

West Nile virus in Algeria: a comprehensive overview

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Abstract

West Nile virus (WNV) is a mosquito-borne virus belonging to the genus *Flavivirus*, related to the Japanese encephalitis antigenic complex of *Flaviviridae* family. It is transmitted by the bite of infected mosquitoes. The virus is maintained in a mosquito–bird–mosquito transmission cycle. WNV has recently dramatically expanded its geographical range and is now considered the most widespread arbovirus in the world, including the Americas, Europe and countries facing the Mediterranean Basin. In Algeria, West Nile disease (WND) infections with human meningoencephalitis cases have been reported in 1994 in Tinerkouk (southwest Sahara). In autumn 2012, one fatal clinical case of WNV neuroinvasive infection was reported in Jijel (coastal east). During the same year, a retrospective serosurvey performed in Algiers and bordering areas highlighted specific anti-WNV IgG in local population. Between 2013 and 2014 two clinical cases were reported, in Timimoune (south) and Guelma (northeast) respectively. Although no case was reported in equids, serosurveys demonstrated its presence: an animal serosurvey was conducted in Djanet (south) in 1975, and in 2014 a seroprevalence of equids in the northeast part of Algeria highlighted a virus circulation. This review aims to evaluate the global epidemiologic situation of West Nile disease in Algeria, with an updated situation based on human cases, equine reports and entomologic investigations. Our study reinforces the need for building the capacity for surveillance in this region to prevent future emergence of WNV and other arboviruses.

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Introduction

West Nile virus (WNV) is a *Flavivirus* transmitted in natural cycles between wild birds and mosquitoes, especially *Culex* species [1]. This virus belongs to the members of the Japanese encephalitis serogroup complex [2]. It is distributed around the world in the Americas, Africa, Europe and Asia. It is naturally maintained in the field by an epidemiologic cycle involving transmission between essentially wild birds and mosquitoes. Otherwise, virus transmission exploits biotic interactions to

persist in a particular area related to environmental conditions. These interactions are strongly influenced by numerous ecologic and environmental factors that may confer unique ecosystem characteristics to the virus cycle associated with the presence of wetlands and the constant appearance of rainfall and flooding, along with abundance of avifauna and mosquitoes [3]. Wild and migratory birds species are mainly involved in its long-distance transmission and spread [4].

Horses, like humans, are epidemiologically considered to be dead-end hosts: they do not have the ability to spread the virus after infection. Disease in horses is manifested by fever, weakness, locomotor dysfunction, ataxia and blindness. In the most severe cases, paraplegia occurs, evolving in 5 to 10 days to death. Viraemia in horses is estimated to be low and does not allow the infection of mosquitoes after a blood meal [5].

In humans, West Nile disease (WND) is represented by an asymptomatic or mild febrile illness in 80% of WNV infections,

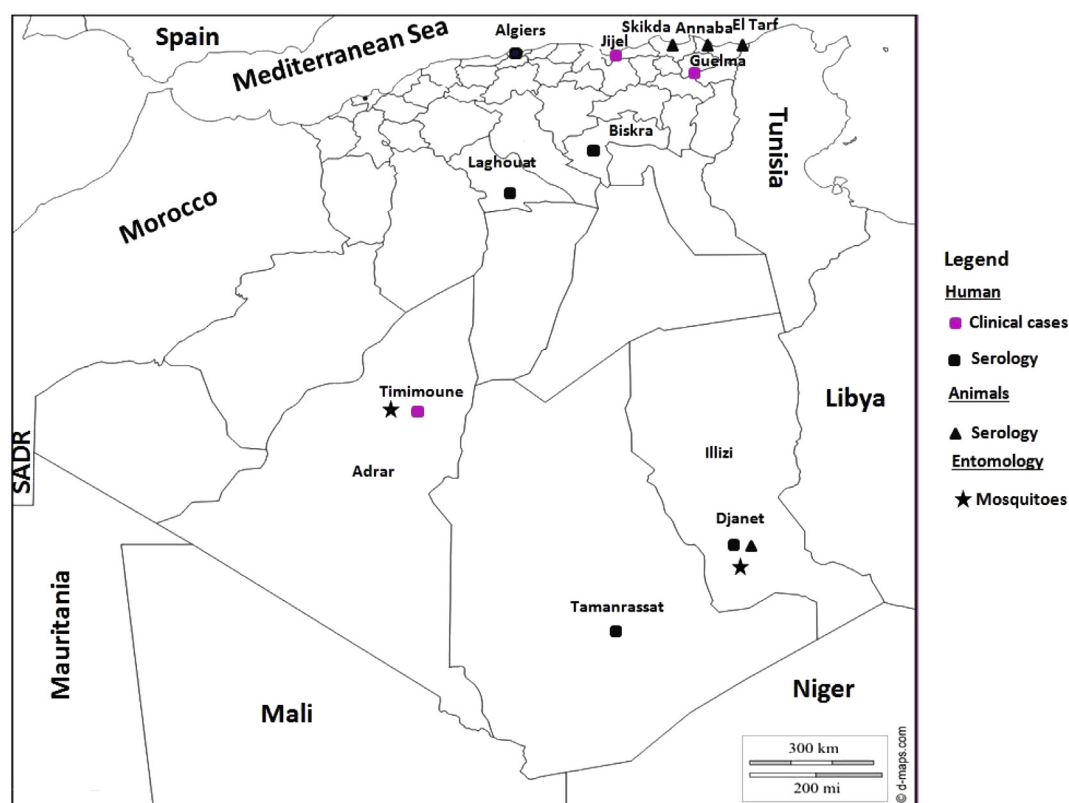


FIG. 1. West Nile virus in Algeria reflecting current known evidence, August 2018.

but approximately 20% of those infected may develop symptoms of WNV disease. West Nile fever (WNF) presents as a minor influenza-like illness along with some clinical signs (e.g. fever, headache, malaise, lymphadenopathy, myalgia, fatigue, skin rash, diarrhea and vomiting), only to develop later into meningoencephalitis episodes or flaccid paralysis (a polioliike syndrome) and, less frequently [6], death. Hepatitis, pancreatitis and myocarditis have also infrequently been described to occur [7].

WNV transmission has been confirmed during the last years in the Mediterranean Basin as a result of the virus's repeated introduction by infected migratory birds and/or to endemic circulation within sedentary bird populations [8]. Many outbreaks causing severe human encephalitis were observed during the mid-1990s in Maghreb, including Algeria in 1994 (50 cases, eight fatalities) and Tunisia in 1997 (111 cases, eight fatalities) [9]. Animal WNF evidence has been described in Morocco, with horse encephalitis outbreaks in 1996 [10], 2003 [11] and 2010 [12]; and in seroprevalence studies conducted in Tunisia and Algeria [13,14]. WND infection has been reported in Algeria, and serologic evidence has been found in humans and animals, although some epidemics in humans without any clinical cases in horses have been reported [14].

In this review, we highlight the current situation of WND in Algeria. The information gathered in this review was obtained via online literature searches using the PubMed and Google search engines, as well as personal research of data. A comprehensive literature search using the terms 'West Nile virus' and 'Algeria' was conducted (Fig. 1, Table 1).

Virus isolation and detection

WNV was first isolated in Algeria in 1968 as part of an investigation of sickness outbreaks in African horses that occurred in the oasis of Djanet (south) from a pool of 215 mosquitoes of the *Culex* genus. Virus identification was carried out at the Pasteur Institute of Dakar [15]. The virus (WNV lineage I) was also detected in a mosquito pool of *Culex perexiguus* collected from the oasis of Aougrou in Timimoune (south) [16] (Fig. 1). In North Africa, the WNV strain isolated in Morocco belong to WNV lineage I, clade Ia [17]. This strain is similar to mosquitoes of WNV Senegal/93 strain and equids of France/2000 strain [11]. WNV isolated in Tunisia also belonged to lineage I, but it was very close to the virulent strains isolated in Israel in 1998 and in New York in 1999 [18].

TABLE 1. Report of West Nile disease surveillance in humans and animals in Algeria, current known evidence, August 2018

Species	Year	Study	Area	Tested	Results
Human	1965	Bouguermouh 1980 [20]	Algiers, Laghouat	281	p = 0
	1973	Bouguermouh 1980 [20]	Djanet (Illizi)	171	14.6%
	1975	Bouguermouh 1980 [20]	Illizi, Tamanrassat	48, 143	58.3%, 3.5%
	1976	Bouguermouh 1980 [20]	Ouled Djellal (Biskra)	24	3.5%
	1994	Le Guenno 1996 [21] ^a	Timimoune (Adrar)	18	83.3%
	2012	Leparc-Goffart 2012 (personal communication) ^a	Jijel	1	100%
	2012	A. Hachid et al., 'First serological evidence of human circulation of West Nile virus in central-north Algeria,' poster presented at the 23rd European Congress of Clinical Microbiology and Infectious Diseases, Berlin, Germany, 2013	Algiers	164	6.7%
	2013	Unpublished data ^a	Timimoune (Adrar)	1	100%
	2014	Unpublished data ^a	Guelma	1	100%
	2014	Lafri 2017 [14]	Skikda, Annaba, El Tarf	293	17.4%
Rodents	1975	Bouguermouh 1980 [20]	Djanet (Illizi)	19	0
Birds	1975	Bouguermouh 1980 [20]	Djanet (Illizi)	188	0
Equids	1975	Bouguermouh 1980 [20]	Djanet (Illizi)	52	9.6%
	2014	Lafri 2017 [14]	Skikda, Annaba, El Tarf	293	17.4%

^aMeningoencephalitis cases.

WND in humans

Arboviruses do not seem to be an important problem for the health services of Algeria. The investigations carried out were therefore fragmentary and limited to specific regions. The clinical picture of the disease caused by WNV seems to be differentiated by the local population and is called *loumet* [19], which signifies measles as well as all febrile states. The first report of this disease occurred in 1965; 92 serum samples from adults and 175 serum samples from children collected from Algiers and Laghouat respectively were found to be negative against arboviruses antigens [20]. In 1973 a total of 171 human serum samples were collected in Djanet, with 25 positive samples against WNV [20]. In 1975, among 143 serum samples collected in the Illizi and Tamanrasset oases respectively, only five serum samples were found to be positive against WNV [20].

The first confirmed clinical cases were reported in 1994 in an outbreak that occurred in the Tinerkouk oasis (Table 1) [9]. In total, 50 notifiable suspect cases and eight deaths were declared [21]. The patients presented with high fever associated with neurologic signs reported as WND symptoms; some patients were comatose. Among 18 serum samples collected, 83.3% were positive. However, the virus could not be isolated. In autumn 2012, a fatal human case of WNV neuroinvasive infection occurred in Jijel (northeast coast) [22]. During the same year, a retrospective epidemiologic serosurvey in Algiers and bordering localities reported IgG against WNV in 11 of 164 serums tested (A. Hachid et al., 'First serological evidence of human circulation of WNV in central-north Algeria,' poster presented at the 23rd European Congress of Clinical Microbiology and Infectious Diseases, Berlin, Germany, 2013). Between 2013 and 2014, two clinical cases were described in Timimoune and Guelma respectively [16] (Table 1).

WND in animals

In Algeria no clinical cases in animals were documented [14]. Because many reports have suggested that several species of

wild mammals are commonly exposed to WNV, occasionally with associated high seroprevalence rates, some studies concerning small animals were carried out. However, few serosurveys demonstrated WNV circulation and appearance (Table 1). In 1975 several animals were analysed for the presence of WNV in Djanet, including 188 birds, 19 rodents and 52 donkeys. The isolation of WNV from the blood clot and brain of rodents was negative. A total of 131 serum samples of birds studied serologically were also negative. Among serum samples collected from 52 donkeys, only five were found to be positive, with a nonspecific serology to WNV [20–23] (A. Hachid et al., 'First serological evidence'). In 2014 a serologic investigation against WNV was conducted in the northeastern part of Algeria (Skikda, Annaba, El Tarf). Serum samples were collected from 293 healthy and unvaccinated equids. Each sample was systematically tested for IgG against WNV by using an in-house enzyme-linked immunosorbent assay with precipitated and inactivated WNV as an antigen. Serum samples were considered to be positive if the ratio of the optical density at 450 nm of the sample on WNV antigen and on the negative antigen was over 3. Owing to antigenic cross-reactivity among flaviviruses, all positive samples were confirmed as truly positive by both Western blot test and seroneutralization of WNV [14]. Anti-WNV antibodies were detected in 19 horses (seroprevalence 26.8%) and 32 donkeys (seroprevalence 14.4%) for a total seroprevalence of 17.4%. Seroconversion was reported in two horses from El Tarf (El Kala wetland), which confirms the existence of an active WNV circulation in 2014 in Algeria [14] (Table 1).

Discussion

The spectacular panzootic of WNV in the Americas has drawn attention to this arboviral disease, and it has frequently been suggested that it is also an emerging pathogen worldwide. The

emergence of WNV is difficult to predict and even more difficult to prevent. Data collected on the WND in North Africa on clinical cases of meningoencephalitis due to WND in humans and horses suggest that WNV is endemic in the North African countries [24]. In 2014 a single confirmed human clinical case was reported in Guelma from the northeast of Algeria [16]. Otherwise, Guelma is situated 134 km from El Kala, where Lafri et al. [14] detected a circulation of WNV in the same year by seroconversion in two horses. Equine WND cases and evidence were also reported in these countries: nine cases were reported in Morocco in horses, with disease caused by lineage I in 2003 [11], and a WNV seroprevalence of 42.3% was reported in Tunisian equids [25]. In 2014 Lafri et al. [14] described the first seroprevalence against WNV equid antibodies, as previously described. Only equid outbreaks of WND have been reported in Morocco [26]. However, in Algeria and Tunisia, it is exactly the opposite situation: human meningoencephalitis epidemics with deaths have been reported without any clinical cases in animals [27]. We could explain this situation by the fact that the virus's strains circulating in North Africa may have different modalities in sensitivity and clinical expression of disease [14].

It is necessary to implement a passive comprehensive WNF surveillance system in Algeria, including advanced laboratory diagnoses for virus isolation and fine characterization related to the national reference centre of arboviruses at the Pasteur Institute of Algiers [14]. Once the genetic background of virus is identified, commercial vaccines against WNV will be available and can be used to vaccinate valuable animals [28]. Because many reports have suggested that several species of wild mammals are commonly exposed to WNV, occasionally with high associated seroprevalence rates, no studies concerning small animals were carried out in the region. Serologic surveys should be completed including entomologic aspects in order to better understand the epidemiologic WNV cycle.

The relation between the human case report and animal detection of WNV in Algeria indicates that the presence of WNV may have a cross link between migratory birds and the abundance of mosquitoes in this wetland region [29] (Fig. 1, Table 1). Elsewhere, the role of migratory birds in relation to the introduction of WNV in the Mediterranean Basin and Europe was clearly demonstrated [30], although monitoring areas of serologic evidence of the virus and clinical cases reported are represented by Sahara oases and coastal plains [14]. The existence of wetlands is favorable to the concentration and confluence of different migratory bird species around water points; this increases contact between WNV vectors and the wild birds that are considered its natural hosts, thus putting humans and horses at the greatest risk of acquiring this disease, resulting in a public health threat [14].

Algeria has favorable conditions for maintaining the WNV transmission cycle, which was proved by a virus circulation in 2014 detected in horses from El Kala [14]. WNV evidence and modalities of circulation are different in the Maghreb countries. Data about the link between vectors and WNV indicate that the experimental demonstration of *Culex pipiens* originated from Maghreb countries as an efficient vector of WNV in the region [14,31]. There is molecular evidence of *Culex pipiens* complex forms and consequences in WNV transmission [32] as well as an inventory of mosquitoes in some regions of Algeria [33] and the recent detection of WNV lineage I *Culex perexiguus* collected from the oasis of Aougrout in Timimoune (south) [16]. Moreover, mosquito distribution and population dynamics would be useful for this purpose [14]. Otherwise, bird mortality must be reported, and a passive seroprevalence programme of peridomestic and wild bird species [34] should be implemented and maintained in areas at risk for WNV circulation. In addition, the adoption of sentinel chicken serosurveys may detect transmission of WNV in Mediterranean countries [35,36], proving promising results. This epidemiologic WNV survey should be implemented in the exposed areas of WNV circulation as previously described and as represented by the coastal wetlands and Sahara oases [14].

Conclusion

WNV remains endemic in Algeria and the surrounding Mediterranean areas. Virus circulation becomes permanent and is probably maintained by insect vector movements and reintroduction of migratory birds. WNV circulation needs further monitoring programmes, including a permanent serosurvey of resident and migratory birds species involved in the reintroduction of this arboviral threat. Therefore, the entomologic identification of mosquitoes species through risk areas determine the role of other vectors in the dissemination and maintenance of WNV such as argasid ticks. Wetlands and surrounding areas should be rigorously assessed by a passive monitoring programme. The control of some anthropogenic and environmental factors could help prevent extension and reemergence of WNV epidemics. Regional and International collaborations would certainly upgrade the knowledge of WNV dynamic circulation and demonstrate unknown aspects of this arboviral disease. Finally, understanding WND epidemiology will certainly contribute to prevent the reoccurrence and spread of the infection among humans and animals in Algeria and the Mediterranean region.

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Conflict of Interest

None declared.

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