# Chikungunya: an arbovirus infection in the process of establishment and expansion in Brazil

## Chikungunya: uma arbovirose em estabelecimento e expansão no Brasil

## Chikungunya: una arbovirosis en establecimiento y desarrollo en Brasil

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Within the group of emerging and reemerging infectious diseases, mosquito-borne arboviruses like dengue virus (DENV) and chikungunya virus (CHIKV) are considered important public health challenges. In addition to the scenario caused by DENV, which is endemic in nearly all of Brazil and has caused epidemics for decades, the movement of CHIKV into Brazilian territory has raised major concern. Both viruses are transmitted by mosquitoes of the genus *Aedes*, particularly *Ae. aegypti* and *Ae. albopictus*, two invasive and cosmopolitan species. *Aedes aegypti* displays anthropophilic behavior and is mostly found in places with human clustering, taking its blood meals and resting inside homes. *Aedes albopictus* displays diversified feeding behavior and is more common in areas with lower human density, preferentially feeding and resting in the peridomicile [1].

CHIKV is an alphavirus originated in Africa, where it is maintained in sylvatic cycles involving vector species of the *Aedes* genus and non-human primates, with three genotypes: West Africa, East/Central/South Africa, and Asian. First isolated in 1952, in Tanzania, the first documented emergence of CHIKV occurred with its introduction in Southeast Asia and India, circulating in a sporadic urban cycle that still continues to this day, with *Ae. aegypti* acting as the main vector [2]. The second emergence occurred in Kenya, in 2004, and in the following years it was disseminated through several Indian Ocean islands, reaching India and Southeast Asia. In 2006, on Réunion Island, an epidemic resulted from viral mutations leading to more effective transmission by *Ae. albopictus* [3]. Autochthonous transmission was also detected in Italy and France, where *Ae. albopictus* acted as vector. In October 2013, CHIKV reached the Americas through the Caribbean, resulting in thousands of infections. In Brazil, autochthonous transmission was first detected in September 2014 in the city of Oiapoque, Amapá State. Over the course of 2014, 2,772 cases of CHIKV were confirmed in Brazil, distributed in six Federation Units: Amapá (1,554 cases), Bahia (1,214), Distrito Federal (2), Mato Grosso do Sul (1), Roraima (1), and Goiás (1). In 2015, as of the 12th epidemiological week, 1,513 cases, 735 had been confirmed in Amapá, where the CHIKV genotype was determined to be the Asian and 778 cases in Bahia, caused by the African genotype [4,5].

CHIKV infection produces a debilitating febrile syndrome with a sudden onset and intense joint symptoms which gave rise to the name chikungunya, which means "to walk bent over" in Makonde, an African language. Arthralgia appears to affect 80% of patients and can persist for months and even years. The spectrum of post-chikungunya rheumatic and musculoskeletal manifestations includes persistent pain, even rheumatoid arthritis, which develops

in approximately 5% of patients [6]. The chronic joint symptoms interfere in the patient's quality of life, with significant economic impacts due to reduced work productivity. According to a study using disability-adjusted life years (DALYs) as the indicator during the epidemic in 2005-2006, in the Réunion Islands, there were approximately 55,000 DALYs lost, the majority of which in the working-age population (20-60 years), 86% of which due to the chronic phase of the disease. This profile differs from dengue, in which some 80% of DALYs are due to premature mortality [7]. The clinical spectrum of the disease can vary,with severe cases and deaths occurring eventurally in patients with comorbidities, the elderly and children. CHIKV causes neurological disease in newborns and the elderly and can be fatal. Vertical transmission was first reported during an epidemic in the Reunion Island and occured in 50% of viremic pregnant women at delivery. Mother-to-child transmission is uncommon, but all the neonates infected during labor presented symptomatic disease, with severe manifestations (50%), including encephalopathy in 90% of the cases [8]. The severity of chikungunya disease in newborns and the burden of cerebral palsy require preventive and therapeutic measures that should be preceded by confirmation of maternal viremia.

Although the combination of fever and arthralgia shows excellent positive predictive value during a chikungunya outbreak, the majority of suspected cases live in endemic areas for dengue, where the odds of clinical diagnostic error are high [9]. Severe infections such as *Staphylococcus* or malaria in travelers returning from the tropics may be underestimated during chikungunya outbreaks and may involve high morbidity and case-fatality. Rapid laboratory confirmation is crucial for adequate clinical therapeutic management and to initiate responses to control measures. Reverse transcriptase polymerase chain reaction (RT-PCR) is a sensitive, specific, and rapid assay for CHIKV diagnosis but is not available outside of research centers in Brazil, where other rapid assays are being tested and validated.

Passive immunization is a therapeutic and preventive option for many viral infections, especially those acquired by vertical transmission. The use of specific antibodies can be an effective drug intervention for individuals at risk of developing severe disease [10]. Since there is no specific antiviral therapy for CHIKV infection, treatment of the other cases consists of supportive care, including the administration of analgesics and steroids to relieve joint symptoms.

The scenario in Brazil raises the possibility of large epidemics due to the following factors: (1) wide infestation of both CHIKV vectors in the brazilian territory [11]; (2) simultaneous circulation of DENV and CHIKV, hindering both the diagnosis and the therapeutic approach; (3) possible adaptation by CHIKV to *Ae. albopictus*, as described in other countries [3]; (4) higher proportion of symptomatic cases compared to dengue; (5) longer viremia (up to 8 days after onset of fever); (6) susceptibility of the entire human population, favoring rapid dissemination of the virus; (7) abundance of primate species together with culicid species never exposed to CHIKV, offering opportunities for the establishment of wild cycles previously present only in Africa [12]; and (8) Brazil's large territory, which hinders surveillance and access by many health services to diagnostic laboratory tests.

Several lessons can be learned from chikungunya outbreaks. First, economic development does not protect countries from vector-borne diseases. Modern lifestyles can amplify an epidemic through traveling, population aging, and production of solid waste, generating breeding sites for *Aedes* vectors. From the clinical point of view, considering that the signs and symptoms are highly variable, with the possibility of chronification of joint manifestations, CHIKV infection should be considered when investigating patients with recent symptoms of symmetrical polyarthritis, and treatment should be oriented by specialists. The effectiveness of CHIKV surveillance depends on rapid diagnosis in locations where the competent vector exists and the population is susceptible. Early recognition of local transmission followed by rapid and effective vector control and other public health measures are the only ways to prevent explosive outbreaks. It is necessary to plan actions to increase the sensitivity of surveillance by better recognition of the disease; make rapid and validated tests available; improve communications and the flow of results and notifications between commercial and state laboratories and public health agencies; share information with the population and encourage social mobilization programs that can expand preventive measures and minimize the risk of the virus spreading. Active entomological and epidemiological surveillance should be maintained in Brazil due to the wide distribution of different populations of *Ae. aegypti* and *Ae. albopictus*, which show high vector competence for CHIKV [13]. Finally, accurate models that incorporate ecological, entomological, and virologic components could be explored to assist the prediction of facilitating factors for spread of the disease and occurrence of outbreaks, similar to the models developed for dengue and other arbovirus infections.

## Contributors

All authors contributed equally in the production of the paper.

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