Antiviral Research 106 (2014) 24–32

Contents lists available at ScienceDirect

Antiviral Research

journal homepage: www.elsevier.com/locate/antiviral

Review

One Health approach to Rift Valley fever vaccine development

Jeroen Kortekaas *

Department of Virology, Central Veterinary Institute, Part of Wageningen University and Research Centre, P.O. Box 65, 8200 AB Lelystad, The Netherlands

ARTICLE INFO

Article history:
Received 5 February 2014
Revised 10 March 2014
Accepted 15 March 2014
Available online 26 March 2014

Keywords:
Rift Valley fever virus
Vaccine
Veterinary
Human
One Health

ABSTRACT

Since its discovery in the 1930s, Rift Valley fever virus (RVFV) spread across the African continent and invaded the Arabian Peninsula and several islands off the coast of Southeast Africa. The virus causes recurrent outbreaks in these regions, and its continued spread is of global concern. Next-generation veterinary vaccines of improved efficacy and safety are being developed that can soon be used for the widespread vaccination of livestock. However, due to regulatory and economic challenges, vaccine manufacturers have been reluctant to develop a human vaccine. Recent innovations in veterinary vaccinology, animal models and licensing strategies can now be used to overcome these hurdles. This paper reviews the historical impact of RVFV on human health and proposes strategies to develop and license a next-generation vaccine for both animals and humans.

Contents

1. Introduction

Rift Valley fever virus (RVFV) is a zoonotic arbovirus endemic to the African continent, the Arabian Peninsula and several islands of the Indian Ocean located to the southeast of Africa. In these areas, the virus causes recurrent outbreaks among animals and humans. Domesticated ruminants, particularly sheep, are the most susceptible to disease. Infection of gestating ewes results almost exclusively in abortion and mortality ratios in newborn lambs can approach 100%. Cattle, goats and ruminant wildlife species are somewhat less susceptible, but losses among these herds can also

* Tel.: +31 320238198.
E-mail address: Jeroen.kortekaas@wur.nl

http://dx.doi.org/10.1016/j.antiviral.2014.03.008
0166-3542/

be considerable. Although most human infections are benign, the virus is feared for its ability to cause hemorrhagic fever and encephalitis. RVFV has been isolated from over 30 mosquito species of which several have a global distribution. Collectively, these features explain why RVFV is considered one of the most serious arbovirus threats to human and animal health.

Next-generation veterinary vaccines will soon be available to control future epizootics. However, due to regulatory and economic challenges, vaccine manufacturers have been reluctant to develop a human vaccine. This paper reviews the historical impact of RVFV on human health and argues to use a common approach to develop vaccines for animals and humans by making use of recent innovations in veterinary vaccinology, animal models and licensing strategies.

2. The history of Rift Valley fever in humans

The first recorded epizootic of Rift Valley fever (RVF) occurred in 1930 on a farm located near the shores of Lake Naivasha in the Rift Valley of Kenya (Daubney et al., 1931a). The outbreak was characterized by hyperacute mortality among newborn lambs and abortions (Daubney, 1931; Daubney et al., 1931a,b; Findlay, 1932; Findlay and Daubney, 1931). A potential role for mosquitoes in the transmission cycle of the causative agent was recognized by scientists investigating the outbreak, who demonstrated that animals could be protected by mosquito netting or by moving the animals to the highlands, which were free from mosquitoes (Daubney et al., 1931b). All four Europeans engaged in the investigation of the outbreak developed symptoms reminiscent of dengue fever and further inquiries made clear that native shepherds experienced similar symptoms. This first confirmed outbreak of RVF is believed to have caused 200 human cases without fatalities (Daubney et al., 1931a,b).

Apart from infections acquired in the field, the first laboratory-acquired infections were reported by Findlay (1932) and Kitchen (1934), all without serious complications. In 1934, Schwentker and Rivers reported a laboratory-acquired infection in the United States (Schwentker and Rivers, 1934). After the acute phase, the patient developed thrombophlebitis during convalescence, and died from a pulmonary embolus 45 days after the onset of illness. This was the first indication that RVFV infection in man can result in life-threatening complications.

After the apparent absence of the disease for twenty years, a serious epizootic among sheep occurred in 1951 in South Africa. After performing a necropsy on a deceased bull, three veterinarians and two assistants became acutely ill. RVFV was isolated from the blood of one of the assistants, confirming the diagnosis (Mundel and Gear, 1951). In the same year, Joubert et al. (1951) and Gear et al. (1951) reported over 50 and 13 human cases, respectively, of a similar illness affecting veterinary surgeons, farmers and native labourers. A subsequent serosurvey suggested approximately 20,000 human cases had occurred without fatalities (Schulz, 1951). During this outbreak, retinal changes and loss of vision were for the first time described in detail (Freed, 1951; Schrire, 1951).

In 1975, South Africa again experienced a serious epizootic in which thousands of lambs and hundreds of sheep and cattle died. During this epidemic, the first human fatalities directly attributable to RVFV infection were reported (McIntosh et al., 1980; van Velden et al., 1977). The clinical manifestations of RVFV infections in 17 patients admitted to hospitals in Bloemfontein were reported by Van Velden et al. (van Velden et al., 1977). The onset of disease was generally sudden and involved chills, painful eyes, headache, backache, limb pains and tender muscles. Neurological complications were noted in 12 patients, which included meningeal irritation, confusion, coma, hypersalivation with teeth grinding, visual hallucinations, lock-in syndrome and rapid involuntary jerky movements. Two patients developed encephalitis which was fatal in both cases. Three fatal cases of hemorrhagic fever were reported, with symptoms including epistaxis, hematemesis, melena and hematuria (van Velden et al., 1977). McIntosh et al. reported 110 laboratory-confirmed cases and 7 fatal cases (McIntosh et al., 1980).

In 1977, a human RVFV epidemic occurred in Egypt, which is believed to represent the largest epidemic to date (Hoogstraal et al., 1979; Meegan, 1979; Meegan et al., 1979). The outbreak followed the completion of the Aswan dam, which was built to regulate the irrigation of the Nile delta and significantly increased the number of mosquito breeding sites. The Egyptian government reported 18,000 cases with 598 deaths, although others suggested that the number of clinical cases could have exceeded 200,000 (Meegan, 1979). A feature that may have contributed to the large number of human cases that occurred during the Egyptian outbreak was the involvement of mosquitoes from the *Culex* (*Cx.*) *pipiens* complex, which were not associated with RVFV epidemics before that time (Hoogstraal et al., 1979).

As in other RVFV outbreaks, the slaughtering of diseased animals is also believed to have played a major role in transmission of the virus to humans. In Egypt, sick animals are customarily slaughtered for consumption and this custom is intensified during epizootics. The efficient transmission of RVFV via this route was exemplified by Hoogstraal et al., who reported illness in all 8 persons who attended the slaughtering of a diseased sheep, of which 6 did not have physical contact with the animal (Hoogstraal et al., 1979). It is furthermore worthwhile to note that the large number of severe human cases that occurred during the Egyptian outbreak may be explained by a high incidence of schistosomiasis, a disease caused by parasites that target the liver (Meegan, 1979).

In 1986, the completion of the Diama dam resulted in the permanent presence of fresh stagnant water in the Senegal river basin and a dramatic increase in mosquito numbers. The year after, Mauritania experienced a serious outbreak of RVF resulting in an estimated 224 fatal human cases (Jouan et al., 1988). The virus re-emerged in this area and caused human fatalities in 1998, 2010 and 2012 (Nabeth et al., 2001; El Mamy et al., 2011; WHO, 2012).

The largest RVFV outbreak of Sub-Saharan Africa occurred in 1997–1998 in Kenya. In the Garissa district only, 171 fatalities were reported among an estimated 27,500 infected humans (Woods et al., 2002). The total number of human cases in Kenya and south Somalia was estimated at 89,000 with more than 400 being fatal (CDC, 1998). The outbreak spread to the south into Tanzania (Woods et al., 2002), resulting in an estimated 40,000 human cases (Anyamba et al., 2010). Mohamed et al., reported 511 suspected cases and a fatality ratio among 144 confirmed severe cases of 28.2% (Mohamed et al., 2010). The massive expansion of RVFV in these areas is believed to have resulted in the spread of the virus to the Arabian Peninsula.

In the fall of 2000, an outbreak occurred in the southern coastal provinces Asir and Jizan of the Kingdom of Saudi Arabia (CDC, 2000a,c) and another occurred in the El Zuhrah district of the Hodeidah governorate in Yemen (CDC, 2000b; WHO, 2000). An estimated 2000 people developed complications varying from ocular impediments to hemorrhagic fever and encephalitis. At least 245 people did not survive the infection, suggesting a case fatality ratio (CFR) among severe cases of 12% (Al-Hazmi et al., 2003; Madani et al., 2003). It was reported that most patients resided in or visited the floodplains of seasonal riverbeds, which contributed to the conclusion that the majority of human cases in this outbreak resulted from mosquito bites (Madani et al., 2003). Entomological studies demonstrated that two mosquito species were abundant in the outbreak areas, *Cx. tritaeniorhynchus* and