

The story of chikungunya virus



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Chikungunya Virus: Advances in Biology, Pathogenesis, and Treatment

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For more on CHIKV diagnosis see Antiviral Res 2019; **66:** 66–81 DOI:10.1016/j. antiviral.2019.03.009

For more on CHIKV vaccines see PLoS Negl Trop Dis 2019; 17: 13. DOI:10.1371/iournal. pntd.0006919

For more on CHIKV therapy see Expert Rev Anti Infect Ther 2018; 16: 333-344. DOI:10.1080/1478 7210.2018.1450629 The word chikungunya ("that which bends up" in the Kimakonde language) indicates a hunched posture resulting from recurrent joint pain. Chikungunya virus (CHIKV) is an emerging arbovirus from the Togaviridae family and the Alphavirus genus, that causes a crippling musculoskeletal inflammatory disease characterised by fever, polyarthralgia, myalgia, rash, and headache. Since the first confirmed CHIKV epidemic in the coastal area of Tanzania in 1952, the virus has caused outbreaks in eastern and central Africa, the Indian Ocean islands, southeast Asia, Central and South America, US territories, and Europe, with more than five million cases reported in the past 15 years.

Chikungunya Virus: Advances in Biology, Pathogenesis, and Treatment, edited by Chioma Okeoma, is one of the most informative books on the subject and offers reviews on CHIKV biology and many other topics—eg, clinical aspects of infection and pathogenesis, including host immune responses, vaccine developments, epidemiology, and ecological data.

In the book, experts from Martinique who dealt with a major CHIKV epidemic in 2013-14 highlight current approaches to manage chikungunya symptoms, in the absence of a definitive therapy. The failure of promising candidates, such as chloroquine, in the management of acute infection draws attention to the urgent need for new anti-CHIKV therapies that efficiently block virus entry and propagation in the cell. Ideally, a vaccine should be capable of inducing neutralising antibodies in immunised hosts to block infection. Different vaccines have been developed in an attempt to accomplish this goal, but only three candidates have reached clinical trials, and so far effectiveness has been disappointing. From these vaccine approaches, attenuated CHIKV was shown to act as one of the best immunogens, but was also associated with sideeffects such as arthralgia. Other tested vaccines include the recombinant measles virus vector expressing CHIKV structural proteins (MV-CHIKV), and a non-replicative virus like-particles (CHIK-VLPs), both very effective in inducing seroconversion, but with short-lived responses.

The book gives an overview of challenges and limitations to fully understand CHIKV chronicity, with helpful illustrations depicting the delivery of the virus into the skin during a vector blood meal, the intracellular sites of viral replication, and the mechanisms allowing virus dissemination within the host. Of special interest is the dual role of the immune responses, initiated by the innate and followed by the adaptive cellular and humoral immunities to control infection, but precipitating continuous inflammation, flaring pain in joints and tendons, resulting in chronic disease.

An exciting chapter in the book is about the interaction of CHIKV with the mosquito vector. The authors describe the distribution, ecology, and behaviour of CHIKV vectors around the world, explaining the transfer of CHIKV from enzootic to urban transmission, by migration of people living or working near forests into urban areas inhabited by Aedes aegypti or Aedes albopictus. The authors also discuss other factors that affect CHIKV transmission by mosquitoes, including antiviral defenses by activation of innate immune mechanisms, the inhibitory role of siRNA pathways, and viral interaction with the mosquito microbiome (eg, the presence of wolbachia bacteria stabilising the CHIKV replication in the insect). Additionally, extrinsic factors like environmental temperature, insecticide exposure, availability of food resources, mosquito population density, and predation are also discussed as influencing vector susceptibility to CHIKV infection. The authors shed light on viral genetic mutations favouring the emergence of novel CHIKV strains with enhanced epidemic potential, as the intriguing adaptation of CHIKV to A albopictus, which resulted in one of the largest outbreaks of CHIKV in Réunion. The authors emphasise the limitations in predicting CHIKV epidemics, discuss ecological factors determining the scope and duration of any given outbreak, and forecast problematic CHIKV evolutionary trajectories. One worrying prophesy from the authors was that "further A. albopictus adaptive evolution of CHIKV will favor the selection of "super-adapted" strains with even greater potential for global expansion as this vector continues to invade new regions".

Ongoing chikungunya epidemics in large CHIKV-naive populations will result in more information on this evolving disease. In our Acute Febrile Clinic at FIOCRUZ (Rio de Janeiro, Brazil), we have seen until now 1000 confirmed CHIKV infections, 15% of which were in pregnant women. Chikungunya Virus: Advances in Biology, Pathogenesis, and Treatment could provide more information on the consequences of acute CHIKV infection during pregnancy, and its effect on disability and neonatal mortality. Some hope exists that ongoing trials using intravenous hyperimmune anti-CHIKV immunoglobulin might indeed prevent neonatal CHIKV infection in viraemic mothers and will eventually be an affordable option for health practitioners to treat this population at risk.

This book is an excellent and comprehensive review of this emergent disease for researchers, students, educators, and medical professionals who are interested in understanding many aspects of the disease, or who want to learn more about specific topics of such a well adapted virus.

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