

## MONTHLY SCIENTIFIC REVIEW ON **CHIKUNGUNYA VIRUS**

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## Situation at a glance

- Chikungunya is an infectious disease caused by an arbovirus, the chikungunya virus. Between 2010 and 2024, not a single case had been detected on the Reunion Island. Since August 2024, Reunion Island has recorded 192 confirmed native cases of chikungunya, spread over seven active areas as of January 13, 2025.
- This situation led the authorities to activate alert level 3 of the ORSEC "Arbovirosis" plan corresponds to an epidemic of low intensity.
- The IXCHIQ Chikungunya vaccine is available, but there is no vaccine recommendation from the HAS.

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## **Scientific articles**

This section presents relevant articles published on peer-reviewed scientific journals or pre-print platforms.

This week, discover breakthroughs in chikungunya diagnostics, vaccines, and vector control, advancing prevention and surveillance of this global health threat.

#### Diagnosis

## RT-RPA as a dual tool for detection and phylogenetic analysis of epidemic arthritogenic alphaviruses. Sridhar S, Tonto PB, Lumkong L, Netto EM, Brites C, Wang WK, Herrera BB.

#### Published in Sci Rep on December 2024.

In this study, authors report the development and validation of three virus-specific Real time- Recombinase polymerase amplification (RT-RPA)-based rapid tests for Chikungunya (CHIKV), o'nyong-nyong (ONNV), and Mayaro (MAYV) viruses. These tests demonstrated both speed and sensitivity, capable of detecting 10–100 viral copies within 20 min of amplification, without exhibiting cross-reactivity. Furthermore, the clinical potential of these tests was evaluated using serum and tissue samples from CHIKV, ONNV, and MAYV-infected mice, as well as CHIKV-infected human patients. We demonstrate that the RPA amplicons derived from the patient samples can be sequenced, enabling cost-effective molecular epidemiological studies. These findings highlight the significance of these rapid and specific diagnostics in improving the early detection and management of these arboviral infections.

## A rapid, specific and ultrasensitive detection of the Chikungunya virus based on RT-RPA:CRISPR/Cas12a one-pot dual mode end-point detection system. Bhardwaj P, Gulafshan S, Singh R.

#### Published in Anal Chim Acta on November 2024.

In this study, the authors aimed to develop a one-pot reverse transcription recombinase polymerase amplification (RT-RPA) mediated CRISPR/Cas12a based detection platform for rapid, specific, and ultrasensitive detection of chikungunya virus (CHIKV) in clinical samples (VRACCH). They have successfully integrated CRISPR/Cas12a technology with reverse transcription recombinase polymerase amplification (RT-RPA) for the detection of Chikungunya virus (CHIKV). The developed assay enabled rapid detection of CHIKV within 35 min, requiring minimal handling process and instrumentation. The assay utilized Envelope 1 (E1) gene for target recognition. The sensitivity and specificity was analyzed using whole blood samples obtained from AFI/AES patients and compared to RT-PCR method. Further, to facilitate ease of result interpretation, VRACCH was integrated with a novel detection approach facilitating naked-eye detection by both fluorescence and dipstick methods in a single tube reaction.

## Salivary detection of Chikungunya virus infection using a portable and sustainable biophotonic platform coupled with artificial intelligence algorithms. Guevara-Vega M, Rosa RB, Caixeta DC, Costa MA, de Souza RC, Ferreira GM, Mundim Filho AC, Carneiro MG, Jardim ACG, Sabino-Silva R.

#### Published in Sci Rep on September 2024.

In this study, the portable Fourier-transform infrared coupled with Attenuated Total Reflection (ATR-FTIR) platform was applied explore the use of this platform for salivary diagnostic of viral diseases. Authors aimed to identify unique vibrational modes of salivary infrared profiles to detect CHIKV infection using chemometrics and artificial intelligence algorithms. Thus, authors intradermally challenged interferon-gamma gene knockout C57/BL6 mice with CHIKV ( $20 \mu I$ ,  $1 \times 105 PFU/mI$ , n = 6) or vehicle ( $20 \mu I$ , n = 7). Saliva and serum samples were collected on day 3 (peak of viremia). CHIKV infection was confirmed by RT-PCR in the serum of CHIKV-infected mice. The best pattern classification showed a sensitivity of 83%, specificity of 86%, and accuracy of 85% using support vector machine (SVM) algorithms. These results suggest that the salivary ATR-FTIR platform can discriminate CHIKV infection with the potential to be applied as a non-invasive, sustainable, and cost-effective detection tool for this emerging disease.

#### Vaccine



# Safety and immunogenicity of a live-attenuated chikungunya virus vaccine in endemic areas of Brazil: interim results of a double-blind, randomised, placebo-controlled phase 3 trial in adolescents. Buerger V, Hadl S, Schneider M, Schaden M, Hochreiter R, Bitzer A, Kosulin K, Mader R, Zoihsl O, Pfeiffer A, Loch AP, Morandi E Jr, Nogueira ML, de Brito CAA, Croda J, Teixeira MM, Coelho IC, Gurgel R, da Fonseca AJ, de Lacerda MVG, Moreira ED Jr, Veiga APR, Dubischar K, Wressnigg N, Eder-Lingelbach S, Jaramillo JC.

#### Published in Lancet Infect Dis on January 2025.

The authors recruited 754 adolescent (aged 12-18 years) in this double-blind, randomised, placebo-controlled phase 3 trial, funded by the Coalition for Epidemic Preparedness Innovation and EU Horizon 2020, evaluating the immunogenicity and safety of the vaccine VLA1553. Randomisation was stratified by baseline serostatus in a 2:1 ratio to receive VLA1553 or placebo. The primary endpoint was the proportion of baseline seronegative participants with chikungunya virus neutralising antibody levels of 150 or more in  $\mu$ PRNT50 (a micro plaque reduction neutralisation test), which was considered a surrogate of protection. VLA1553 induced seroprotective chikungunya virus neutralising antibody levels 98-8% (95% CI 96·5–99·8) in participants who were seronegative at baseline. In seropositive participants, the baseline seroprotection rate of 96·2% increased to 100% after vaccination. VLA1553 was generally safe. The authors conclude that these data support the use of VLA1553 for the prevention of disease caused by the chikungunya virus among adolescents and in endemic areas.

### First immunogenicity and safety data on live chikungunya vaccine in an endemic area. Freedman DO, Wilder-Smith AB, Wilder-Smith A.

#### Published in Lancet Infect Dis on January 2025.

In this paper, the authors comment the research article above. They commend this trial as more safety and immunogenicity data are now available for populations with previous chikungunya exposure and people aged 12 years. The also mention the US Centers for Disease Control recommendations for vaccination, the EMA position, the WHO and the regional and national immunisation technical advisory groups ongoing discussions regarding the vaccine use policy.

## Antibody persistence and safety of a live-attenuated chikungunya virus vaccine up to 2 years after single-dose administration in adults in the USA: a single-arm, multicentre, phase 3b study. McMahon R, Toepfer S, Sattler N, Schneider M, Narciso-Abraham M, Hadl S, Hochreiter R, Kosulin K, Mader R, Zoihsl O, Wressnigg N, Dubischar K, Buerger V, Eder-Lingelbach S, Jaramillo JC.

#### Published in Lancet Infect Dis on December 2024.

The authors report antibody persistence and safety up to 2 years in participants from a precursor phase 3 trial from professional vaccine trial sites in the USA. 363 participants, out of 2724 participants in the precursor study who received one dose of VLA1553, were analysed in this single-arm, multicentre, phase 3b study. Strong seroprotection was observed at 1 year (98.9%) and 2 years (96.8%) after vaccination, and was very similar between those aged 18–64 years and those aged 65 years and older. No adverse events of special interest were ongoing at the time of transition.

## Safety and immunogenicity of a single-shot live-attenuated chikungunya vaccine: a double-blind, multicentre, randomised, placebo-controlled, phase 3 trial. Schneider M, Narciso-Abraham M, Hadl S, McMahon R, Toepfer S, Fuchs U, Hochreiter R, Bitzer A, Kosulin K, Larcher-Senn J, Mader R, Dubischar K, Zoihsl O, Jaramillo JC, Eder-Lingelbach S, Buerger V, Wressnigg N.

#### Published in Lancet on June 2024.

The authors evaluated VLA1553 live-attenuated vaccine candidate in a double-blind, multicentre, randomised, phase 3 trial done in 43 professional vaccine trial sites in the USA. 4128 healthy volunteers aged 18 years and older, with no history of chikungunya virus infection, were enrolled and randomised (3:1) to receive VLA1553 or placebo. The primary endpoint was the proportion of baseline negative participants with a seroprotective chikungunya virus antibody level 28 days after vaccination. In the per-protocol analysis, after a single vaccination, VLA1553 induced seroprotective chikungunya virus neutralising antibody levels in 98-9% of participants in the VLA1553 group (95% CI 96·7–99·8; p<0·0001) 28 days post-vaccination, independent of age. VLA1553 was generally safe with an adverse event profile similar to other licensed vaccines. The authors conclude VLA1553 is an excellent candidate for the prevention of disease caused by chikungunya virus.

## Safety and Immunogenicity of an Adjuvanted Chikungunya Virus (CHIKV) Virus-like Particle (VLP) Based Vaccine in Two Pivotal Phase 3 Trials, ≥12 Years of Age. Richardson JS, Anderson D, Mendy J. Muhammad S, Tindale L, Loreth T, Tredo SR, Jenkins V, Aiibove P, Bedell L.

#### Published in Open Forum Infect Dis on November 2024.

The authors evaluated VLA1553 live-attenuated vaccine candidate in a double-blind, multicentre, randomised, phase 3 trial done in 43 professional vaccine trial sites in the USA. 4128 healthy volunteers aged 18 years and older, with no history of chikungunya virus infection, were enrolled and randomised (3:1) to receive VLA1553 or placebo. The primary endpoint was the proportion of baseline negative participants with a seroprotective chikungunya virus antibody level 28 days after vaccination. In the per-protocol analysis, after a single vaccination, VLA1553 induced seroprotective chikungunya virus neutralising antibody levels in 98.9% of participants in the VLA1553 group (95% Cl 96·7–99·8; p<0·0001) 28 days post-vaccination, independent of age. VLA1553 was generally safe with an adverse event profile similar to other licensed vaccines. The authors conclude VLA1553 is an excellent candidate for the prevention of disease caused by chikungunya virus.

#### Vector control

Mosquito-disseminated pyriproxyfen for mosquito-borne disease control in Belo Horizonte, Brazil: a pragmatic, before-after control-intervention paired-series trial. Abad-Franch F, Carvajal-Cortés JJ, Rabelo ACL, Gusmão EVV, Soares SSS, Luz SLB.

#### Published in Lancet Infect Dis on September 2024.

This study evaluated whether mosquito-disseminated pyriproxyfen (MDPPF), a larvicide and pupicide delivered by mosquitoes themselves, can reduce dengue transmission. Conducted in Belo Horizonte, Brazil, from 2017 to 2019, 2481 dissemination stations were deployed in nine high-risk neighborhoods, with neighboring and citywide areas as buffers and controls. Dengue incidence data (2016–2019) were analyzed using a BACIPS approach and negative-binomial generalized linear mixed models. Findings showed that MDPPF deployment reduced dengue cases by 29% in intervention neighborhoods and 21% in buffer areas, while incidence remained unchanged in control areas. For a hypothetical outbreak of 100,000 cases, MDPPF could potentially reduce symptomatic cases by 21,000 to 36,000, alleviating health system strain. This indicates MDPPF's promise as a strategy to combat mosquito-borne diseases, though further studies are needed for diseases like Zika and chikungunya due to insufficient data.

## Effectiveness of Wolbachia-mediated sterility coupled with sterile insect technique to suppress adult Aedes aegypti populations in Singapore: a synthetic control study. Bansal S, Lim JT, Chong CS, Dickens B, Ng Y, Deng L, Lee C, Tan LY, Kakani EG, Yoong Y, Du Yu D, Chain G, Ma P, Sim S, Ng LC, Tan CH.

#### Published in Lancet Planet Health on September 2024.

This study assessed the impact of combining Wolbachia-mediated sterility with the sterile insect technique (SIT) to control Aedes aegypti populations in Singapore's urban areas from 2018 to 2022. Wolbachia-infected sterile male mosquitoes were released twice weekly across 117 sectors, leading to a 62% reduction in female mosquito populations within three months, 78% within six months, and over 91% after 18 months. Spillover effects also reduced mosquito abundance in adjacent non-release areas by 61%. The intervention helped mitigate dengue incidence, despite slight increases in Aedes albopictus populations in some areas. Using synthetic control methods, the study demonstrated the feasibility of large-scale, long-term mosquito control in dense urban settings. Challenges included sustaining releases and addressing migration of wild-type mosquitoes, but the findings underscore the potential of IIT-SIT as a robust tool against vector-borne diseases.





## Detection of dengue virus and chikungunya virus in wastewater in Portugal: an exploratory surveillance study. Monteiro S, Pimenta R, Nunes F, Cunha MV, Santos R.

#### Published in Lancet Microbe on September 2024.

In this study, authors aimed to explore wastewater-based surveillance (WBS) plans for dengue virus (DENV) and chikungunya virus (CHIKV) tracking. RNA concentrations of DENV and CHIKV (non-structural viral protein 1 [nsP1] and envelope protein [E1] genes) were quantified by RT-PCR in 11 wastewater treatment plants in three regions of Portugal, once every 2 weeks for 11 months (May 2022 to April 2023). 273 samples were collected. DENV was detected in 68 (25%) of 273 samples, with a median viral load of  $1.1 \times 10-4$  (IQR  $3.2 \times 10-5$  to  $8.0 \times 10-4$ ). CHIKV was detected in 30 (11%) of 273 samples, with median viral loads of  $3.1 \times 10-4$  ( $1.6 \times 10-4$  to  $6.4 \times 10-4$ ; nsP1 gene) and  $7.8 \times 10-4$  ( $4.2 \times 10-4$  to  $2.0 \times 10^{-3}$ ; E1 gene). The pattern of occurrence of CHIKV was similar between regions whereas slight differences were found for DENV. When combining results for the three studied regions, DENV prevalence and viral load had two seasonal peaks (summer and winter) and CHIKV prevalence and viral load had a single peak during March and April of 2023. This study highlights the potential of WBS as a potent tool for gauging the epidemiological landscape of DENV and CHIKV in Portugal, where autochthonous cases have not yet been detected.

#### Epidemiology

Chikungunya: a decade of burden in the Americas. de Souza WM, Ribeiro GS, de Lima STS, de Jesus R, Moreira FRR, Whittaker C, Sallum MAM, Carrington CVF, Sabino EC, Kitron U, Faria NR, Weaver SC.

#### Published in Lancet Reg Health Am on January 2024.

Chikungunya virus (CHIKV), first detected in the Americas in 2013, has caused over 3.6 million reported cases across 50 countries by 2023. Transmitted by Aedes aegypti and Aedes albopictus mosquitoes, CHIKV causes acute and chronic illnesses, with significant public health and economic impacts. Brazil became the epidemic epicenter, hosting the dominant ECSA-American CHIKV lineage, while other regions experienced outbreaks followed by periods of reduced incidence due to herd immunity. Challenges to CHIKV control include underreporting, co-circulation with other arboviruses, and limited genomic surveillance. Recent advancements, such as the first FDA-approved vaccine and novel mosquito control strategies (e.g., Wolbachia-infected mosquitoes), show promise. However, scaling up vaccination, strengthening diagnostics, and improving vector control are critical to mitigating CHIKV's burden and potentially eliminating it from the Americas. Comprehensive, multi-scale surveillance and international collaboration are essential for success.

## **Relevant news**

This section presents official reports from health agencies, manufacturers and press releases with reliable sources.

## Chikungunya : en raison de l'accélération de la diffusion de l'épidémie, le préfet déclenche le niveau 3 du plan ORSEC à La Réunion

Published by ARS La Réunion on 13 January 2025.

Depuis le 23 août 2024, le territoire réunionnais comptabilise 192 cas de chikungunya. En raison de l'augmentation du nombre de cas et de la dispersion des foyers, et sur proposition du directeur général de l'ARS Gérard COTELLON, Patrice LATRON, préfet de La Réunion, déclenche le niveau 3 du dispositif ORSEC « Arboviroses », ce qui correspond à la circulation d'une épidémie à faible intensité.

#### Areas at Risk for Chikungunya

Published CDC on 19 December 2024.

Outbreaks have occurred in most parts of the world, including in Africa, the Americas, Asia, Europe, and islands in the Indian and Pacific Oceans.

#### Chikungunya worldwide overview

Published by ECDC on 17 December 2024.

In 2024 and as of 30 of November, approximately 480 000 CHIKVD cases and over 200 deaths have been reported worldwide.

## Chikungunya moving into new regions, disabling millions and racking up billions in costs, data suggest

Published by CIDRAP on 4 December 2024.

Globalization, urbanization, and climate change have significantly raised the risk of "explosive, unpredictable" outbreaks of the mosquito-borne disease chikungunya, which disabled millions and likely amassed close to \$50 billion in healthcare and disability-related costs in 110 countries from 2011 to 2020, researchers report in *BMJ Global Health*.





### Fact sheets

This section provides a short overview of of the epidemiology, virology, clinical features and risk assessment related with the disease.

#### **Overview**

CHIKV is an RNA virus from the Alphavirus genus, part of the Togaviridae family, originating in Africa. The disease's name means "the one who walks bent over," due to joint and muscle pain. There are four known clades: West African, Asian, ECSA (East/Central/South African), and IOL (Indian Ocean Lineage). The virus is mainly transmitted to humans through Aedes mosquitoes (Aedes aegypti and Aedes albopictus). Less common transmission can occur via contact with infected blood, especially in laboratory and healthcare settings (<1%). Vertical transmission from mother to child during the second trimester of pregnancy and intra-partum transmission during viremia at delivery have also been reported.

#### Diagnosis

For suspected cases, PCR testing should be done as soon as possible after symptoms appear (viremia lasts about 8 days). Isolated IgM antibodies require a second sample at least 10 days later to confirm seroconversion (IgG appearance). IgM presence alone does not confirm recent infection due to their prolonged persistence.

#### Symptoms

CHIKV infection is symptomatic in 80% of cases and typically progresses through three clinical stages: acute (day 1–21), postacute (day 21–3 months), and chronic (beyond 3 months). Initial symptoms are non-specific (fever, headache, rash, muscle pain, and joint pain). Severe forms are more likely in patients with comorbidities, pregnant women, immunocompromised individuals, and people at extreme ages. Mortality for severe cases ranges from 0.5% to 1.3%. Chronic forms, which significantly affect quality of life, impact 20–60% of patients depending on the viral lineage and care quality.

#### Treatment

### There is no approved specific treatment for CHIKV. Management focuses on relieving symptoms and treating rheumatologic complications.

#### Vaccine

IXCHIQ, developed by Valneva, is the only approved chikungunya vaccine. It is a live-attenuated vaccine given as a single intramuscular dose. It has FDA and EMA approval for individuals aged 18 and older who are not immunocompromised.

## **Guidelines and practical information**

This section lists official manuals of recommendations for clinical practice or public health policy published by leading health organizations.

| CDC  | Information for traveller's : Chikungunya (2024)                                    |
|------|-------------------------------------------------------------------------------------|
| WHO  | Guidelines on Clinical Management of Chikungunya Fever (2019)                       |
| ECDC | Guidelines for mosquito surveillance                                                |
| PAHO | Preparedness and Response for Chikungunya Virus Introduction in the Americas (2011) |
| WHO  | Guidelines for prevention and control of Chikungunya fever (2009)                   |