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Review

# Chikungunya fever: Epidemiology, clinical syndrome, pathogenesis and therapy

Simon-Djamel Thiberville [a,b,*], Nanikaly Moyen [a,b], Laurence Dupuis-Maguiraga [c,d], Antoine Nougairede [a,b], Ernest A. Gould [a,b], Pierre Roques [c,d], Xavier de Lamballerie [a,b]

[a] UMR_D 190 "Emergence des Pathologies Virales" (Aix-Marseille Univ. IRD French Institute of Research for Development EHESP French School of Public Health), Marseille, France
[b] University Hospital Institute for Infectious Disease and Tropical Medicine, Marseille, France
[c] CEA, Division of Immuno-Virologie, Institute of Emerging Diseases and Innovative Therapies, Fontenay-aux-Roses, France
[d] UMR E1, University Paris Sud 11, Orsay, France

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ABSTRACT

Chikungunya virus (CHIKV) is the aetiological agent of the mosquito-borne disease chikungunya fever, a debilitating arthritic disease that, during the past 7 years, has caused immeasurable morbidity and some mortality in humans, including newborn babies, following its emergence and dispersal out of Africa to the Indian Ocean islands and Asia. Since the first reports of its existence in Africa in the 1950s, more than 1500 scientific publications on the different aspects of the disease and its causative agent have been produced. Analysis of these publications shows that, following a number of studies in the 1960s and 1970s, and in the absence of autochthonous cases in developed countries, the interest of the scientific community remained low. However, in 2005 chikungunya fever unexpectedly re-emerged in the form of devastating epidemics in and around the Indian Ocean. These outbreaks were associated with mutations in the viral genome that facilitated the replication of the virus in *Aedes albopictus* mosquitoes. Since then, nearly 1000 publications on chikungunya fever have been referenced in the PubMed database. This article provides a comprehensive review of chikungunya fever and CHIKV, including clinical data, epidemiological reports, therapeutic aspects and data relating to animal models for *in vivo* laboratory studies. It includes Supplementary Tables of all WHO outbreak bulletins, ProMED Mail alerts, viral sequences available on GenBank, and PubMed reports of clinical cases and seroprevalence studies.



**Contents**



* Corresponding author. Current address: UMR_D 190, Faculté de Médecine Timone, 5ème étage Aile Bleue, 27 Bd Jean Moulin, 13385 Marseille Cedex 05, France. Tel.: +33 91 32 44 20; fax: +33 91 32 44 21.
*E-mail address:* djamt@yahoo.fr (S.-D. Thiberville).

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## 1. Introduction

Chikungunya virus (CHIKV) is an arthropod-borne virus that is transmitted by *Aedes* (*Ae.*) mosquitoes. It was first isolated in 1952 in the Makonde Plateau of the southern province of Tanzania (former Tanganyika). The virus transmission cycle requires infection of female mosquitoes via a viraemic bloodmeal taken from a susceptible vertebrate host and, following a suitable extrinsic incubation period, transmission to another vertebrate host during subsequent feeding (Solignat et al., 2009). After an incubation period, most patients suffer from polyarthralgia and myalgia, with a significant impact on their quality of life. Chikungunya fever is characterised by a very high viraemic load and concomitant abnormalities such as pronounced lymphopenia and moderate thrombocytopenia. The rate of asymptomatic cases is lower, and the percentage of infected patients requiring medical attention is higher, than in most other common arboviral infections. After the acute stage, some patients experienced relapse, persistent arthralgia or musculoskeletal pains. Increase of age is the most obvious risk factor associated with severe disease or persistent symptoms in adults, whilst in paediatric populations, newborns have a higher risk of severe disease.

Since the first reports of chikungunya fever in Africa in the early 1950s, more than 1500 scientific publications on different aspects of the disease and its causative agent have been produced. Analysis of these publications shows that, following a number of studies in the 1960s and 1970s, and in the absence of autochthonous cases in developed countries, the interest of the scientific community remained low (Fig. 1). However, in 2005 chikungunya fever unexpectedly re-emerged in the form of devastating epidemics in and around the Indian Ocean. These outbreaks were associated with mutations in the viral genome that facilitated the replication of the virus in *Aedes albopictus* mosquitoes. Since then, nearly 1000 publications on chikungunya fever have been referenced in the PubMed database. The reader is referred to Supplementary Tables 1–6 for lists of all WHO outbreak bulletins, ProMED Mail alerts, viral sequences available on GenBank, and PubMed reports of clinical cases and seroprevalence studies.

Two distinct transmission cycles have been described for CHIKV: a sylvatic cycle in Africa and an urban human–mosquito–human virus transmission cycle seen in Asia, the Indian Ocean, Africa and more recently, in Europe. The two major vectors of the disease currently identified are *Ae. aegypti* and since 2006, *Ae. albopictus*. The important role of *Ae. albopictus* in recent outbreaks is

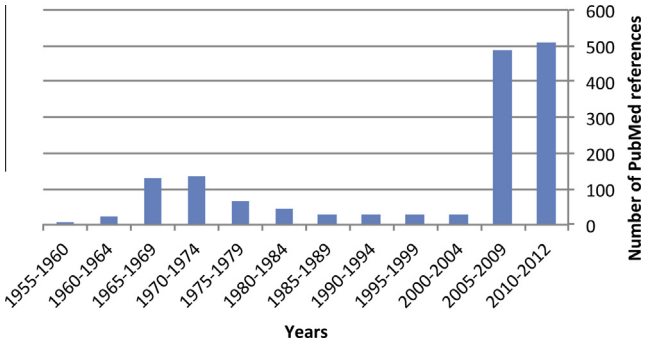


**Fig. 1.** Publications related to outbreaks of chikungunya fever in the PubMed database. Articles published between 1950 and September, 2012 were identified using the MeSH term "chikungunya," and are reported by 5-year periods.