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Emergence of *Wesselsbron* virus among black rat and humans in Eastern Senegal in 2013

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ABSTRACT

Wesselsbron disease is a neglected mosquito transmitted *Flavivirus* infection that causes abortions and has teratogenic effects on sheep and cattle in Africa. Human can also be infected. The detection of human or animal cases is complicated by the non-specific symptoms close to Rift Valley Fever (RVF) in domestic livestock species or Dengue like syndrome in humans. Then, these detections are usually made during RVF investigations in sheep. These domestic animals should take a role in the life cycle of the virus but some evidences of *Wesselsbron* virus (WSLV) presence in wild animals suggest that the latter may be involved in the virus maintenance in nature. However, the reservoir status of wild vertebrate in general and rodents particularly for WSLV is only based on an isolation from a Cape short-eared gerbil in southern Africa. Most of WSLV isolations are from southern parts of Africa even if it has been found in western and central Africa or Madagascar. In Senegal, there are serological evidences of WSLV circulation in human since the 1970s and some isolations, the last one of which dates back in 1992. Despite the detection of the virus on mosquitoes until the 2000s in different parts of the country, no new human case has been noted. In this paper, we report the WSLV re-emergence in eastern Senegal in 2013 with 2 human cases and its first isolation from a black rat *Rattus rattus*. Sequencing analyses show the circulation of the same strain between these humans and the commensal rodent. The putative impact on WSLV transmission to human populations could be more important if the reservoir status of the black rat is confirmed. Focused survey in human populations, specific entomological and mammalogical investigations would permit a better understanding of the life cycle of the virus and its impact on public health.

1. Introduction

Wesselsbron disease (WSL) is a mosquito borne infection of sheep and cattle in Africa which can also infect human in whom fever and myalgia are the most common symptoms. It is caused by *Wesselsbron* virus (WSLV) which belongs to the *Flavivirus* genus. WSLV was first isolated in blood of a febrile man and dead lamb during an outbreak in 1955 in Wesselsbron in the Free State Province, South Africa [17,34].

The disease in sheep is clinically similar to Rift Valley fever (RVF) with abortions and 20% mortality in pregnant ewes. Hydrops amnii and teratogenic effects such as arthrogryposis, hydrocephaly or neurogenic muscular atrophy are also observed in lambs [4] whereas infection causes less severe fever in goat, cattle, and pig [5]. WSL has been described as a cause of neurological disease in two horses of South Africa (Venter et al., 2008) [38]. WSL outbreaks can be unnoticed as they are often concomitant with RVF epidemics in South Africa [35] and its incidence can be underestimated. In humans, the infection causes arthralgia, myalgia and fever during a short and mild acute phase [33].

WSLV has a wide geographic distribution in Africa [34] and viral isolations from mosquitoes have been reported in South Africa, Botswana, Zimbabwe, Uganda, Mozambique, Uganda, Cameroon, Central African Republic, Mauritania, Senegal, Nigeria, DR Congo and Madagascar [36]. *Aedes* mosquitoes are generally associated with virus detection [18].

WSLV was also isolated from several domestic livestock species including camels, cattle, pigs, donkeys and horses, and serological evidence of its circulation was found in wild animals including South African zebras [2] and wild ruminants from Chad [2,34] which raised the question of its reservoir. The reservoir status of wild vertebrate for

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WSLV is also suspected since an isolation from Cape short-eared gerbil *Desmodillus auricularis* in southern Africa (Kokernot et al., 1960) [39].

Between 1955 and 2011, 35 WSLV isolates were obtained from humans, mostly from Central African Republic (CAR) and South Africa [34,37], Jupp and Kemp, 1998 [40], [13,39]. In western Africa, most human isolates are from Senegal (4 strains in 1965, 1974, 1982 and 1992).

In Senegal, WSLV was serologically detected in most of the children from Upper Casamance and Eastern Senegal between 1972 and 1975 [29]. Swanepoel [34] reports a laboratory-acquired infection in 1965 and another one in 1974. A human infected isolation was also obtained in 1992 in the capital city Dakar (Annual report of Institut Pasteur de Dakar (IPD), 1992) after a previous one 10 years before.

Even if Monlun et al. [26] found that WSLV did not seem to represent a major public health concern in southeastern Senegal, entomological investigations between 1998 and 1999 in some parts of Senegal and Mauritania, spanning the Senegal River basin permitted to detect 51 WSLV strains from *Aedes vexans* [11]. Already, >40 strains were found from 1974 to 1999 in Kedougou, Barkedji and Yonofere, a village in Saint Louis region (Annual report of IPD, 1999).

Moreover, recent emergences of viruses within populations initially naive showed the necessity of anticipation of risk factors. In this purpose, in the Kedougou region (southeastern Senegal), a surveillance of arboviruses has been undertaken on mosquitoes and human populations.

In this paper, we report on the re-emergence WSLV in Eastern Senegal in 2013 with 2 human cases and its first isolation from the rodent *Rattus rattus* (the black rat).

2. Material and methods

2.1. Study sites

In the Kedougou region (Fig. 1), a surveillance of acute febrile illness (AFI) on human populations has been led since 2009 [31]. Patients presenting AFI were recruited from seven healthcare facilities of the Kedougou region, including Ninefesha rural hospital, Kedougou and Saraya health centres, Bandafassi and Khossanto health posts, the Kedougou military health post, and the Catholic Mission mobile team, which targets populations in remote areas.

2.2. Samples collection

Samples were collected from human presenting acute febrile illnesses and from rodent trapped in Kedougou. Serum or blood specimens of patients with AFI, as well as brain, serum and blood collected from rodents, are then submitted to the Arboviruses and Hemorrhagic Fever viruses Unit of IPD for a diagnostic of arboviruses.

Trapping sessions targeting rodents and shrews have been undertaken in a number of localities of Eastern Senegal to study the putative circulation of arboviruses in these small mammal populations. Briefly, traps (wire-mesh locally made and folding aluminium Sherman© traps) were set inside buildings for trapping sessions of one to six consecutive days with peanut butter as bait [6]. One of each type of traps was set per room and inspected for captures each morning. Each trapped specimen was identified to the species level based on morphological or geographical knowledge [14,16] or, in case of ambiguity, by further molecular or chromosomal analyses (see details in [12,15,21]). Trapped individuals were euthanatized by cervical dislocation as recommended by Mills et al. [25]. The brain, the tissues and the serum of each individual were separated and put in dry ice for transportation to IPD. Permission to work within the different villages was obtained from appropriate authorities, and animals were correctly treated following Sikes et al. [32].

2.3. Viral isolation and identification

Each sample was inoculated into 2- to 3-days-old suckling mice for isolation of live virus (Shope and Sather, 1979) [41] according to a protocol approved by the National Health Laboratory Service Animal Ethics Committee (reference number, 107/06).

Suckling mice derived viruses were identified by reverse transcription PCR targeting a segment at the partial NS5 gene using the generic

Fig. 1. Map of Kedougou region with the different localities of origin of the different isolates of this study.