

Caribbean Chikungunya outbreak should move vaccine back onto the agenda

LONDON, UK----24th June 2014----ExpertREACT. The cyclical pattern of Chikungunya outbreaks and low case fatality rate when compared to other vector borne diseases e.g. JE, dengue and yellow fever has historically lowered priority for vaccine development. This may change with the latest disease resurgence in the Caribbean; close to Brazil and the continental US.

Chikungunya (CHIK) is an RNA alphavirus transmitted by *Aedes* spp. mosquitoes which causes an acute illness characterized by fever, headache and severe arthralgia (joint pain). The latter can last longer than 12 months. On rare occasions, CHIK infection may lead to neurologic and hepatic disease with high illness and mortality rates. CHIK, first described in 1952 in modern day Tanzania and in Asia in 1958, is endemic in Africa and Southeast Asia with unpredictable outbreaks occurring at irregular intervals of between 7 to 20 years. Since 2005, CHIK outbreaks have been reported in several countries with major epidemics occurring in India (2006), several Indian Ocean islands (Reunion), Indonesia, Malaysia and Gabon. Recently, CHIK outbreaks have also occurred in previously CHIK free countries, including China, Papua New Guinea, Laos, New Caledonia, Bhutan and the Americas (Caribbean).

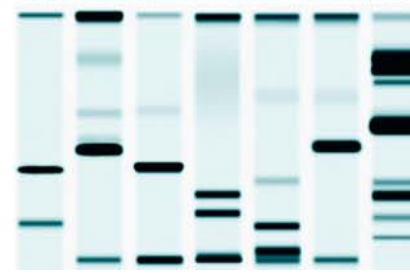
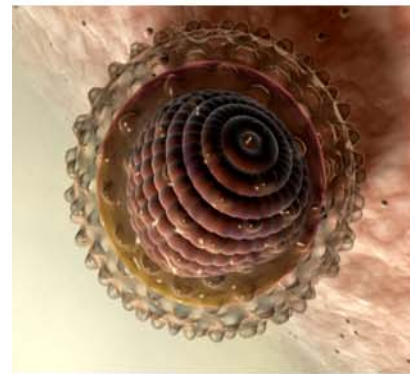
CHIK infection is difficult to diagnose because it is often subclinical and symptoms mimic those of dengue fever and other alpha virus infections. Specific diagnosis requires laboratory confirmation with serology been the most widely used method (CHIK IgM can be detected as 3-6 days after clinical onset). In response to recent outbreaks, several countries/territories have made CHIK notifiable including Singapore, Australia, Thailand and Hong Kong. Reporting became mandatory in France in 2006 and a system for the early identification of imported cases was introduced in 2008 in areas where *Aedes albopictus* exists (mainly the southern coast). CHIK is not notifiable in the United States although cases can be reported to ArboNET, the national surveillance system for arthropod-borne diseases.

CHIK is not generally considered a life-threatening disease, with an estimated case-fatality rate of 0.1% based upon the outbreak in Reunion Island (1). However, the increasing spread of its geographical range is of concern due to the high morbidity associated with infection and so its potential burden on productive members of society. The first documented outbreak in the Americas, which first occurred in December 2012 is particularly striking. As of June 17, 2014 nineteen Caribbean islands had reported local transmission of the virus, meaning mosquitoes in the area were infected and facilitating transmission to people (known as autochthonous transmission) (2).

Data produced by the Pan American health organisation (PAHO) (updated June 13, 2014) lists >170,000 suspected cases in the Caribbean, 4,576 of which are confirmed with 14 deaths (2). The majority of suspected cases have been recorded in the Dominican Republic, Guadeloupe and Martinique. Because transmission is rampant in the region, US travellers have brought the virus home to the continental US in at least 12 states, mostly Florida (3). Although currently no transmission between people in the US has been documented, this is highly probable because *Aedes albopictus* mosquitoes are widely distributed in the US. Moreover, autochthonous (native) transmission has previously occurred in north-east Italy in 2007, south-eastern France in 2010 proving such a phenomenon can occur in temperate countries.

What is the next step for Chikungunya virus? And should we be worried? Epidemiologists suspect that it is inevitable that autochthonous CHIK transmission will occur in LATAM following the outbreak in the Caribbean. The LATAM region has high-density mosquito populations and immunologically uninfected CHIK populations. *Aedes aegypti*, the primary CHIK virus vector in India and South-East Asia, is also a vector for dengue in most of Central and South America. The first autochthonous CHIK outbreak in South America (French Guiana) was confirmed in 2014; the first recorded imported CHIK infection occurred in Brazil in 2010. Thus the pre-requisites for autochthonous CHIK transmission (vectors, returning viremic travelers and climatic conditions) are present in large areas of Central and South America. Additionally, Brazil is at high risk of an imported outbreak as it is the host nation for the 2014 FIFA World Cup (June/July 2014) and the Olympics (2016).

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Moreover, a recent article in Eurosurveillance stated (4):

“Further spread and establishment of the disease in the Americas is likely, given the high number of people travelling between the affected and non-affected areas and the widespread occurrence of efficient vectors.”

There is no specific treatment for CHIK infection. Current prevention of CHIK infection relies on avoidance of mosquito bites and elimination of mosquito breeding sites. Because *Aedes* mosquitoes are primarily aggressive daytime feeders mosquito nets are of little value.

A live-attenuated CHIK vaccine was being developed by the US Army but discontinued due to operational reasons (5). The vaccine was shown to immunogenic and well tolerated, although some CHIK vaccinees developed transient mild arthralgia following a single subcutaneous dose. Recent reports have indicated that the US Army transferred the vaccine technology to five (undisclosed) vaccine manufacturers which may soon progress the candidate to clinical trials (5). Other programs include a VLP vaccine being developed by the National Institute of Allergy and Infectious Diseases (NIAID), which is apparently available for licensing. Also in November 2013, THEMIS (Austria) and Institut Pasteur also began a Phase I trial (6) with a recombinant measles VLP vaccine which has recently reported positive data.

Chikungunya is undergoing a resurgence, but those countries that have recently experienced large epidemics such as India, enter a silent phase due to acquisition of population wide herd immunity. This cyclical pattern and long intervals between outbreaks have in part historically dampened efforts to develop a vaccine due to uncertain market demand. Thinking may change if local transmission occurs in Brazil, or even the continental United States. Vaccine developers should heighten their interest level in a Chikungunya vaccine.

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References and Notes:

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