

Chikungunya Virus: A Major Emerging Threat

Stephen Higgs

IT HAS BEEN 15 YEARS SINCE the mosquito-borne West Nile virus (WNV) was introduced into the Americas. Following initial misidentification as the closely related, indigenous Saint Louis encephalitis virus, it was an astute veterinarian, and *VBZ* editorial board member, Tracey McNamara who led the way to the realization that something new had arrived. Intensive mosquito control measures were implemented in the affected areas of New York. By the end of the year, some experts declared victory over the virus based upon their belief that the WNV had been controlled and eliminated from the U.S. *Mission accomplished!*

The detection of the virus early in 2000 was the beginning of the steady spread of WNV to all contiguous states and the permanent establishment of WNV in the U.S. and several other countries. As a consequence of the introduction, the Centers for Disease Control and Prevention received an infusion of much needed funds which supported training programs to address the decline in expertise and capabilities related to vector-borne diseases and to implement the ArboNET surveillance system, that is still being used to great effect. New diagnostic tools were developed, new blood screening protocols were implemented to prevent infections resulting from transfusion and organ transplantation, and vaccines to protect horses were commercialized; although there is currently no approved vaccine for humans.

The U.S. experienced years of intense activity as the virus moved to the Southern and Western states. Periods of declining activity seemed to lead to complacency and an attitude that WNV was old news and had reached an epidemic plateau. Resurgence, as seen, for example by the dramatic increase in cases that occurred in the Dallas–Ft. Worth area during 2012 demonstrated that zoonotic pathogens could not be ignored. According to the excellent CDC WNV webpage (www.cdc.gov/westnile/index.html) and the U.S. Geological Survey site (http://diseasemaps.usgs.gov/wnv_background.html), there have been over 22,000 non-neuroinvasive cases, over 17,000 neuroinvasive cases, and over 1,600 fatalities due to WNV infections. With a high asymptomatic/non-reporting rate of perhaps 80% it could be assumed that since 1999, there have been over 2 million people infected with WNV.

When I became involved in research on mosquito-borne viruses in the mid 1980's, it surprised me to learn that we did not know everything about the relationship between the viruses and their arthropod vectors or indeed fully understand the ecology and many other aspects of the diseases that have

taken a huge toll on humans and domestic animals. How could this be, when the transmission of yellow fever virus by mosquitoes was discovered over 100 years ago? One might have assumed that the advent of innovative, seemingly revolutionary, molecular techniques that are now routinely used would have filled most, if not all, of the gaps in our knowledge and understanding of these vector-borne pathogens. Although we now have sequenced the genomes of key mosquito vectors and can genetically engineer a wide variety of viruses, the reality is that we still do not understand some of the basic aspects of the transmission of pathogens by arthropods. For the most part, we still do not understand species specificity and vector competence, for example: why particular viruses are transmitted by certain species of mosquitoes and not others, and why different populations of a particular species of mosquito vary with respect to its susceptibility.

As part of studies to improve our understanding of these relationships, in the early 2000s, my research group was working with two relatively obscure alphaviruses, which although genetically similar, were transmitted by very different mosquitoes: o'nyong nyong virus by *Anopheles gambiae* and chikungunya virus (CHIKV) by *Aedes aegypti*. How quickly things can change. Chikungunya virus has moved from obscurity to notoriety and has now become a major emerging threat on a global scale. Studies based on an infectious clone of CHIKV developed by my group¹ revealed that during an epidemic on several islands in the Indian Ocean a single amino acid change in the E2 protein increased viral infectivity for the Asian Tiger mosquito, *Ae. albopictus*. The combination of this increased infectivity along with the global spread of this highly invasive mosquito² has likely been the major contributing factor that has driven the ongoing spread of CHIKV. During late 2013, CHIKV was detected on islands in the Caribbean. As of July 11, 2014, the Pan American Health Organization (PAHO) has reported 259,723 suspected and 4,721 confirmed cases of locally-acquired chikungunya fever in the Americas with 22 countries or territories involved (http://www.paho.org/hq/index.php?option=com_content&view=article&id=9053&Itemid=39843)

Local transmission cycles have now been reported in El Salvador in Central American and in Suriname and Venezuela in South America. Data from the CDC's ArboNET national surveillance system (www.cdc.gov/chikungunya/geo/united-states.html) reports 138 imported cases in the US as of July 14, 2014. Although 25% of the cases have been in

Florida, cases have been widespread with diagnoses in over 20 other States.

To date, all of the cases have been imported, that is in travelers returning from other countries where the virus is circulating. A key question of course is: could the CHIKV become established in the U.S. as WNV did? One thing that I learned from other people associated with the WNV experience is not to make predictions! As demonstrated by the 2007 outbreak of CHIKV in Italy, that was initiated by an infected traveler from Asia introducing the virus into the local *Ae. albopictus* population, the potential for CHIKV transmission in temperate climates certainly exists and must not be ignored. In the U.S., we certainly have competent vectors, namely *Ae. aegypti* and *Ae. albopictus* in many areas and we have susceptible vertebrate amplifying hosts, *i.e.*, people. What may be the critical difference between WNV and CHIKV, that enabled WNV spread and establishment in the U.S. is that whilst WNV is a zoonotic pathogen that infects multiple species of mosquitoes and is transmitted primarily in a bird-mosquito cycle, the CHIKV transmission cycle is primarily restricted to human-*Aedes spp.* interactions. By the time that WNV was detected and identified in the U.S., the process of dispersal from the introduction site by infected birds had likely already began, and so vector control measures although locally effective, could not prevent establishment. Ironically, a difference between these two viruses that might make control measures more effective in the event of local CHIKV transmission is that most people infected with CHIKV become symptomatic, in contrast to WNV where perhaps 80% are asymptomatic. People with chikungunya fever would seek medical attention and in the absence of a recent travel history to endemic areas, this should alert authorities of local transmission of the virus. One would hope that vector control measures and effective communications made to the community, advising the use of insect repellents and reducing mosquito breeding sites, etc., would be immediately implemented in order to contain the outbreak. For the general public, information is already available from websites listed herein, there has been a great deal of local news coverage, and government agencies are on alert. However, although much was learned and achieved from the WNV experience, I do worry that the failure to sustain the training programs will

compromise our ability to respond quickly enough if CHIKV transmission occurs in the U.S., especially if it is in an area that does not have appropriate vector control programs established.

The emergence of CHIKV and other pathogens provides a constant reminder of the interconnectedness between humans and other animals and our vulnerability to known and unknown threats. Awareness, knowledge and understanding of these agents is critical for the development of effective preparedness and responses to these threats. The uniquely broad scope of articles published by the expert contributors to *Vector-Borne and Zoonotic Diseases*, and our sister Mary Ann Liebert, Inc., journals (including *Biosecurity and Bio-terrorism* and *Viral Immunology*) represents an unequalled resource for anyone interested in these important pathogens. Stay informed by subscribing to *Vector-Borne and Zoonotic Diseases*, and the excellent agency websites mentioned herein.

References

1. Tsetsarkin K, Higgs S, McGee CE, De Lamballerie X, Charrel RN, Vanlandingham DL. Infectious clones of Chikungunya virus (La Réunion isolate) for vector competence studies. *Vector Borne Zoonotic Dis.* 2006;6:325–337.
2. Mark Q. Benedict, Rebecca S. Levine, William A. Hawley, L. Philip Lounibos. Spread of the tiger: global risk of invasion by the mosquito *Aedes albopictus*. *Vector-Borne Zoonotic Dis.* 2007;7:76–85.

—Stephen Higgs, PhD, FRES, FASTMH
Editor-in-Chief
Vector-Borne and Zoonotic Diseases

Associate Vice President for Research
Director, Biosecurity Research Institute
University Distinguished Professor, Diagnostic
Medicine and Pathobiology
Peine Professor of Biosecurity
Professor Diagnostic Medicine & Pathobiology
Kansas State University
Manhattan, KS

Email: shiggs@bri.ksu.edu