. Over 200 human deaths were reported in Mauritania in 1987 [3]. In 2007-2008, 738 human cases were officially reported in Sudan, including 230 deaths

[4]. It is likely that the number of cases was underreported because RVF mostly affects rural populations living far from public health facilities. The occurrence of RVF in northern Egypt is evidence that RVF may occur in Mediterranean countries, thus directly threatening Europe. In the Indian Ocean, RVF has been introduced in the French island of Mayotte, with several clinical cases reported in humans [5]

Transmission, epidemiology and clinical symptoms

The RVFV transmission cycle involves ruminants and mosquitoes. Host sensitivity depends on age and animal species [6] (Table 1). Humans are dead-end hosts. The epidemiological cycle is made more complex by direct transmission from infected ruminants to healthy ruminants or humans, by transovarian transmission in some mosquito species, and by a large number of potential vectors with different bio-ecology [6]. The existence of wild reservoir hosts has not been clearly demonstrated to date (Figure 1).

Transmission mechanisms

The bite of infected mosquitoes is the main transmission mechanism of RVF in ruminants during inter-epizootic periods. More than 30 mosquito species were found to be infected by RVFV [6,7] (Table 2), belonging to seven genera of which *Aedes* and *Culex* are considered as the most important from the point of view of vector competence (other genera are *Anopheles*, *Coquillettidia*, *Eretmapodite*, *Mansonia* and *Ochlerotatus*).

In mosquitoes, transovarian RVFV transmission has been observed in *Aedes mcintoshi*. It appears to be a likely phenomenon in several other species, including the widespread *Ae. vexans* species complex. In some of these *Aedes* species, infected, diapaused eggs may survive in dried mud during inter-epizootic and/or dry/cold periods [8] and hatch infected imagoes.

Ruminant-to-human transmission is the main infection route for humans, although they can also be infected

by mosquito bites [9]. Body fluids such as the blood (during slaughtering and butchering), foetal membranes and amniotic fluid of viraemic ruminants are highly infective for humans. Fresh and raw meat may be a source of infection for humans, but the virus is destroyed rapidly during meat maturation. Empirical

field observations indicate that ruminants can also become infected by contact with material containing virus (e.g. fetus and fetal membranes after abortion), however, this route of transmission has not yet been confirmed [10].

TABLE 1
Species susceptibility and sensibility to the Rift Valley fever virus

Mortality >70%	Mortality 10-70%	Severe disease with low fatality rate (<10%)	Antibody production	Not susceptible
Lamb	Sheep	Human	Camel	Bird
Kid	Calf	Cattle	Horse	Reptile
Puppy	Some rodents	Goat	Cat	Amphibian
Kitten		African Buffalo	Dog	
Mouse		Asian Buffalo	Swine	
Rat		Monkey	Donkey	
			Rabbit	

Reproduced from Lefèvre et al. [5] with permission from the publisher (Lavoisier, France)

FIGURE 1
Epidemiological cycle of Rift Valley fever

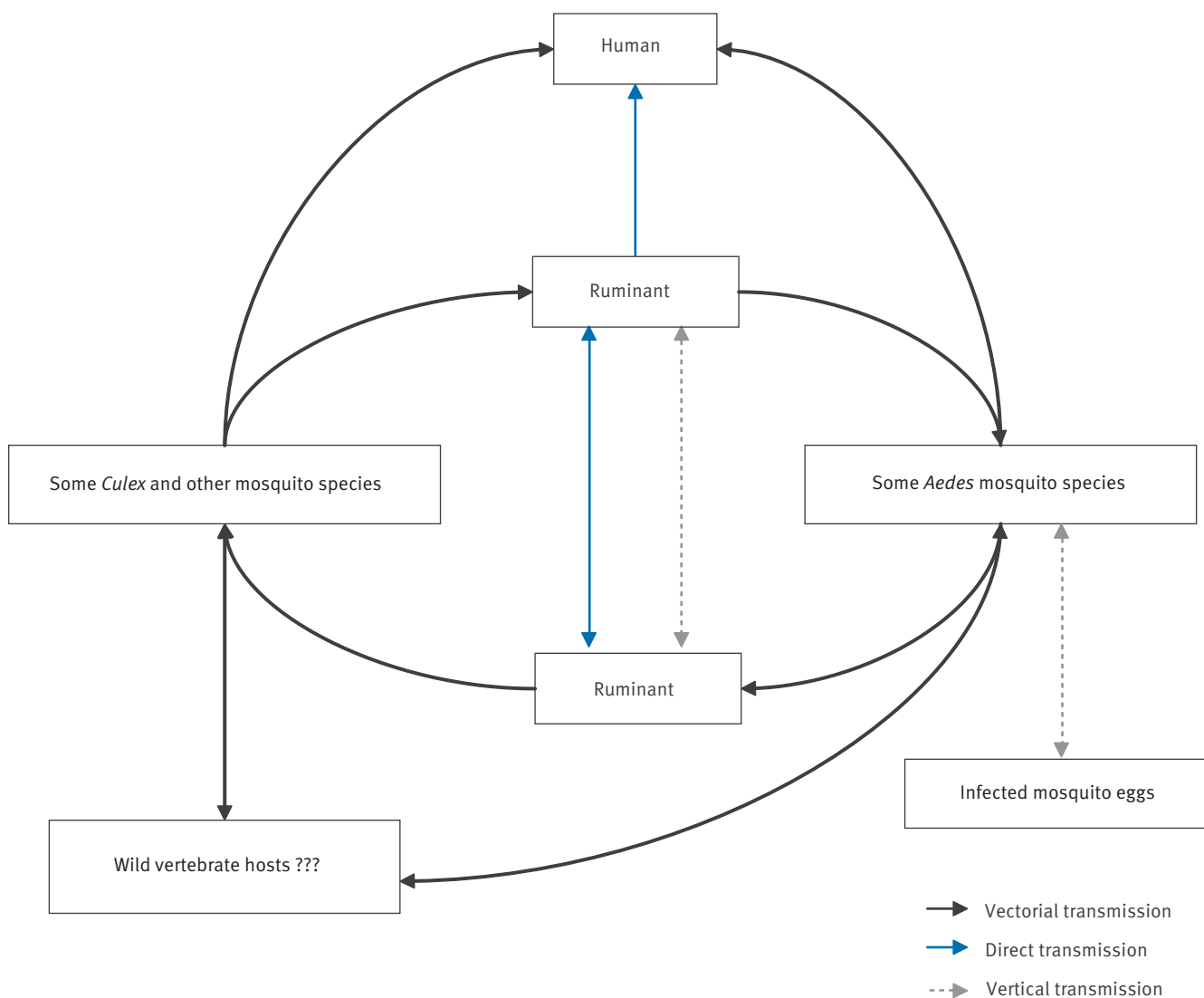


TABLE 2
Arthropods naturally infected by Rift Valley fever virus

Genus	Species	Country (year)	
<i>Aedes (Aedimorphus)</i>	<i>cumminsii</i>	Kenya (1981-1984)	
		Burkina Faso (1983)	
	<i>dalzieli</i>	Senegal (1974, 1983)	
	<i>dentatus</i>	Zimbabwe (1969)	
	<i>durbanensis</i>	Kenya (1937)	
	<i>ochraceus</i>	Senegal (1993)	
	<i>tarsalis</i>	Uganda (1944)	
	<i>vexans arabiensis</i>	Senegal (1993) Saudi Arabia (2000)	
<i>Aedes (Neomelaniconion)</i>	<i>circumluteolus</i>	Uganda (1955) South Africa (1955, 1981)	
	<i>mcintoshii</i>	Zimbabwe (1969) South Africa (1974-1975) Kenya (1981-1984)	
	<i>palpalis</i>	Central African Republic (1969)	
<i>Ochlerotatus (Ochlerotatus)</i>	<i>caballus</i>	South Africa (1953)	
	<i>caspius</i>	Suspected, Egypt (1993)	
	<i>juppi</i>	South Africa (1974-1975)	
<i>Aedes (Stegomyia)</i>	<i>africanus</i>	Uganda (1956)	
	<i>demeilloni</i>	Uganda (1944)	
<i>Aedes (Diceromyia)</i>	<i>furcifer group</i>	Burkina Faso (1983)	
<i>Anopheles (Anopheles)</i>	<i>coustani</i>	Zimbabwe (1969) Madagascar (1979)	
	<i>fuscicolor</i>	Madagascar (1979)	
<i>Anopheles (Cellia)</i>	<i>chrityi</i>	Kenya (1981-1984)	
	<i>cinereus</i>	South Africa (1974-1975)	
	<i>pauliani</i>	Madagascar (1979)	
	<i>pharoensis</i>	Kenya (1981-1984)	
<i>Culex (Culex)</i>	<i>spp.</i>	Madagascar (1979)	
	<i>antennatus</i>	Nigeria (1967-1970) Kenya (1981-1984)	
	<i>neavi</i>	South Africa (1981)	
	<i>pipiens</i>	Egypt (1977)	
	<i>poicilipes</i>	Senegal (1998, 2003)	
	<i>theileri</i>	South Africa (1970) Zimbabwe (1969)	
	<i>tritaeniorhynchus</i>	Saudi Arabia (2000)	
	<i>vansomereni</i>	Kenya (1981-1984)	
	<i>zombaensis</i>	South Africa (1981) Kenya (1981-1984, 1989)	
	<i>Culex (Eumelanomyia)</i>	<i>rubinotus</i>	Kenya (1981-1984)
	<i>Eretmapodites</i>	<i>chrysogaster</i>	Uganda (1944)
		<i>quinquevittatus</i>	South Africa (1971) Kenya (1981-1984)
<i>Coquillettidia</i>	<i>fuscopennata</i>	Uganda (1959)	
	<i>grandidieri</i>	Madagascar (1979)	
<i>Mansonia (Mansoniodes)</i>	<i>africana</i>	Uganda (1959, 1968) Central African Republic (1969) Kenya (1989)	
	<i>uniformis</i>	Uganda (1959) Madagascar (1979)	
<i>Other diptera</i>	<i>Culicoides spp.</i>	Nigeria (1967)	

Adapted from [1].

Direct human-to-human transmission has not been reported, and RVF is not considered to be a nosocomial disease. Transplacental RVFV transmission may occur in vertebrates, including humans. It results in abortion and high newborn mortality rates [11].

Rodents may be infected during epizootic periods [12-15] but their epidemiological role in virus transmission and maintenance is not clear. Bat species also have been suspected [16]. Finally, wild ruminants may play a role in the epidemiology of RVF in areas where their population density is high [17].

Clinical features

Animals

Clinical manifestations vary depending on age and animal species. In sheep, a fever of up to 41-42°C is observed after a short incubation period. Newborn lambs (and sometimes kids) usually die within 36 to 40 hours after the onset of symptoms, with mortality rates sometimes reaching 95%. Older animals (from two weeks to three months-old) either die or develop only a mild infection. In pregnant ewes, abortions are frequent, ranging from 5% to 100%. Twenty per cent of the aborting ewes die. Vomiting may be the only clinical sign presented by adult sheep and lambs older than three months. However, these animals may experience fever with depression, haemorrhagic diarrhoea, blood-stained muco-purulent nasal discharge, and icterus. Case-fatality rates vary between 20% and 30%. Adult goats develop a mild form of the disease, but abortions are frequent (80%). Mortality rates are generally low [10]. Calves often develop acute illness, with fever, fetid diarrhoea, and dyspnoea. Mortality rates may vary from 10% to 70%. Abortion is often the only clinical sign and mortality rates are low (10-15%).

Humans

In most cases, human infections remain unapparent, or with mild, influenza-like symptoms. However, infected people may experience an undifferentiated, severe, influenza-like syndrome and hepatitis with vomiting and diarrhoea. Complications may occur. Severe forms are manifested in three different clinical syndromes. The most frequent one is a maculo-retinitis, with blurred vision and a loss of visual acuity due to retinal haemorrhage and macular oedema. Encephalitis may also occur, accompanied by confusion and coma. This form is rarely fatal but permanent sequelae are encountered. The third and most severe form is a haemorrhagic fever, with hepatitis, thrombocytopenia, icterus, and multiple haemorrhages. This form is often fatal [10,18,19]. Human case-fatality rates have been lower than 1% in the past, however, an increase has been reported since 1970 [19]. In the RVF epidemic in Saudi Arabia in the year 2000, the fatality rate reached 14% [20].

Diagnostic methods

RVFV presents a high biohazard for livestock farmers, veterinarians, butchers, slaughterhouse employees, and laboratory staff handling infected biological samples. International public health agencies have set a bio-safety level (BSL) of BSL₃ for facilities in Europe handling the virus and of BSL₄ for facilities in the United States (US).

Appropriate diagnostic samples are peripheral blood collected on EDTA, plasma or serum of infected animals or patients, and the liver, brain, spleen or lymph nodes of dead animals. When samples can be conveyed rapidly to a diagnostic laboratory (<48 hours), they should be stored at a temperature below +4 °C. When this is not the case, samples should be frozen at -20 °C (or below). Small fragments of organs may be stored in a 10-20% glycerol solution

Virus isolation can be performed in suckling or weaned mice by intracerebral or intraperitoneal inoculation or in a variety of cell cultures including Vero, BHK21, or mosquito line cells. RVFV can be identified in cell cultures by immunofluorescence, virus neutralisation test, reverse transcriptase polymerase chain reaction (RT-PCR), and/or genome sequencing. Virus isolation is the gold standard for RVF diagnosis. However, its sensitivity is rather low: RVFV isolation is not easy to achieve. Alternatively, the detection of RVFV ribonucleic acid (RNA) can be done using RT-PCR performed on RNA extracted directly from biological samples [21]. Results are available within a few hours, which makes RT-PCR the priority test when a case of RVF is suspected.

Serological tests to detect antibodies against RVFV include the virus neutralisation test (VNT), and enzyme-linked immunosorbent assays (ELISA). VNT is very specific, cross reactions with other Phleboviruses being limited [22;23]. It is the gold standard serological test. However, it is costly, time consuming, and requires a BSL₃ or 4 laboratory.

(Indirect) immunoglobulin (Ig) detection ELISAs are quick, sensitive and specific. They are progressively replacing VNT [24]. A competition ELISA (cELISA) is also commercially available to detect IgG and IgM. It allows serological diagnosis in ruminants and humans. At the earliest, it can detect antibodies as soon as four days following infection or vaccination in animals reacting very early, and eight days post-vaccination for 100% of animals [25]. More recently, another indirect ELISA based on a recombinant RVFV nucleoprotein has been developed. Its sensitivity is 98.7% and specificity 99.4% [26-28].

The cELISA has been evaluated with human and animal sera collected in Africa, and also with sera from French livestock (cattle, sheep and goats) to check their specificity with European ruminant breeds which turned out to be excellent with a predictive negative value of

100% (n = 502), 95% confidence interval: 99.3 to 100% [29].

Treatments

There is no specific treatment for either humans or animals.

Prevention

Vaccines

A human vaccine (inactivated with beta-propiolactone) has been produced in the US and was used to protect laboratory staff and military troops. However, its production has been stopped [30].

Given that domestic ruminants are involved in the epidemiological cycle and that humans mostly become infected after contact with viraemic animals, the vaccination of ruminants is the method of choice to prevent human disease. Both live and inactivated vaccines are available for livestock.

The Smithburn vaccine is a live attenuated vaccine. It is inexpensive to prepare and immunogenic for sheep, goats, and cattle. It protects these species against abortion caused by a wild RVFV, and post-vaccinal immunity is life long. However, it has a residual pathogenic effect and may induce foetal abnormalities and/or abortion in ruminants. It is also pathogenic for humans (febrile syndrome). Despite these drawbacks, it is recommended by the Food and Agriculture Organization of the United Nations (FAO) [31] and remains the most widely used vaccine against RVF in Africa.

The inactivated RVF vaccine provides a lower level of protection and its production is more expensive. Moreover, it requires at least two inoculations and frequent booster shots to induce the desired level of protection, rendering it inappropriate in countries where large portions of ruminant herds are nomadic. However, it was used by the Israeli veterinary services to prevent RVF introduction to Israel after the 1977-1978 epidemic in Egypt [32], as well as by the Egyptian veterinary services to prevent re-introduction of RVF from Sudan after an epidemic hit that country in 2007.

Other candidate vaccines are being evaluated such as the so-called “clone 13” which is an attenuated strain of RVFV that was isolated from a moderately ill patient in the Central African Republic [33]. This vaccine induces neutralising antibodies against RVFV. New-generation vaccines are also under study: recombinant vaccines using a poxvirus or an *Alphavirus*-based vector [34,35] and DNA vaccines [34*,36*]. However, these vaccines are still in the preliminary stages of development.

Smithburn and inactivated vaccines are produced and commercially available in Egypt, South Africa, and Kenya. There is no Community pharmaceutical legislation prohibiting companies from producing RVF vaccines on EU territory and there is no obligation to notify such production to the European Commission.

Moreover, quoting Council Directive 2001/82/EC (EC 2001b), “in the event of serious epizootic diseases, Member States may provisionally allow the use of immunological veterinary medicinal products without a marketing authorisation, in the absence of a suitable medicinal product and after informing the Commission of the detailed conditions of use (article 8)” [37*].

Insecticide treatments

Larvicide treatments may provide a control alternative where mosquito breeding sites are well identified and cover limited surface areas. Both Methoprene, a hormonal larval growth inhibitor, and *Bacillus thuringiensis israeliensis* (BTI) preparations, a microbial larvicide, are commercially available and can be used successfully to treat temporary ponds and watering places where mosquitoes proliferate. Adulticide treatments (e.g. using pyrethroids) are expensive and difficult to implement. Moreover, because this usually involves treating large areas, the environmental and ecological consequences may be important.

Other measures

Preventive measures should also include restrictions on animal movements, the avoidance or control of the slaughter and butchering of ruminants, the use of insect repellents and bed nets during outbreaks, information campaigns, and increased and targeted surveillance of animals, humans and vectors.

Current geographical distribution

RVF is either enzootic, or is reported in most sub-Saharan African countries, Egypt and Madagascar (Figure 2).

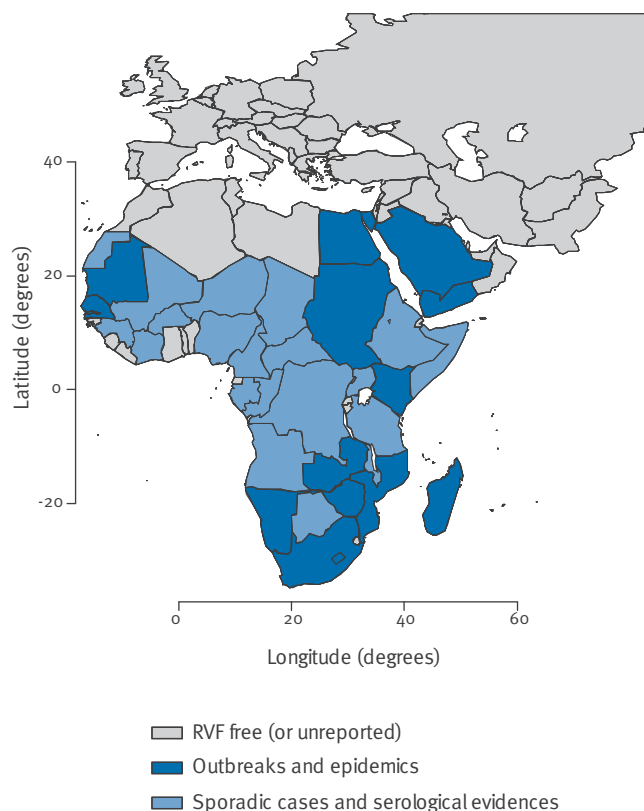
During the first large epidemic, reported in Egypt in 1977-1978, over 600 people died of RVF [39]. The epidemic reached the Mediterranean shore (Nile delta) but did not spread to neighbouring countries. In September 2000, RVF was detected for the first time outside of the African continent in Saudi Arabia and Yemen, and led to human deaths and major livestock losses [40]. By the end of 2006, the disease had re-emerged in Kenya [41], followed by Tanzania and Somalia [42]. Another large epidemic hit the Sudan in 2007 in the Nile Valley around Khartoum [4]. In May 2007, RVF was diagnosed on the French island of Mayotte in a young boy who had been evacuated from Anjouan, one of the other islands of the Comoros archipelago. The RVFV was probably introduced there by the trade of live ruminants imported from Kenya or Tanzania during the 2006-2007 epidemics. Studies conducted after this first human case was reported have shown that 10% of cattle had antibodies against RVFV (ELISA, IgG and/or IgM) - without any clinical suspicions reported by the public and private veterinary services. A retrospective study was then conducted in 2008, using blood samples collected from clinically suspected human cases of dengue or chikungunya illness who had tested negative for these two diseases, between 1 September 2007 and 31 May 2008. Ten human RVF cases were

found (including IgM- and/or RT-PCR-positive samples), seven of them (70%) occurring from January to April, during the hot, rainy season [5]. This study has

demonstrated that RVF had been circulating in Mayotte at least since early 2007, probably introduced there by the illegal importation of live infected ruminants from other Comoros islands.

FIGURE 2

Geographical distribution of Rift Valley fever



Source: United States Centers of Disease Control and Prevention [38*].

In 2008, a RVF epidemic occurred in Madagascar with over 500 human cases [43]. Several outbreaks were reported in South Africa in late 2007 and 2008 without any reported human cases [44].

Factors of change

Factors that could cause a change in the epidemiology of RVF are summarised in Table 3. Irrigated areas, including rice fields, constitute favourable breeding sites for many mosquito species. Dambos are temporary surface water bodies found in semi-arid eastern Africa. With heavy rainfall and consecutive flooding, considerable mosquito proliferation may occur (mostly *Aedes* and *Culex* spp.). Wadi are temporary rivers encountered in arid areas (e.g. Yemen or Saudi Arabia): when they stop flowing, surface water remains available in ponds and mosquitoes may proliferate.

Livestock trade and the Mediterranean region

Livestock trade and transport may affect the geographical distribution of RVF and contribute to a large scale – sometimes continental - spread of the disease and to the introduction of the virus into disease-free areas via livestock movements. RVF cases were reported in irrigated areas of the Sudan during the 1970s. Antibodies were detected in camels that crossed the border from Sudan to Egypt, suggesting that infected camels may have introduced RVFV into Egypt [39].

TABLE 3

Main outbreaks of Rift Valley fever and factors causing them

Year	Country	Ecosystem	Vector	Hosts	Triggering factor
1975	South Africa	?	?	?	?
1976	Sudan	Irrigated area	?	Small ruminants	Irrigation (?)
1977	Egypt	Irrigated area	<i>Culex pipiens</i>	Small ruminants, camels, humans	Irrigation, cattle trade
1987	Mauritania, Senegal	Irrigated area	<i>Culex pipiens</i>	Small ruminants, cattle, camels, humans	?
1993	Egypt	Irrigated area	?	Small ruminants, humans	Irrigation
1997	Egypt	Irrigated area	?	Small ruminants, humans	Irrigation
1997-1998	Kenya	Dambos	<i>Aedes</i> spp. <i>Culex zombaensis</i>	Small ruminants	Rainfall
2000	Yemen, Saudi Arabia	Wadi	<i>Aedes vexans</i> <i>Culex tritaeniorhynchus</i>	Small ruminants, cattle, camels, humans	Rainfall and virus introduction
2006-2007	Kenya, Tanzania, Somalia	Dambos	?	Small ruminants, cattle, humans	Rainfall
2007	Sudan	Irrigated area	?	Small ruminants, cattle, humans	?
2007-2008	Mayotte	Island	?	Small ruminants, cattle, humans	Virus introduction
2008	Madagascar	Rice field in highlands	<i>Culex?</i> <i>Anopheles?</i>	Small ruminants, cattle, humans	?

During the outbreak in Saudi Arabia in 2000, six viral strains of RVFV were isolated from *Aedes* mosquitoes. These strains were genetically close to the strain isolated in Kenya (1997-1998), suggesting that the virus was probably introduced into Saudi Arabia from the Horn of Africa by ruminants [45]. It remains unknown whether the virus has survived in Saudi Arabia since 2000. In any event, the risk of re-introduction from the Horn of Africa is high. During the period of religious festivals in Mecca, 10 to 15 million small ruminants are imported from there to Saudi Arabia.

A similar pattern in sheep trade is observed between sub-Saharan Africa and northern Africa. In the coming years, the Muslim feasts of *Eid-ul-Fitr* and *Eid al-Adha* will occur between September and November, i.e. when the activity of mosquito populations is high (end of the rainy season in Sahelian Africa) [46].

Therefore, the introduction of RVF-infected animals on the eastern and southern shores of the Mediterranean Sea is a likely event. Once introduced there, RVFV may find ruminant hosts, as well as competent mosquito species [47]. However, because livestock trade from northern Africa and the Middle East to Europe is forbidden, the introduction of RVF-infected animals to Europe looks unlikely [48].

Climate

Climate warming is likely to have an impact on the geographical distribution of RVF. Higher temperatures increase mosquito feeding frequency and egg production and decrease the duration of their development cycle, as well as the extrinsic incubation period of RVFV in mosquitoes. Therefore, higher temperatures associated with increased rainfall may result in higher vector densities and vector competence and, subsequently, a higher RVFV transmission rate. In addition, transovarian transmission processes could be altered.

If the virus were introduced to northern Africa or southern Europe, mosquitoes such as *Ae. vexans* could play a role as vectors in many Mediterranean countries. Several *Ochlerotatus* species, which breed in wetlands, might also be able to transmit the virus. *Culex pipiens*, a ubiquitous species, is locally abundant (in wetlands, rice fields, irrigated crops, sewers etc) and may act as an amplifier in the biological cycle. Increased temperatures could also have an impact on the vector competence and capacity of other endemic European mosquito species [49], although this is difficult to quantify (it has already been proved in controlled conditions with other arboviruses). Indeed, if introduced, several potential vector species that have so far not been investigated may become involved in the transmission of the RVFV.

In East Africa, RVFV causes major epidemics at irregular intervals of 5-15 years. Climate models for this region predict an increase in the mean annual rainfall as well as an increase in the frequency and intensity

of extreme rainfall events [50]. These changes may induce more severe and more frequent outbreaks in East Africa, which would thus represent a high risk area for neighbouring regions with livestock trade relationships such as the Indian Ocean islands.

Vectors

The flight capacities of *Aedes* and *Culex* mosquitoes are somewhat limited, ranging from a few hundred meters to more than 10 km [51,52]. However, these distances are long enough to allow a local spread of RVF.

Wind transportation of infected mosquitoes has been reported for other arboviruses [53,54]. Presently, no information is available for RVFV vectors. Passive transportation of infected mosquitoes in boats or planes travelling from Africa has been reported for *Anopheles* mosquitoes infected by *Plasmodium* parasites [55]. However, for RVFV to be introduced this way, such infected mosquitoes would need to find susceptible hosts to initiate a local cycle. This event looks unlikely.

Predictive models

Risk mapping

East Africa (Kenya)

In Kenya, a correlation has been demonstrated between heavy rainfall events and the occurrence of RVF outbreaks. Maps of remotely sensed rainfall as well as vegetation index maps have been used together with ground data to monitor and predict vector population dynamics and RVFV activity and have established a correlation between these two parameters. The main advantage of remote sensing for the prediction of RVF occurrence in East Africa is the relatively low cost. It is readily available on a country and regional basis and its use may allow preventive measures to be taken such as the vaccination of susceptible livestock and the control of mosquito larvae [56,57].

Predictive models have been improved over the past decade through the addition of Pacific and Indian Ocean surface temperature anomalies and rainfall and normalised difference vegetation index (NDVI) data. An accuracy of 95-100% was estimated for the prediction of Kenyan epizootics of RVF, with a lead time of two to five months [57]. The FAO has used the technology to warn countries facing an increased risk of RVF. However, the geographic scope of these models is limited because ecological and epidemiological processes are different in other areas of Africa [58]. The outlook for the use of these models is even worse for the Mediterranean basin and Europe where climate determinants differ significantly from those of East Africa and the potential ecological and epidemiological processes are unknown as the disease has never been reported in these areas.

West Africa (Senegal)

RVF is endemic in the Ferlo area (northern Senegal) [59]. This area is characterised by a temporary pond ecosystem. These ponds are filled at the beginning

of the rainy season (July) and dry up from October to January, according to their size and the intensity of rainfall, and are favourable environment to the development of *Aedes* mosquito populations.

However, the East African model can not be applied in West Africa: abundant rainfall is not often associated with RVF outbreaks. The epidemiological process leading to RVF epidemics looks much more complex,

TABLE 4

Competent mosquito vectors of Rift Valley fever virus with known distribution in the European Union and candidate countries

Country	<i>Aedes vexans vexans</i>	<i>Ochlerotatus caspius</i>	<i>Culex theileri</i>	<i>Culex pipiens</i>	<i>Culex perexiguus</i>
Austria	X	X	?	X	?
Belgium	X	X	?	X	?
Bulgaria	X	X	X	X	X
Croatia ¹	X	X	?	X	?
Cyprus	?	X	?	X	?
Czech Republic	X	X	?	X	?
Denmark	X	X	?	X	?
Estonia	X	X	?	X	?
Finland	X	X	?	X	?
France (mainland)	X	X	X	X	?
France (Corsica)	X	X	X	X	?
Germany	X	X	?	X	?
Greece	X	X	X	X	X
Hungary	X	X	X	X	?
Ireland	?	X	?	X	?
Italy (mainland)	X	X	X	X	X
Italy (Sardinia)	X	X	X	X	?
Italy (Sicily)	X	X	X	X	X
Latvia	X	X	?	X	?
Lithuania	X	X	?	X	?
Luxembourg	?	?	?	?	?
Former Yugoslav Republic of Macedonia ¹	X	X	X	X	X
Malta	?	X	?	X	?
The Netherlands	X	?	?	X	?
Poland	X	X	?	X	?
Portugal	X	X	X	X	X
Romania	X	X	X	X	?
Slovakia	X	X	X	X	?
Slovenia	X	X	?	X	?
Spain (mainland)	X	X	X	X	X
Spain (Balearic Islands)	X	?	?	X	?
Sweden	X	X	?	X	?
Turkey ¹	X	X	X	X	X
United Kingdom	X	X	?	X	?

X: vector present; ?: unknown to the authors, or not found yet.

¹EU candidate country.

Adapted from [1].

involving the joint dynamics of hosts movements (transhumance), host immunity, and a vector population with brief activity during the rainy season.

In this region, the risk of transmission was shown to be heterogeneous and linked to pond type [59]. A very high spatial resolution remote sensing image was used to characterise the temporary ponds and their environment and derive indices linked to mosquito biology [60]. However, this work is not advanced enough to be used in surveillance programmes.

Risk analysis for Europe

A detailed, qualitative risk analysis was performed in 2005 by The European Food Safety Authority (EFSA) [1]. The main conclusions of this study are summarised below.

Ruminant importations

The importation of infected ruminants is the greatest hazard for RVF introduction to the European Union (EU). Clinical signs may not be observed rapidly in livestock living in remote, humid areas such as the Camargue region in France or the Danube delta in Romania. Such a scenario would allow RVFV to amplify and endemic foci to develop, if suitable ecological and entomological conditions were met [1].

Official RVF-free status is required for a country to export livestock and livestock meat to the EU. Such a status depends on a country's ability – relying on observable evidences - to implement an efficient disease surveillance system and willingness to report possible RVF outbreaks. These constraints are the same as for foot-and-mouth disease and other epizootic diseases. They were instituted in 1972 (directive 72/462/CEE [61], later modified to be more stringent). The practical consequence is that any introduction of live ruminants and their products from Africa and the Middle East to the European Union is forbidden. However, illegal and unknown ruminant importations probably occur between the Middle East and central Europe, and between northern Africa and southern Europe. This is also a major component of the risk of introduction of many other important animal and zoonotic diseases, like peste des petits ruminants, foot-and-mouth disease, bluetongue disease, Crimean-Congo haemorrhagic fever, etc. For instance, a risk analysis has recently been conducted to assess the risk of introduction of peste des petits ruminants virus (a *Morbillivirus*) from Maghreb to France. The conclusion was that the risk was extremely low, ranging from 0 to 2 on a scale from 0 (impossible event) to 9 (certain event) [48].

Vectors

Several potential RVFV vectors are present in the EU (Tables 4 and 5). Differences in climate, seasonal variations of vector and host density, and genetic drift may result in differences in vector competence (the biological suitability of the vector to transmit the pathogen) and vectorial capacity (external factors such as

number and lifespan of the vector, feeding preferences of the host) compared with the situation in Africa. Nevertheless, there is almost no doubt that several of the mosquito species in the EU, e.g. *Cx. pipiens*, would be competent vectors for RVF [62]. Moreover, the introduction and spread of new vector species represents a further risk. For example, *Ae. albopictus* can transmit RVFV [62-64], and many epidemiological concerns arise from this species' current distribution in Europe: Albania, Bosnia and Herzegovina, Croatia, Italy (including Sicilia and Sardinia), south eastern continental France and Corsica, limited areas of Germany (north of the Alps), Greece, Monaco, Montenegro, the Netherlands (green houses), San Marino, Slovenia, eastern Spain, southern Switzerland, and the Vatican city [65].

Virus survival

Blood, organs, fresh meat, fetal fluids and tissues as well as hides all represent a serious hazard to at-risk occupational groups (farmers, veterinarians, slaughterhouse employees, butchers, etc). The virus persists in the liver, spleen and kidneys, but rapidly disappears from meat as the pH decreases with meat maturation. The importance of blood, bone and offal meal products as a vehicle for RVFV has not been evaluated [4]. Milk is not considered to constitute a risk. However, due to a lack of data, transmission by ingestion of milk can not be definitively ruled out.

Accidental RVF infections have been recorded in laboratory staff handling blood and tissues from infected animals.

Conclusion

Several national and Commission-supported analyses have been conducted to assess the risk of the introduction and spread of RVF within the EU. The conclusions have been that the overall risk was low. However, the recent reappearance of RVF in East Africa, including Sudan, the Nile Valley, and the Indian Ocean, has shown that the RVFV is very active and sensitive to climate and other environmental as well as socio-economic changes. These changes, together with growing human populations and an associated increased demand for meat, will promote greater controlled and uncontrolled movements of livestock. Consequently, the Mediterranean basin, central Europe, and the Middle East will probably be increasingly exposed to the risk of introduction of RVF. It is important to promote risk analyses that rely on accurate estimations of livestock movements between endemic and RVF-free areas. Moreover, high-risk ecosystems should be catalogued and the data updated on a regular basis to account for environmental changes. This latter activity has been initiated under the EU-funded Emerging Diseases in a changing European eNvironment (EDEN) project and should be continued once the project ends in 2010. Research programmes are needed to better characterise the bionomics of RVFV vectors in Europe and to develop RVFV introduction, installation, and

spread models to improve disease surveillance and provide more efficient decision-making tools.

Furthermore, more efficient vector and disease control methods are needed to enable the implementation of efficient contingency plans:

- For vector control, a systematic assessment of existing methods and tools should be undertaken (laboratory and field experiments) and research programmes developing new technologies should be supported, including options for the development of genetically modified mosquitoes designed either to reduce population sizes or to replace existing populations with vectors unable to transmit the disease.

- For disease control in European ruminants, the existing vaccines should be tested, preferably in collaboration with pharmaceutical companies. Because the cheapest and most efficacious existing vaccine (the Smithburn RVFV strain) has residual pathogenic effects in ruminants and humans, research on new-generation vaccines (e.g. recombinant, or reverse-genetic vaccines) should also be supported, both for human and animal populations.

- Because a large-scale RVF epidemic appears unlikely in Europe (where a low proportion of people have direct contact with ruminants and their body fluids), human vaccination should target the population subgroups at high risk of exposure (farmers, veterinarians, slaughterhouse employees, butchers etc), once human vaccines have been developed.

- Finally, the most relevant long term strategy is to control RVF where it is endemic. A substantial effort is needed to better understand the bio-ecology of RVFV vectors and viruses and epidemiological processes in Africa, to develop predictive and quantitative risk models and maps, and to implement risk-based surveillance and control methods.

Acknowledgements

This review was conducted in the framework of the European Centre for Disease Prevention and Control funded V-borne project "Assessment of the magnitude and impact of vector-borne diseases in Europe", tender no. OJ/2007/04/13-PROC/2007/003. It was compiled, edited and reviewed using EDEN and Arbozoonet funding, (EU grant GOCE-2003-010284 EDEN; EU grant agreement 211757). The paper is catalogued by the EDEN steering committee as EDEN0197 (<http://www.eden-fp6project.net/>). The contents of this publication are the responsibility of the authors and do not necessarily reflect the views of either the European Centre for Disease Prevention and Control or the European Commission.

* Erratum: This reference was corrected on 18 March.

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