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Assessing the zoonotic potential of arboviruses of African origin

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Several African arboviruses have emerged over the past decade in new regions where they caused major outbreaks in humans and/or animals including West Nile virus, Chikungunya virus and Zika virus. This raise questions regarding the importance of less known zoonotic arboviruses in local epidemics in Africa and their potential to emerge internationally. Syndromic surveillance in animals may serve as an early warning system to detect zoonotic arbovirus outbreaks. Rift Valley fever and Wesselsbronvirus are for example associated with abortion storms in livestock while West Nile-virus, Shuni virus and Middelburg virus causes neurological disease outbreaks in horses and other animals. Death in birds may signal Bagaza virus and Usutu virus outbreaks. This short review summarise data on less known arboviruses with zoonotic potential in Africa.

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Introduction

African arboviruses in the families *Flaviviridae* (West Nile Virus (WNV); Zika virus; Yellow Fever (YFV); Usutu virus); *Togaviridae* (Chikungunya virus) and *bunyaviridae* (Rift Valley fever (RVF) and Crimean Congo Haemorrhagic Fever (CCHF) were some of the major emerging and re-emerging zoonotic pathogens of the last decade [1,2]. These viruses were largely unnoticed as diseases in Africa before they emerged internationally. Arboviruses often circulate between mosquito vectors and vertebrate hosts and spill over to sensitive species during climatic events where they may cause severe disease. One Health surveillance for syndromes associated with arboviruses in animals; screening of mosquito vectors and surveillance for human disease may help to identify less known zoonotic arboviruses and determine their potential to emerge internationally (Figure 1). This lead to identification of Shuni virus [3•,4•], Middelburgvirus [5•], Usutu [6] and Bagaza virus [7] in Africa and Europe raising questions on the potential of further zoonotic pathogens to emerge internationally.

The purpose of this review is to summarise data on arboviruses with zoonotic potential detected in humans, animals and vectors in Africa.

Arboviruses and their ecology

Zoonotic arboviruses mainly belong to the genera *Alphavirus*, family *Togaviridae*; *flavivirus* (*Flaviviridae*) and *Bunyavirus Nairovirus* and *Phlebovirus* genus (*Bunyaviridae)*. A few zoonotic viruses belong to the *orbivirus genus* (family *Reoviridae*); the *Rhabdoviridae* and *thogotovirus* genus (family *Orthomyxoviridae*) however these are mainly animal pathogens [1]. Arboviruses mostly cause mild febrile disease but may progress to encephalitic, haemorrhagic fever signs, birth defects and death in humans and animals [2]. Arboviruses utilise animal hosts for amplification and arthropod vectors, including mosquitoes, *Culicoides* biting midges, sandflies and ticks for transmission and occasionally spill over into humans or domestic animals where they may cause disease. Their ecology is complex with several reservoir, amplification hosts and bridging vectors contributing to the amplification of virus and potential spill-over into humans and sensitive animals (Figure 2).

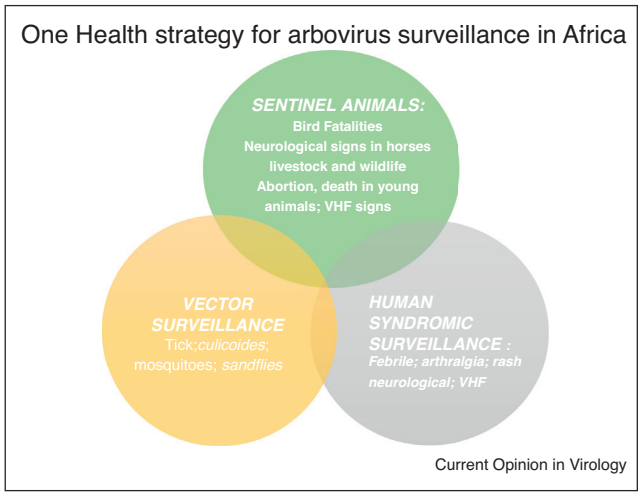
The vector epidemiology in combination with the availability of animal reservoirs and favourable environmental conditions determines the capacity to cause outbreaks, infect different species and emerge internationally [1,8].

Zoonotic arboviruses in Africa

Many arboviruses were identified between 1930s and 1970 by the Rockefeller foundation in Africa in arthropod vectors, animals and humans. Subsequent virus isolations from individual human and animal cases or larger outbreaks defined zoonotic associations [9–11,12•] although burden of disease data is still lacking for many.

Table 1 summarises the African arboviruses with known zoonotic links from natural human infections in Africa, as collected in the International Catalogue of Arboviruses [13•] and reviews [14,15,16•,17]. The most important zoonotic viruses are summarised below. Yellow Fever

Figure 1



One Health Surveillance for arboviruses in Africa. Disease outbreaks in animals may act as an early warning system for arbovirus epidemics. RVF and WSLV are both associated with abortion and haemorrhagic manifestations in livestock [46•,50], while neurological infections in horses and other species may signal WNV outbreaks [51,52]. Bird die-offs may indicate WNV [53] or Usutu infections [54] however, endemic birds appear to have genetic resistance to WNV [55]. Passive surveillance for neurological disease in horses and other animals in South Africa over 8 years facilitated the description of the epidemiology of WNV lineage 2 [26•] and several other neurotropic arboviruses with zoonotic potential including Shuni virus (SHUV) [3•], Middelburgvirus, Sindbisvirus [5•], and Wesselsbronvirus (unpublished). These viruses were also detected in several wildlife species with neurological signs. Investigation of serological evidence in humans and syndromic surveillance for febrile disease, arthralgia and neurological signs identified arboviruses in unsolved meningo-encephalitis cases [27•]. Collection and screening of arthropod vectors in areas where clinical cases are detected may help to describe the epidemiology of these pathogens.

[18] and Dengue [19] are well described and mainly human pathogens so not covered in this short review.

Flaviviruses

The *Flaviviruses* are transmitted by mosquitoes and ticks. WNV and Wesselsbronvirus are the best described in Africa.

WNV, first isolated in 1937 in Uganda, spread across Africa the Western hemisphere, Europe and Asia to become one of the most important emerging vectorborne pathogens globally [20–22]. WNV circulates between ornithophilic mosquitoes, in particular *Culex univittatus* and *C. pipiens* and birds from where it may spill over into humans, horses and other sensitive animals [23] (Figure 1). Two major lineages, 1 and 2 and several minor lineage are recognised with lineage 1 occurring mainly in Central to North Africa and the Western hemisphere, while lineage 2 is endemic in Southern Africa and Madagascar and now in Central Europe [24]. Surveillance for neurological disease in horses and other animals in South Africa suggest horses are highly sensitive to WNV lineage 2. Neurological infections with fatality rates of 30% occur annually in late summer and autumn in horses [25•,26•]. Human cases also occur every year with large epidemics reporting in 1974 and 1981. Severe disease may be missed with ~3% of unsolved meningoencephalitis cases in hospitals in Pretoria identified as WNV [27•]. Detection of WNV lineage 1 in ticks collected from wildlife in Kenya suggests a potential mechanism for spread of the virus through attachment to migratory birds [28]. The burden of disease due to WNV in humans and animals across Africa is likely underappreciated.

Wesselsbronvirus (WSLV) is associated with high mortalities in newborn lambs and kids, congenital malformation of the central nervous systems of the ovine foetus and *hydrops amnii* and abortion in ewes. Human cases are rare and mainly associated with non-fatal influenza-like illness [23]. A case of encephalitis was reported in an entomologist investigating an outbreak in South Africa [29]. The reservoir host is not known but recently isolations were made from black rats in Senegal [30•]. The virus is thought to be transmitted by *Aedes caballus juppi* mosquitoes and is a differential diagnosis for Rift Valley fever [29]. WSLV antibodies have been detected throughout Africa although cases remain rare. Human cases of febrile disease were identified during a RVF outbreak in South Africa in 2011 [31].

Other Flaviviruses

Zikavirus has mainly been associated with mild infections in Africa since its discovery in Uganda in 1947. Primates are considered to be the natural host. The African lineage is postulated to cause less severe disease than the Asian strain that emerged in the Americas, since neurological infections and microcephaly have not been reported in Africa [32•]. Recent serological and mosquito investigations demonstrated 6% seroprevalence in Senegal and Nigeria [33•] and identified Zikavirus in 5/4313 febrile cases in Gabon as well as 2/137 *Aedes albopictus* pools [34]. The Asian strain has only been reported in travellers in a few countries following its international emergence but did not establish locally (http://www.healthmap.org/zika/#timeline).

Bagaza virus was isolated in 1966 from mosquitoes in Bagaza, Central African Republic but also in domestic turkeys in South Africa in 1980 [35]. Emergence in birds in Europe [7] and serological evidence in encephalitis patients in India [36] raise questions on its disease association in Africa. Recent isolation from exotic European pheasants with neurological signs in 2016 and 2017 in South Africa suggests local circulation and that Bagaza virus should be considered in febrile cases in humans (unpublished data, Venter M).