

Chikungunya

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Chikungunya

Summary

- Togavirus family, genus alphavirus
- Vector: mosquito, *Aedes* species
- Main clinical presentation: arthralgia/ rash, febrile disease (AR, FD), frequently post-Chikungunya rheumatic syndrome

Virus

Chikungunya virus (CHIKV) is a single-strand RNA virus of positive polarity; its genome encodes 4 non-structural (nsP1-4) and three structural proteins (C, E1, E2). Phylogenetically, there are 3 distinct genotypes: the West African, the Asian and the Eastern-Central-South African genotype.

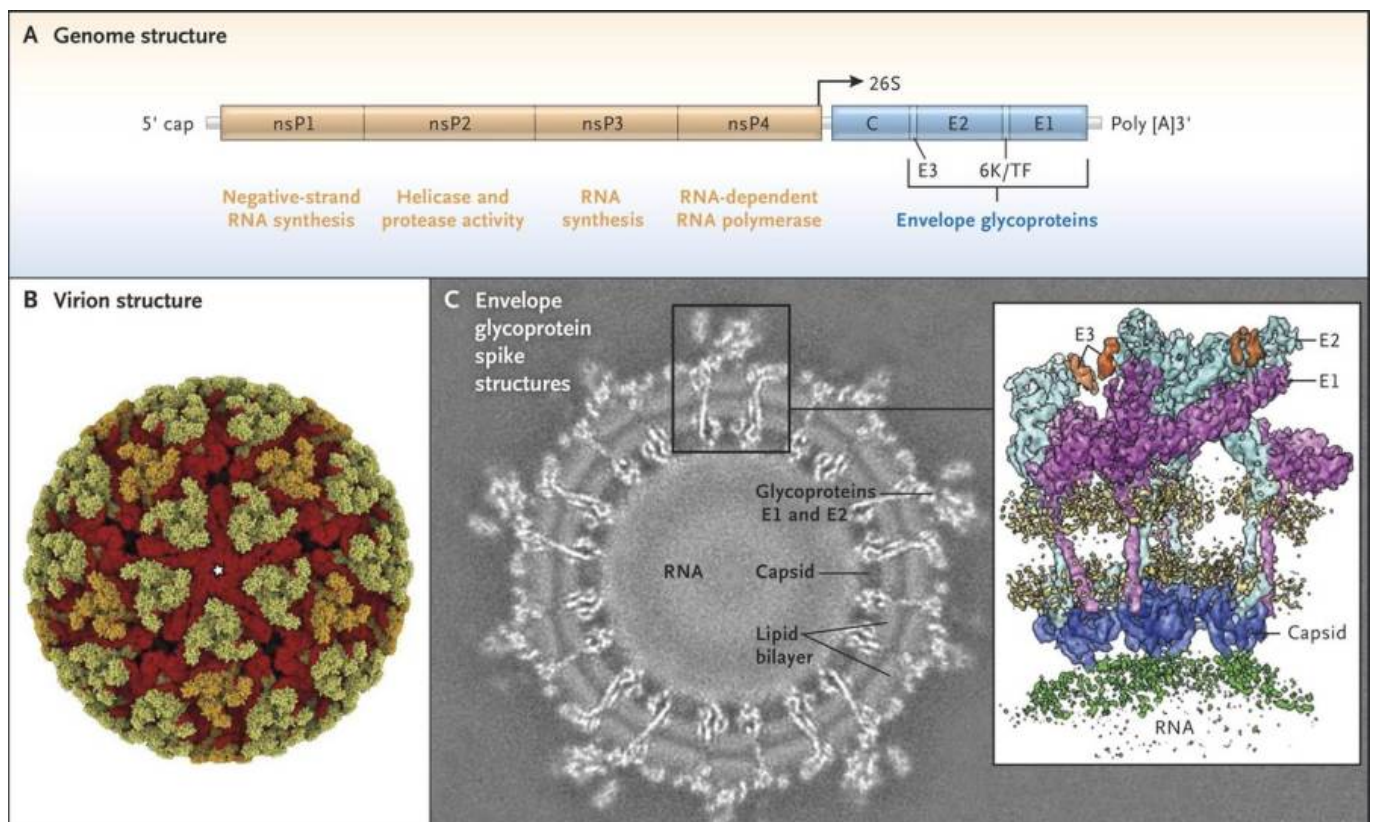


Figure: Structure of Chikungunya virus (Weaver et al, NEJM)

Transmission

Chikungunya virus was isolated during an epidemic in Tanzania in 1952 from both patients and mosquitoes. It has since been isolated frequently from humans and mosquitoes in tropical Africa, India and Southeast Asia, where large epidemics occur from time to time. Non-human reservoir species have not been identified unequivocally. Both *Aedes aegypti* and *A. albopictus* are vectors.

In 2004, there was an outbreak of Chikungunya fever in Kenya. The next year it reached the Comores. In 2005-6, outbreaks followed in Reunion (with 265,000 clinical cases out of a population of 770,000), Mauritius, Madagascar and other islands in the Indian Ocean. In Reunion, mortality was 237 deaths, about 1 per 1000 clinical cases. A single mutation (A236V) was identified in chikungunya virus strains in the 2005-2006 Reunion Island outbreak, that facilitated transmission by the Asian tiger mosquito (*A. albopictus*). CHIKV was capable of spreading via travellers, as was witnessed in July 2007, when about 160 people in Ravenna province, Italy fell ill. This was the first example of Chikungunya transmission via exotic mosquitoes (*Aedes albopictus*) outside the tropics.

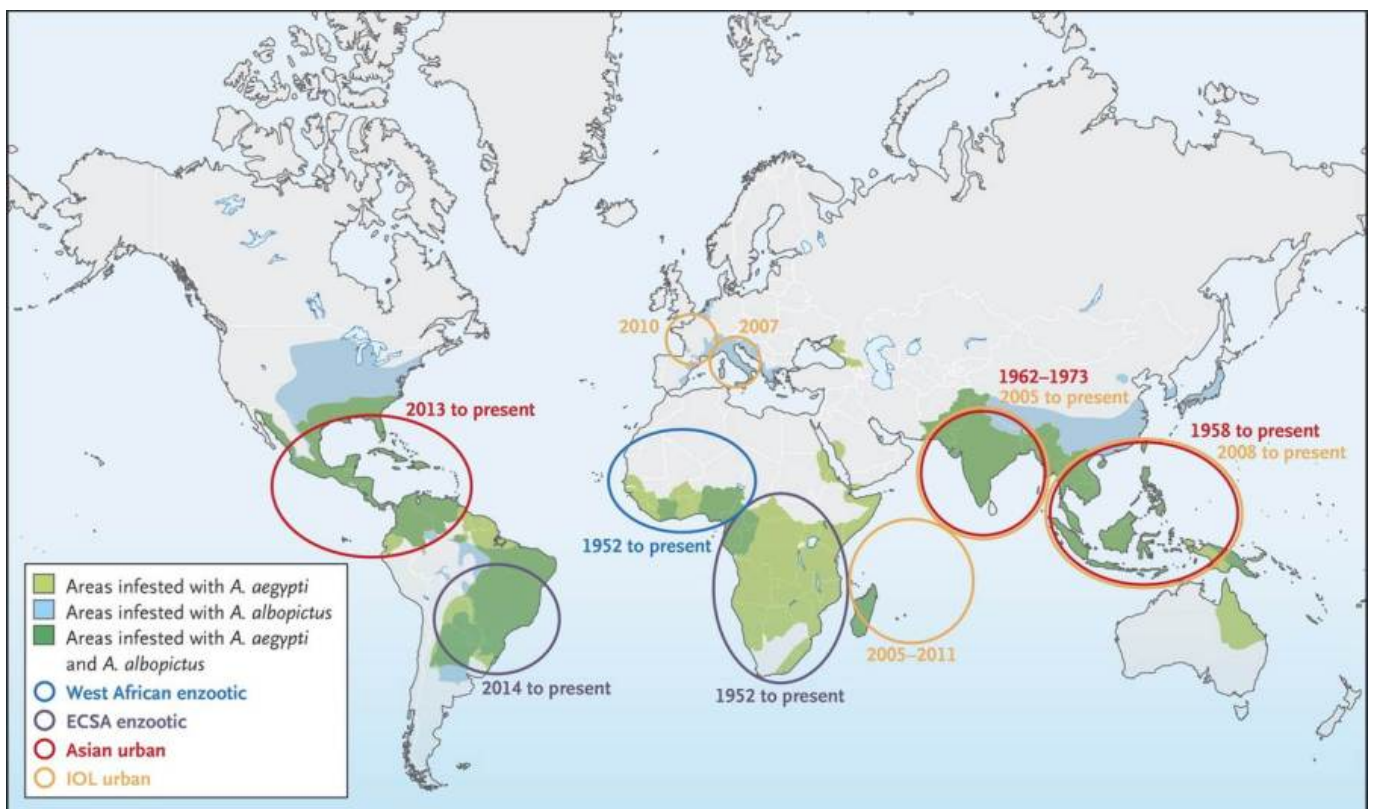


Figure: Distribution of Chikungunya (Weaver et al, NEJM)

Contrary to expectations and reports of introduction of so-called Indian Ocean Lineage of the ECSA genotype by travellers into the Americas, it was an Asian-lineage Chikungunya virus strain that caused a major epidemic in the Americas. The strain was introduced into the island of St. Martin in October 2013.

Clinical aspects

The clinical picture resembles that of classic dengue fever with which chikungunya fever is often confused. After a brief incubation period of 2 to 5 days, there is sudden onset of fever followed by crippling joint pains that may temporarily incapacitate the patient. In the Makonde language, “chikungunya” means “doubled up; that which bends up”, referring to this important arthralgia. Conjunctivitis and skin rash are common. Arthralgias occur in around 70 percent of cases and can persist for weeks to months. If no complications ensue, recovery takes 5 to 7 days. New severe clinical forms were reported in Reunion, including cases caused by peripartum mother-to-infant transmission. Rare complications include meningoencephalitis (also in newborns) and probably hepatic failure (possible role of high doses of acetaminophen). Common hematologic abnormalities in the acute phase include lymphopenia and thrombocytopenia that may lead to bleeding. Hepatic enzymes are commonly increased.

Chronic joint pains can be persistent or relapsing. These arthralgias are located mostly in the distal joints and may be associated with arthritis and may mimic rheumatoid arthritis (chronic inflammatory, erosive, and rarely deforming polyarthritis) in up to 50% of patients.

Diagnosis

Diagnosis in endemic areas is clinical, although it is very difficult to discriminate from co-circulating arboviral infections. A definitive diagnosis relies on virus detection through reverse-transcriptase-polymerase-chain-reaction (RT-PCR) testing during the viraemic phase (the first week). RT-PCR can be designed in a multiplex format to simultaneously detect several other arboviruses, such as dengue virus, which can be very useful for triage of patients. Chikungunya virus culture in a variety of cells permits further virologic characterization but has no added value over RT-PCR in clinical practice and is not performed routinely.

Sero-diagnosis is facilitated by the limited antigenic diversity of chikungunya virus and extensive cross reactivity of the antibodies induced by different strains. Serum IgM is detectable from day 5 (and even earlier) to several months after the onset of illness and is also considered diagnostic. Seroconversion can also be detected as a fourfold increase in IgG between acute-phase and

convalescent-phase serum samples.

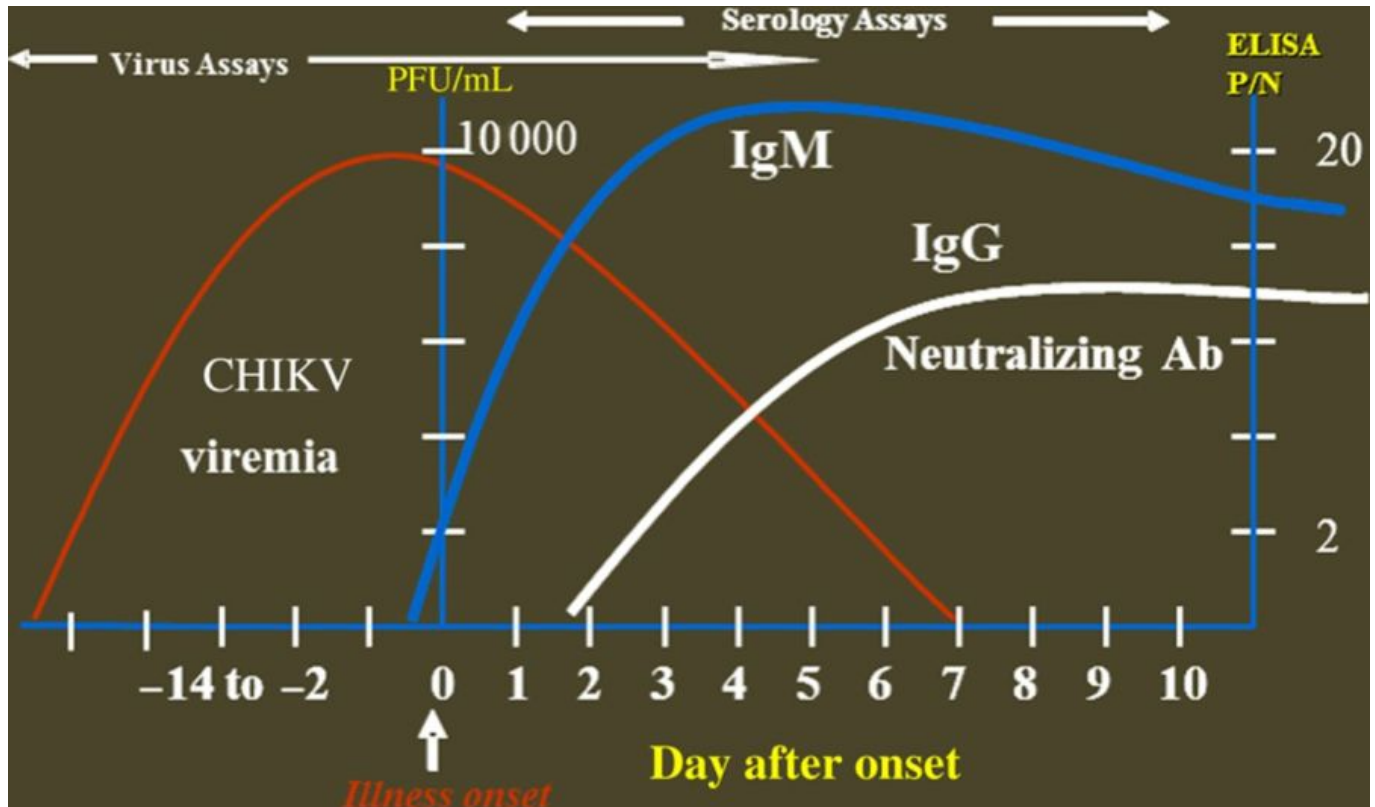


Figure: Chikungunya diagnostics in relation to kinetics of viremia and antibody response (Johnson et al, J Infect Dis)

Treatment

Treatment is symptomatic. Post-chikungunya rheumatism may require long-term treatment with nonsteroidal anti-inflammatory drugs or Disease Modifying Anti Rheumatic Drugs (DMARDs) such as methotrexate, although their safety and efficacy also have yet to be demonstrated in clinical trials.