Rev. Inst. Med. Trop. Sao Paulo
57(3):276, May-June, 2015
http://dx.doi.org/10.1590/S0036-46652015000300017

LETTER TO THE EDITOR

WEST NILE FEVER IN BRAZIL: SPORADIC CASE, SILENT ENDEMIC DISEASE OR EPIDEMIC IN ITS INITIAL STAGES?

May 21, 2015

Dear Editor

During the initial reports in some countries of Africa and Asia and until the 1990s, West Nile fever (WNF) was only considered a "minor" public health problem. The disease gained awareness after outbreaks occurred in Israel, Australia and European countries and, in particular, due to the large number of people and animals affected in the United States of America between the end of the 1990s and the beginning of the new century. Thereafter, signs of West Nile virus (WNV) circulation were detected in the Cayman Islands, El Salvador, Guatemala, Belize, Colombia, Venezuela, and Argentina. However, viral isolation was rarely achieved, and records of human, equine and avian morbidity in Latin America are lacking. Moreover, for unclear reasons, there was no correspondence between the expansion of the geographic range of viral circulation and the occurrence of significant animal or human morbidity by WNF in these regions[7]. Given the evidence of WNV circulation in South American countries beginning in 2003, the Brazilian Ministry of Health adopted the reporting of suspected human cases of WNF[7]. In parallel with the implementation of surveillance strategies for monitoring the introduction of the virus into the country, Brazilian researchers posed the question: "*West Nile Encephalitis: our next epidemic?"*[3]. Between 2002 and 2013, serological evidence of viral circulation was found in horses and birds in the Amazon and Pantanal regions[4,6,8]. Serological surveys conducted in the states of Rio Grande do Sul (2002) and Rio Grande do Norte (2003), which included a significant number of birds of various species, found no evidence of WNV circulation in the country[1].

In 2010, despite the negative results of the study "*Is West Nile virus a potential cause of central nervous system infection in Brazil*?", SOARES *et al.*[10] concluded that *"With the recent activity in Argentina, it is fundamental to continue to monitor for this virus as an emerging cause of neurological disease in South America"*. Similarly, in early 2014 FIGUEIREDO & FIGUEIREDO[2] advised: *"It is necessary to improve the surveillance of SLEV, ROCV, and WNV in Brazil. Therefore, doctors must include flaviviruses (not only dengue) and other arboviruses in their differential diagnosis of acute febrile disease and of meningoencephalitis. In fact, if the doctors do not think on these pathogens, it will perpetuate the mistaken idea that these diseases do not exist here"*.

In August 2014, a ranch worker from a rural area of Aroeiras do Itaim municipality (Piauí State, Brazil) was admitted to the Natan Portella Institute for Tropical Diseases (Teresina, Piauí State, Brazil) with clinical symptoms of acute encephalitis. Since June 2013, a sentinel surveillance program of viral encephalitis has been instituted by the Municipal Health Department of Teresina. A research protocol established in partnership with the Evandro Chagas Institute (Ananindeua, Pará State, Brazil) enabled the shipment of blood, cerebrospinal fluid and fecal samples in an attempt to isolate and molecularly and serologically detect herpes viruses, enteroviruses and arboviruses. From the start of the program until the admission of this patient, samples from 36 patients had been examined. In the second half of November 2014, the Evandro Chagas Institute released the results of the examinations that undoubtedly confirmed that Piauí had recorded the first human case of WNF in Brazil[12].

At the announcement of the first confirmed case of WNF in Brazil, the Ministry of Health released the following statement: *"It is noteworthy that this case was an isolated event; the chain of transmission was not identified, and an in-depth investigation is being performed to clarify the mode of transmission. It does not have epidemiological significance to Brazil nor does it represent a risk to the public health of Piauí or Brazil"*[5]. Thereafter, the Brazilian Society of Tropical Medicine expressed concern about the circumstances in which the diagnosis of the first case of WNF in Brazil was conducted: *"Even though this was an isolated case, the situation is worrisome. Its absence in Brazil, until this case, was enigmatic. After all, why would a virus disseminated throughout North America and the Caribbean not enter into Brazil where its insect vectors and animal reservoirs are present? Then, suddenly it appears in the State of Piauí? (...) This question is even more troublesome because the virus was identified just after routine surveillance was instituted in a referral hospital. The conclusion is obvious: the virus has already been circulating undetected in Brazil for some time"*[11].

The epidemiology news portal from the *International Society for Infectious Diseases*, *ProMED-mail,* also expressed moderate concern following the disclosure of the diagnosis: "*Vector? Isn't missing ... There: all the elements of a transmission cycle are present. To deny that the risks of dissemination and, eventually, that outbreaks are a tangible reality would be naive, reckless and, to some degree, irresponsible"*[9].

The detection of the first case of WNF in Brazil may have distinct epidemiological meaning expressed by the assumptions that the encephalitis surveillance system was able to detect: (1) the initial phase of an outbreak or an epidemic of WNF in the State of Piauí; (2) a case of an already endemic disease at low levels that so far had an unknown occurrence or was undetected in the region or in the country or (3) a sporadic case that emerged under exceptional circumstances that is so far unexplained.

The capacity of Brazilian biomes to provide an ecological niche conducive to the spread of WNV remains enigmatic. To date, there have been no other cases with a confirmed diagnosis of WNF in the country. The team involved in the surveillance of viral encephalitis in Teresina is advocating the hypothesis of a silent endemic (at low levels) of WNF in Piauí and, perhaps, in Brazil. The manifestations of encephalitis caused by various viruses (and even by non-viral agents) have a significant amount of coincident signs and symptoms. The low specificity of clinical, cerebrospinal fluid data, radiological and electroencephalographic "patterns" of WNV encephalitis hinders its recognition. Thus, the reporting of suspected cases, which is an essential step for the national reference laboratories to perform specific diagnostic tests, is fairly limited. The classical assumption of the herpetic nature of viral encephalitis, the lack of specific therapies against most viruses and the lack of diagnostic methods in most Brazilian hospitals are factors that combined lead to the non-recognition of the etiologic agents involved in central nervous system infections. These assertions may indicate that other cases of WNV encephalitis may have occurred without clinical recognition (which is admittedly difficult) of the disease and without performing the tests necessary for an etiological diagnosis. Brazilian clinicians, researchers and epidemiologists have a challenge ahead, given that the clarification of the current status of WNV circulation does have an epidemiological relevance to Teresina municipality, for Piauí State and to Brazil.

Marcelo A. Cunha e Silva VIEIRA(1), Aline de Almeida Xavier AGUIAR(2), Amaríles de Souza BORBA(3), Herlon Clístenes Lima GUIMARÃES(4), Kelsen Dantas EULÁLIO(5), Linduarte Leitão de ALBUQUERQUE-NETO(5), Maria do Amparo SALMITO(3) & Oriana Bezerra LIMA(3)

(1) Natan Portella Institute of Tropical Medicine, Dept. Neurology, R. Governador Artur de Vasconcelos 151, 64001-450 Teresina, PI, Brazil. Telephone: +55 86 3221 3413. E-mail: macsvieira@superig.com.br.
(2) Municipal Health Dept., Zenon Rocha Emergency Hospital, Teresina, PI, Brazil.
(3) Municipal Health Dept., Surveillance Secretariat, Teresina, PI, Brazil.
(4) State Health Dept., Surveillance Secretariat, PI, Brazil.
(5) Natan Portella Inst. of Tropical Medicine, Dept. Infectious Diseases, Teresina, PI, Brazil.
Correspondence to: Marcelo A.C.S. VIEIRA
Funding: This research received no grant from any funding agency in the public, commercial or not-for-profit sectors.

REFERENCES

1. Araújo FAA, Vianna RST, Wada MY, Silva EV, Doretto L, Cavalcante GC, *et al.* Inquérito sorológico em aves migratórias e residentes de Galinhos/RN para detecção do vírus do Nilo Ocidental e outros vírus. Bol Eletrôn Epidemiol. 2004;4(2):1-12.
2. de Figueiredo ML, Figueiredo LT. Review on infections of the central nervous system by St. Louis encephalitis, Rocio and West Nile flaviviruses in Brazil, 2004-2014. Adv Microbiol. 2014;955-61.
3. Luna EJA, Pereira LE, Souza RP. Encefalite do Nilo Ocidental, nossa próxima epidemia? Epidemiol Serv Saúde. 2003;12(1):7-19.
4. Melandri V, Guimarães AÉ, Komar N, Nogueira ML, Mondini A, Fernandez-Sesma A, *et al.* Serological detection of West Nile virus in horses and chicken from Pantanal, Brazil. Mem Inst Oswaldo Cruz. 2012;107:1073-5.
5. Ministério da Saúde, Brasil, 2014. Saúde confirma primeiro caso de Febre do Nilo. (cited 2015 Mar 30). Available from: http://portalsaude.saude.gov.br/index.php/cidadao/principal/agencia-saude/15962-saude-confirma-primeiro-caso-de-febre-do-nilo
6. Ometto T, Durigon EL, de Araujo J, Aprelon R, de Aguiar DM, Cavalcante GT, *et al.* West Nile virus surveillance, Brazil, 2008-2010. Trans R Soc Trop Med Hyg. 2013;107:723-30.
7. Pauvolid-Corrêa A, Varella RB. Aspectos epidemiológicos da febre do oeste do Nilo. Rev Bras Epidemiol. 2008;11:463-72.
8. Pauvolid-Corrêa A, Campos Z, Juliano R, Velez J, Nogueira RM, Komar N. Serological evidence of widespread circulation of West Nile virus and other flaviviruses in equines of the Pantanal, Brazil. PLOS Negl Trop Dis. 2014;8:e2706.
9. ProMED-mail. Febre do Nilo Ocidental: Brazil (PI), humanos, casos suspeitos, surto? International Society for Infectious Diseases. 2014. Archive number 20141224.3052950. (cited 2015 Mar 30). Available from: http://promedmail.org/direct.php?id=3052950
10. Soares CN, Castro MJ, Peralta JM, Freitas MR, Puccioni-Sohler M. Is West Nile virus a potential cause of central nervous system infection in Brazil? Arq Neuropsiquiatr. 2010;68:761-3.
11. Sociedade Brasileira de Medicina Tropical. Caso de febre do Nilo Ocidental no Piauí é preocupante, alertam especialistas. Brasília: Newsletter SMBT; 2014. Edição 41. 15 de dezembro de 2014. (cited 2015 Mar 30). Available from: http://sbmt.org.br/portal/caso-de-febre-do-nilo-ocidental-no-piaui-e-preocupante-alertam-especialistas
12. Vieira MA, Romano AP, Borba AS, Silva EV, Chiang JO, Eulalio KD, *et al.* West Nile virus encephalitis: the first human case recorded in Brazil. Am J Trop Med Hyg. 2015;pii:15-0170. (Epub ahead of print).