Zika Virus

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KEYWORDS

• Arbovirus • Autochthonous • Birth defects • Flavivirus • *Flaviviridae*
• Guillain-Barré syndrome • Microcephaply

KEY POINTS

- Before its emergence in Brazil in 2015, Zika virus was not thought to be endemically transmitted in the Americas. Since then, it has spread across South America and into North America, including the Caribbean and, recently, the United States.
- Zika virus is most commonly transmitted by mosquitoes; however, horizontal and vertical transmission in humans is well documented.
- Zika fever presents with similar symptoms to other arboviral infections, so both molecular and serologic testing are required to distinguish it from similar diseases.
- Birth defects and serious neurologic sequelae have been recorded in association with Zika virus infection.
- Continued epidemiologic monitoring as well as basic research into the biology, pathogenesis, and immunology of Zika virus and Zika fever is needed to develop effective countermeasures and vaccines.

INTRODUCTION

Before 2015, Zika virus (ZIKV), a once obscure mosquito-borne virus, was responsible for sporadic outbreaks of acute febrile illness in parts of the Eastern Hemisphere. In early 2015, a cluster of dengue fever–like illnesses characterized by fever, maculopapular rash, arthralgia/myalgias, and conjunctivitis was reported in the Brazilian city of Camaçari, in the state of Bahia.[1] ZIKV RNA was detected by polymerase chain reaction (PCR) in serum specimens from 7/24 (29.2%) patients who received care at Santa Helena Hospital. By December of that year, between 440,000 and 1,300,000 human ZIKV infections were estimated to have occurred.[2] As of September 2016, widespread

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autochthonous transmission of ZIKV has been documented in nearly every country in the Western Hemisphere, demonstrating the rapidity with which emerging infectious diseases can spread in immunologically naïve populations, especially if competent vectors and potential reservoir species are present in disease-endemic regions.

ZIKV was discovered in April 1947 as a result of investigating the cause of fever in a sentinel rhesus monkey, animal number 766, that was placed in the Zika forest of Uganda as part of a yellow fever research mission sponsored by the Rockefeller Foundation.[3] ZIKV was ultimately isolated from the brains of Swiss albino mice that were intracerebrally inoculated with serum collected from rhesus 766. Nine months later, in January 1948, ZIKV was again isolated, only this time from brain tissue of mice intracerebrally inoculated with clarified homogenates of *Aedes africanus* mosquitoes collected from the Zika forest.[3] It was not until 1954 that the first human cases of Zika fever were documented. Briefly, 3 Nigerian patients, a 30-year-old man (patient 1), a 24-year-old man (patient 2), and a 10-year-old girl (patient 3), presented with mild pyrexia, headache, and other symptoms. ZIKV was later isolated from the serum of patient 3 via intracerebral inoculation of mice, and anti-ZIKV antibodies were detected in the sera of patients 1 and 2.[4] Since then, ZIKV serosurveys have identified human and animal ZIKV exposures throughout Africa and Asia, demonstrating the extensive endemicity of this virus. Results of these studies should be interpreted with caution, however, because serologic tests for ZIKV are prone to cross-reactivity with antibodies generated in response to related viruses, including Spondweni virus, dengue virus (DENV), and others.[5] In 2007, an outbreak of Zika fever on Yap Island in the Western Pacific marked the first time that ZIKV was detected outside of Africa and mainland Asia.[6] In the following years, additional outbreaks across the Pacific region were documented, including a very large epidemic spanning all of the archipelagoes of French Polynesia, and later, in New Caledonia, Cook Islands, Easter Island, Fiji, Vanuatu, and others.[5,7,8] Ultimately, phylogenetic and phylogeographic data conclude that the current epidemic in the Western Hemisphere resulted from the introduction of ZIKV from French Polynesia by way of Easter Island into mainland South America.[9]

To date, little is understood about the dynamics of ZIKV infection, and new modes of transmission, including sexual intercourse, as well as the appearance of severe complications, including birth defects and neurologic diseases, have only recently been described. Newly established animal and cell culture models of ZIKV infection have provided some insight into the pathogenicity of ZIKV, but these systems are still in their infancy and have yet to reproducibly recapitulate the more severe complications observed in human infections. The paucity of information regarding the myriad aspects of Zika fever pathophysiology and the long-term consequences of pregnancy-associated ZIKV infections have prompted a multinational effort to develop targeted therapeutics, effective vector control programs, and vaccines to protect vulnerable populations. Because of the nearly daily release of new publications concerning information about ZIKV and Zika fever, it is impossible to review the entire body of current knowledge; however, the authors have attempted to summarize salient points regarding the epidemiology, basic biology, pathophysiology, diagnosis, treatment, and prevention of ZIKV infection.

EPIDEMIOLOGY

Between 1947 and 2014, ZIKV was associated with sporadic epidemics in parts of Africa, Southeast Asia, and Oceania. The most extensive epidemic during this time period occurred in French Polynesia in 2013; approximately 30,000 cases were