

CDAlert

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CHIKUNGUNYA FEVER

INTRODUCTION

Chikungunya is a relatively rare form of viral fever caused by an alpha virus that is spread by bite of *Aedes aegypti* mosquito. The name is derived from the Swahili word meaning 'that which bends up' in reference to the stopped posture developed as a result of the arthritic symptoms of the disease. Symptoms of chikungunya fever can include sudden onset of fever, chills, headache, nausea, vomiting, joint pain with or without swelling, low back pain, and rash. This disease is almost always self-limiting and rarely fatal.

Chikungunya (CHIK) virus was first isolated from the serum of a febrile human in Tanganyika (Tanzania) in 1953. Between 1960's and 1980's the virus was isolated repeatedly from numerous countries in Central and Southern Africa as well as in Senegal and Nigeria in Western Africa. During this period, the virus was also identified in many areas of Asia. Since 1953, CHIK virus has caused numerous well documented outbreaks in Africa and South Eastern Asia, involving hundreds of thousands of people.

AETIOLOGY

Chikungunya virus is a Group IV (+) (RNA) virus belonging to family *Togaviridae* with genus *Alphavirus* and species *Chikungunya*. Several other togaviruses of the alphavirus genus (Ross river, Onyongnyong etc.) have been associated with similar syndrome.

TRANSMISSION

Chikungunya virus is most commonly transmitted to humans through the bite of an infected mosquito, specifically mosquitoes of the *Aedes* genus, which usually bite during daylight hours.

In Africa, CHIK virus appears to be maintained in sylvatic cycle involving wild primates and forest dwelling *aedes* spp. mosquitoes. Serological studies have repeatedly demonstrated the presence of antibodies in humans and primates throughout the moist forests and semi arid savannas of Africa. A vertebrate reservoir or sylvan transmission cycle has not been identified outside Africa, supporting the historical evidence that CHIK virus originated in Africa and was subsequently introduced into Asia where it is now typically associated with *Aedes aegypti* mosquitoes. Strains from Africa and Asia are reported to differ biologically indicating that distinct lineage may exist.

CLINICAL FEATURES

Chikungunya is an acute viral infection of abrupt onset, heralded by fever and severe arthralgia, followed by other constitutional symptoms and rash and lasting for a period of 1-7 days. The incubation period is usually 2-3 days, with a range of 1-12 days. Fever rises abruptly often reaching 39 to 40 degree centigrade and accompanied by intermittent shaking chills. This acute phase lasts 2-3 days. The temperature may remit for 1-2 days, resulting in a 'saddle back' fever curve.

The arthralgias are polyarticular, migratory and predominantly affect the small joints of hands, wrists, ankles and feet with lesser involvement of larger joints. Pain on movement is worse in the morning improved by mild exercise, and exacerbated by strenuous exercise. Swelling may occur but fluid accumulation is uncommon. Patients with milder articular manifestation are usually symptom free within a few weeks, but more severe cases require months to resolve entirely. Generalized myalgias as well as back and shoulder pain is common.

Cutaneous manifestations are typical with many patients presenting with a flush over the face and trunk. This is usually followed by a rash generally described as maculopapular. The trunks and limbs are commonly involved but face, palms and soles may also show lesions.

During the acute disease, most patients will have headache, but it is not usually severe. Photophobia and retroorbital pain may also occur. Conjunctival infection is present in some cases. Some patients will complain of sore throat and have pharyngitis on examination.

Although rare, the infection can result in meningo-encephalitis especially in newborns and those with pre-existing medical conditions. Pregnant women can pass the virus to their fetus. Severe cases of Chikungunya can occur in elderly, in the very young (newborns), and in those who are immuno-compromised. Chikungunya outbreaks typically result in several hundreds or thousands of cases but deaths are rarely encountered.

Differential diagnosis of chikungunya include Dengue and dengue haemorrhagic fever, Onyong-nyong virus infection and Sindbis virus infection.

MANAGEMENT OF CASES

There is no specific treatment for Chikungunya. The illness is usually self

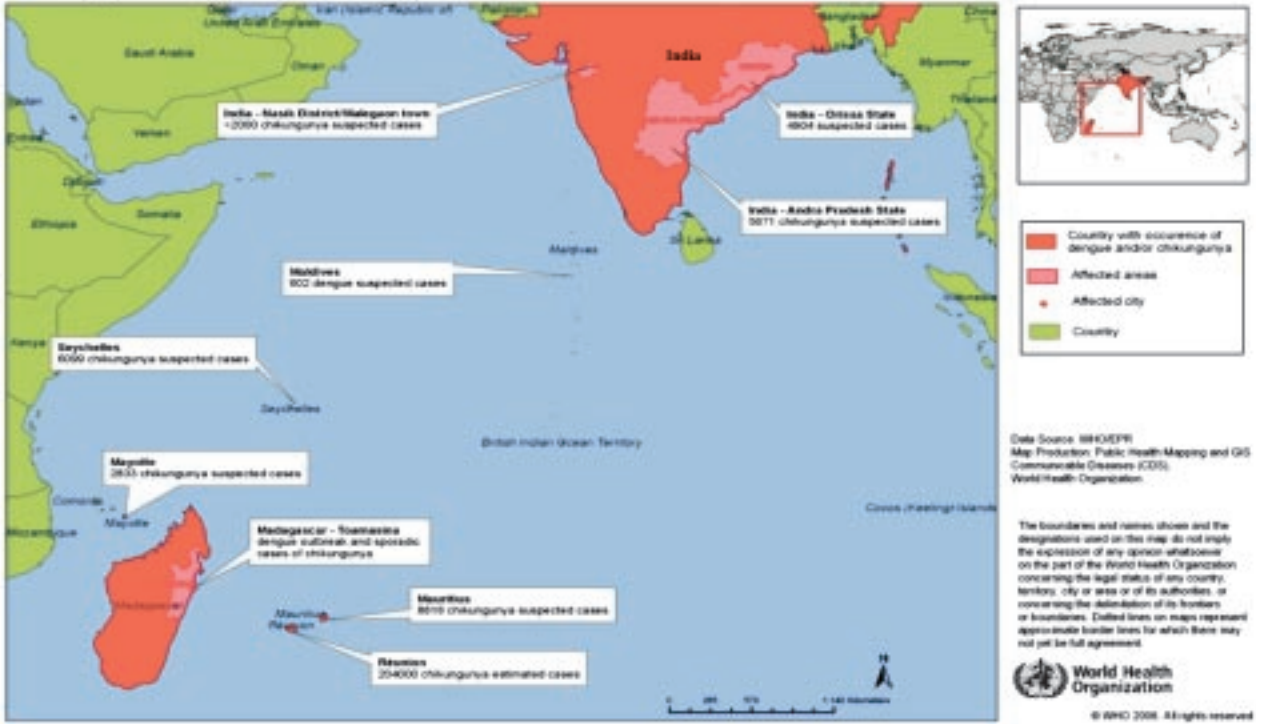
limiting and will resolve with time. Supportive care with rest is indicated during the acute joint symptoms. Movement and mild exercise tend to improve stiffness and morning arthralgia, but heavy exercise may exacerbate rheumatic symptoms. Non aspirin and non - steroidal anti inflammatory drugs are recommended. In unresolved arthritis refractory to NSAID, chloroquine 250mg is recommended.

EPIDEMIOLOGY

Global

Africa - CHIK virus is transmitted in the savannah and forests of tropical Africa by aedes mosquito that belong to the subgenera Stegomyia (Aedes africanus, Aedes luteocephalus, Aedes opok) and Diceromyia (Aedes furcifer, Aedes taylori, Aedes cordellieri). The vertebrate portion of the cycle is provided by non-human primates such as cercopithecus, monkeys or baboons which amplify and maintain virus circulation. It is thought that endemic circulation and moving epidemics in troops of primates are responsible for survival of the virus and local spillover into human population. In African villages, or rural areas these mosquitoes may then infect humans and the substantial viraemia measure suggest that humans, in appropriate setting may contribute to mosquito infection, leading to further virus amplification. This becomes particularly important when domestic breeding of Aedes aegypti is present in large numbers, a situation that may lead to village and large urban epidemics in Africa. The prototype CHIK epidemic which occurred in Tanzania in 1952 to 1953, resulted when Aedes aegypti borne disease moved through multiple villages over an expanse exceeding 5000 km. Another interesting feature of CHIK epidemiology was observed from Tanzania. In studies of individual dwellings, there was a highly significant trend for multiple cases to occur in a hut once a single case occurred. This of course, could be reflection of flight

Chikungunya and Dengue - Indian Ocean update. Status as of 17 March 2006



range of *Aedes aegypti* vectors and human habits but also is a phenomenon that could occur as a result of mechanical transmission or interrupted feeding of competent biological vectors.

Asia - Transmission in Asia follows a different pattern from that seen in Africa, being primarily transmitted from human to human by *Aedes aegypti*. Although Asian monkeys develop significant viraemia after CHIK inoculation and have been found to harbour antibodies to CHIK, they have never been shown to participate in any important way in the maintenance or amplification of the virus in the continent. CHIK activity in Asia has been documented since its isolation in Bangkok, Thailand in 1958. Other south-east Asian countries which have experienced Chikungunya outbreaks include Cambodia, Vietnam and Burma. A series of epidemics usually lasting a single year have been reported from Sri Lanka and India. Antibodies surveys indicate that CHIK has been active further east in the Pacific including Indonesia and Philippines. The first CHIK virus isolation was in Thailand from Bangkok in 1958 in a setting of intense

dengue virus activity. Antibodies surveys indicated that virus continued to be transmitted until 1962 to 1964. During this period, human infections occurred at formidable rates in Bangkok area and its environs. In 1962, an estimated 40,000 patients sought medical attention in the urban complex of 2 million inhabitants. This intensive transmission was accomplished by large population of *Aedes aegypti* breeding in water storage jars ubiquitous in Thai homes as a consequence of the lack of piped water distribution system. These mosquitoes, biting voraciously indoors, had infection rates of 0.8 to 1.4 per 1000. Similar conditions were observed through mid-1970s, before CHIK transmission nearly disappeared. CHIK antibodies were rare in Bangkok children born after 1976, and virus isolation was not obtained from febrile outpatients and haemorrhagic fever suspects tested in 1979 to 1980. The reasons for the decline in the CHIK transmission are unclear because *Aedes aegypti* were abundant and dengue transmission continued. In 1988, evidence of CHIK transmission in Thailand was obtained once again. But the subsequent

CHIKUNGUNYA OUTBREAKS IN INDIA

Year	Locality	Important Characteristics	Reference
1963	Calcutta	<ul style="list-style-type: none"> ➤ Cases in lakhs ➤ 37% haemorrhagic manifestation ➤ Approx. 200 deaths 	ICMR Bulletin, May 1980
1964	Madras	<ul style="list-style-type: none"> ➤ Cases in lakhs ➤ 5.8% haemorrhagic manifestation 	Sarkar et al IJMR 1964 (52); 651-660
1973	Maharashtra	<ul style="list-style-type: none"> ➤ small outbreak ➤ no haemorrhagic manifestation 	
2005*	Andhra Pradesh	<ul style="list-style-type: none"> ➤ 6421 cases ➤ no haemorrhagic manifestation & deaths 	Investigation reports, NICD, Delhi
	Maharashtra	<ul style="list-style-type: none"> ➤ 34725 cases ➤ no haemorrhagic manifestation & deaths 	
	Karnataka	<ul style="list-style-type: none"> ➤ 18529 cases ➤ no haemorrhagic manifestation & deaths 	

*Ongoing

pattern has been one of the occasional outbreaks rather than severe epidemic disease.

India

India, in 1963, experienced an outbreak of viral haemorrhagic fever in Calcutta. Chikungunya virus was responsible for extensive dengue-like infection with occasional haemorrhagic manifestation. Sarkar and his colleagues isolated Chikungunya virus from cases with severe haemorrhagic manifestation.

An epidemiological study was made as one part of a multidisciplinary investigation of an epidemic of a severe febrile illness, sometimes associated with haemorrhagic manifestations and occasionally terminating in death. It began in July, became serious in August, reached a peak in November and then rapidly declined by December coincident with the end of the monsoon rains. Data from hospital records and death registers are consistent in showing that serious cases were most frequent among infants and young children, least frequent among young adults, and frequent again among adults over 40 years of age. By contrast, data from home visits suggested that milder illnesses may have been of

nearly equal frequency among children and adults, leading to a hypothesis that there was an association between age and the likelihood that an infection will eventuate in serious illness or death. It was not possible to make any reasonably precise estimate of the number of infections and mild illnesses that occurred during the course of this epidemic. However, they must have been in lakhs. Similarly, it was not possible to obtain a precise count of the number of cases requiring hospitalization, because the medical profession was unprepared to make definitive diagnosis but they may have numbered in thousands. Examination of death registers revealed that this epidemic may have resulted in nearly 200 deaths within the corporate limits of Calcutta. Thirty-five of the 36 virus isolates from intracerebral inoculation of suckling mice were identified as chikungunya by 'Quick' CF test. One was tentatively recognized as a Group B virus.

The origin of this epidemic remains unknown, although purely circumstantial evidence suggests an introduction from endemic centers in the countries of south east Asia. Calcutta, an important air and sea port, provides an optimal opportunity for any such introduction.

The epidemic occurring in southern India

(Vellore, Madras, Pondicherry) in 1964, provided a glimpse of another pattern of CHIK transmission in Asia which was particularly well documented because Vellore was the site of on-going dengue studies. Retrospective serological work showed that CHIK had not been active in Vellore and Madras areas for about 30 years, although Calcutta had experienced epidemic transmission the previous year. As the rainy season progressed into July, August and September, *Aedes aegypti* population increased to peak. By the end of October, only occasional human cases were seen. Numbers of *Aedes aegypti* decreased further with cool temperatures and drier weather. Same transmission season had been seen with dengue in previous years. Febrile illness usually accompanied by characteristic joint pains, varied from 8% to 86% in different neighbourhoods and correlated with *Aedes aegypti* density. Males and females were equally affected but the clinical attack rates were lower in infants. It is difficult to accurately assess the impact on Vellore but it was substantial. There were 288 laboratory confirmed CHIK infections from whom 233 virus isolations were made including one infant that died.

The activity of Chikungunya virus appeared to decline during the period 1965 to 1972. In 1973, a small localized outbreak was reported from Barsi, Sholapur district, maharashtra state. This happened after eight years of relative quiescence the cause which remains to be understood. No outbreaks were reported from India after 1973 till 2005. The human epidemics have all been in urban areas infested with *Aedes aegypti*. The role of non-human hosts in natural cycle of this virus needs further investigation.

CURRENT SCENARIO – RE-EMERGENCE OF CHIKUNGUNYA INFECTION

Global

The outbreak of Chikungunya was

discovered in Port Klang in Malaysia in 1999 affecting 27 people. From 27th February, 2005 - 28 March 2006, 3115 cases of Chikungunya have been notified by 31 physicians from a sentinel network on La Reunion. Estimations from a mathematical model evaluate that about 2,04,000 people may have been infected by Chikungunya virus since March, 2005 on La Reunion. The presenting clinical symptoms were consistent with Chikungunya infection. Since the beginning of January 2006, other countries in the South West Indian Ocean have reported Chikungunya cases: Mayotee (9 January - 10 March, 2833 suspected cases), Mauritius (1 January - 5 March, 6000 suspected cases including 1200 confirmed cases) and the Seychelles (1 January - 26 February, 8818 suspected cases). Several European countries have reported imported cases in people returning from these islands: France (160 imported cases), Germany, Italy, Norway and Switzerland.

India

After quiescence of about three decades an outbreak of Chikungunya with sporadic cases of dengue is being reported from different parts of India. A total of 6421 cases of fever have been reported from districts of Rayalseema, Nalagonda and Hyderabad in the state of Andhra Pradesh since December 2005. The attack rate varied from 2.3 to 39.1%. 386 sera samples were collected and tested at National Institute of Virology (NIV), Pune. Six samples were positive for IgM antibodies to dengue and 139 samples for IgM antibodies to Chikungunya virus by MAC ELISA. 86 samples were tested at NICD, of which 3 were positive for dengue IgM antibodies and 43 showed HI antibodies for Chikungunya virus in high titres. Out of the 10 samples tested, seven were positive for chikungunya by RT-PCR. There was increase in incidence of fever cases in Maharashtra since December 2005. 258 villages from 15 districts have reported 34,725 fever cases

till 5th April, 2006. Representative samples were collected from Malegaon, Nasik district, Beed and Latur districts. Of the 68 samples tested, 13 showed high titres of HI antibodies against Chikungunya virus and 3 were positive for IgM antibodies to Dengue virus. Similarly, 18,529 cases of fever with arthritis/arthralgia cases have been reported from seven districts (Gulbarga, Bidar, Bellary, Raichur, Tumkur, Koppal, and Chitrdurge) of Karnataka State since December 2005. Attack rate varied from 4 - 45% in different affected villages. Out of 76 sera samples collected from Bidar, 43 show IgM antibodies against Chikungunya virus at NIV Pune. None were positive for Dengue. Seven paired sera samples were tested at NICD. Of these four showed four fold difference in HI antibody titre confirming the diagnosis of Chikungunya.

Attack rates in affected States

States	Attack rate in different affected villages
Andhra Pradesh	2.3 – 39.1%
Karnataka	4 – 45%

In these States, the onset of illness has been observed to be acute with moderate to high fever, chills and associated joint pain. The joints affected are knee, ankle, wrist, elbow and small joint of hands. Lymphadenopathy and rash are not significant presentations. All ages and both sexes are affected with preponderance above 15 years age. No death due to this disease has been reported. Three to four cases from the same family report illness in 2-3 days duration. Cases have been reported from urban and peri-urban area. The piped water supply in these areas is only for half an hour duration forcing people to adopt water storage practices mainly in big cement and plastic tanks. These containers act as potential breeding places for *Aedes aegypti*. Entomological survey carried out in most affected area revealed high House, container and Breteau *Aedes* indices. The outbreak is currently on-going.

LABORATORY DIAGNOSIS

Though definitive diagnosis can only be made by laboratory means, Chikungunya should be suspected when epidemic disease occurs with characteristic triad of fever, rash and rheumatic manifestations.

Case definition

Suspect case

An acute illness characterized by sudden onset of fever with several of the following symptoms: joint pain, headache, backache, photophobia, arthralgia, rash.

Probable case

As above and positive serology (when single serum sample is obtained during acute phase or during the convalescence).

Confirmed case

A probable case with any of the following:

- Four fold HI antibody difference in paired serum samples.
- Detection of IgM antibodies
- Virus isolation from serum.
- Detection of Chikungunya virus nucleic acid in sera by RT-PCR.

Laboratories working on Chikungunya

1. National Institute of Virology, Pune
2. National Institute of Communicable Diseases, Delhi

Laboratory tests

Serological diagnosis

Virus specific IgM antibodies are readily detected by Capture ELISA in patients recovering from Chikungunya infection and they persist in excess of 6 months. No commercial tests are yet available.

Haemagglutination Inhibition (HI) antibodies appear with the cessation of viremia. All patients will be positive by day 5 to 7 of illness. Neutralization antibodies parallel HI antibody. The antigen for HI Test is available from NIV, Pune.

Collection, storage and transportation of sample

Laboratory diagnosis depends on the quality of sample and the time when the sample is obtained during the course of the disease.

For serology

Acute sample - collected upto 5 days after the onset of illness. Convalescent or paired sample should be collected 10 - 14 days after the first sample.

For isolation of the virus and RT-PCR

Blood for isolation of virus and RT-PCR should be collected within first 5 days of illness. These samples should be immediately transported (within 48 hours) to the referral laboratory in cold preferably frozen.

Transportation

Transport specimens to the laboratory at 2 – 8°C as soon as possible. Do not freeze whole blood, as haemolysis may interfere with serology test results.

If more than 24 hours delay is expected before specimen can be submitted to the laboratory, the serum should be separated from the red blood cells and stored frozen.

Vector of Chickungunya

Aedes aegypti mosquitoes are considered as vector of chickungunya virus. The vector bites humans during day time. It breeds in several types of domestic and peri-domestic water containers (metallic, plastic, rubber, cement, earthen materials, etc). This mosquito is mainly found in urban areas but during past 2 decades, due to developmental activities, it has spread to many rural areas of the country. The best way to control *Aedes aegypti* population is source reduction i.e. prevention of mosquito breeding in and around human habitation. This can be achieved by weakly change of water in water containers like coolers and other domestic vessels. Special care should

be taken to prevent accumulation of junk around human habitation and stagnation of rain water in discarded containers.

PREVENTION AND CONTROL

There is no vaccine or specific medication available against *Chikungunya* infection. Vector control is thus very important in controlling or preventing *Chikungunya* transmission. Elimination of breeding sites, or source reduction is an effective method of control. *Aedes aegypti* is typically a container habitat species and breeds primarily in artificial container and receptacles.



Aedes Mosquito

Control of mosquito breeding

- All water tanks, cisterns, barrels, trash containers, etc. need to be covered tightly with a lid.
- Remove or empty water in old tyres, tin cans, buckets, drums, bottles or from other places where mosquitoes breed.
- Clogged gutters and flat roofs that may have poor drainage need to be checked regularly.
- Water in bird baths and plant pots or dip trays should be changed at least twice each week.
- Pets water bowls need to be emptied daily.
- In ornamental water tanks/garden, larvivorous fish (e.g. gambusia, guppy) need to be introduced. They eat mosquito larvae.
- Weeds and tall grass should be cut short; adult mosquitoes look for these shady places to rest during the hot daylight hours.

- In case water containers cannot be emptied on daily/weekly basis, Temephos (1 ppm) should be applied.

Protection from mosquito bites

- Insecticide treated mosquito curtains/nets should be used. Especially children should sleep under ITNs during daytime.
- Insecticide spray should be done to kill mosquitoes. For knockdown effect, well planned fogging operations is strongly recommended with 2% pyrethrum space spray in high risk villages/wards where clustering of cases has been reported.

Surveillance

Epidemiological and entomological surveillance needs to be intensified. Reporting of fever cases is to be monitored closely.

Active surveillance by health workers using the case definitions for 'cases presenting with acute fever associated with arthralgia/arthritis (Painful and stiff joints) is recommended to detect new cases early for treatment. This will help in identifying affected areas so that control measures may be initiated.

Vector surveillance (both adult and aquatic stages of mosquitoes) should be intensified. This will help in identifying high risk areas for initiating control measures and assessing impact.

Medical and health institutions, professional associations, private practitioners, NGOs should be involved for fever reporting and proper case management.

IEC activities

IEC activities are crucial for community sensitization and participation. People need to be educated about the disease, mode of its transmission, availability of treatment and adoption of control measures. The activities have to be identified particularly to effect changes in practice of storage of water and personal protection. They should also be reassured that this a preventable disease. People should be encouraged to use personal protective measures in the form of full sleeve clothes, use of mosquito repellent and insecticide treated mosquito net (even while sleeping during daytime)/curtains etc. They should be advised to cooperate in fogging and take measures for eliminating breeding places. Community ownership has to be encouraged in the long term for sustaining low larval and adult densities of mosquitoes and use of personal protection measures.

Special campaigns may be carried out with the involvement of mass media including local vernacular newspapers/magazines, radio and TV as well outdoor publicity like hoardings, miking, drum beating, rallies etc. Health education materials should be developed and widely disseminated in the form of posters, pamphlets, handbills. Inter-personal communication through group meetings, traditional/folk media particularly must be optimally utilized. Involvement of NGOs, Faith Based Organizations, Community Based Organizations, Women's Self-Help Groups, professional associations like Indian Medical Association, Nehru Yuvak Kendras, NSS/NCC units in schools and colleges in control activities should be promoted actively.

...about CDAlert

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Chief Editor: Dr. R. K. Srivastava

Editorial Board: Dr. Shiv Lal, Dr. R. L. Ichhpujani, Dr. Shashi Khare, Dr. A. K. Harit

Guest Editor: Dr. Veena Mittal, Dr. Mala Chabra & Dr. Saxena

Publisher: Director, National Institute of Communicable Diseases, 22 Sharnath Marg, Delhi 110 054

Tel: 011-23971272, 23971060 Fax : 011-23922677

E-mail: dinricd@bol.net.in and dinricd@del3.vsnl.net.in

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