Chikungunya fever (CF) is a viral illness caused by an arbovirus transmitted by the Aedes mosquitoes. The disease is supposed to have its origin in the African wild (more precisely from Tanzania in 1952). The name is derived from the “makonde” dialect, which means “to bend up.” The most commonly quoted epidemic had happened in the French territory of Reunion islands in Indian Ocean. The disease has now been reported from various World Health Organization (WHO) regions including South East Asia. The spread of the disease in South India from 2004 has affected millions of people and left many with crippling disabilities. Kerala had the worst experience ever in 2007. Besides the usual attributes of a viral fever, this disease may cause involvement of various organ systems including psychological and social sequelae.

Chikungunya virus (CHIK virus in short) is an RNA virus that belongs to the Alphavirus genus of the Togaviridae, the family that comprises a number of viruses that are mostly transmitted by arthropods. Infection with CHIK virus results in CF with its associated symptoms. Epidemics of fever, rash and arthritis resembling CF have been recorded as early as 1824 in India and elsewhere. However, the virus was first isolated between 1952 and 1953 from both human and mosquitoes during an epidemic of fever that was considered clinically indistinguishable from dengue in Tanzania. Subsequent outbreaks have been recorded in Africa, Asia and Europe. An outbreak with 197 cases was described in Italy in 2007 in travelers returning from Indian Ocean islands or India. The recent upsurge of CF in Indian states of Orissa, Maharashtra, Gujarat, Kerala, Karnataka and various Indian Ocean islands including Comoros, Mauritius, Reunion and Seychelles highlight the periodic spread of this disease and raise questions about factors influencing the triggering of outbreaks. Chikungunya epidemics display cyclical and seasonal trends. There is an inter-epidemic period of 4–8 years (sometimes as long as 20 years). Outbreaks are most likely to occur in postmonsoon period when the vector density is very high. India reported CF in 213 districts located in 15 states/union territories. About 1.39 million suspected cases have been reported. Some areas reported attack rates as high as 45%.1

*Aedes aegypti* is the common vector responsible for transmission in urban areas whereas *Aedes albopictus* has been implicated in rural areas. Recent studies indicate that the virus has mutated enabling it to be transmitted by *Aedes albopictus.*2 The Aedes mosquito breeds in domestic settings such as flower vases, water-storage containers, air coolers, etc. and peri-domestic areas such as construction sites, coconut shells, discarded household junk items (tires, plastic and metal cans, etc.). The adult female mosquito rests in cool and shady areas in domestic and peri-domestic settings and bites during day time.

### Clinical Manifestations during the Acute Phase

Chikungunya fever virus causes a febrile illness in the majority of people with an incubation period of 2–4 days from the mosquito bite, but may vary from 2 to 10 days. Viremia persists for up to 5 days from the clinical onset. Fever is the commonest symptom (92%) and is usually associated with arthralgia (87%), backache (67%) and headache (62%).3 The fever varies from low grade to high grade, lasting for 24–48 hours. Fever rises abruptly in some, reaching 39–40°C, with shaking chills and rigor and usually subsides with use of antipyretics. No diurnal variation was observed for the fever.

In the Reunion epidemic as well as Indian, many patients had arthralgia without fever. The joint pain tends to be worse in the morning, relieved by mild exercise and exacerbated by aggressive movements. The pain may remit for 2–3 days and then reappear in a saddle back pattern. Migratory polyarthritis with effusions may be seen in around 70% cases, but resolves in the majority. Ankles, wrists and small joints of the hand were the worst affected. Larger joints like knee, shoulder and spine were also involved. There is a tendency for early and more significant involvement of joints with some trauma or degeneration. Occupations with predominant overuse of smaller joints predisposed those areas to be affected more (interphalangeal joints in rubber tappers, ankle joints in those standing and walking for a long time, e.g. policemen). The classical bending phenomenon was probably due to the lower limb and back involvement, which forced the patient to stoop down and forward.

Transient maculopapular rash is seen in up to 50% persons. The maculopapular eruption persisted for more than 2 days in approximately 10% cases. Intertriginous atrophic-like ulcers and vesiculobullous eruptions were noticed. A few persons had angiomatous lesions and fewer had purpuras. Stomatitis was observed in 25% and oral ulcers in 15%. Nasal blotchy erythema followed by photosensitive hyperpigmentation (20%) was observed more commonly in the recent epidemic. Exfoliative dermatitis affecting limbs and face were seen in around 5% cases. Epidermolyis bullosa was an occasional observation in children. Most skin lesions recovered completely except in few cases where the patches of hyperpigmentation from photosensitivity persisted.

Photophobia and retro-orbital pain has been observed. Although rare in adults, children, particularly neonates have developed vomiting and/or diarrhea and meningencephalitis. Neurologic manifestations such as encephalitis, febrile seizures, meningeval syndrome and acute encephalopathy were reported. Neuroretinitis and uveitis in one or both eyes has also been observed. The main ocular manifestation associated with the recent epidemic outbreak of chikungunya virus infection in South India included granulomatous...
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and nongranulomatous anterior uveitis, optic neuritis, retrobulbar neuritis and dendritic lesions. The visual prognosis was generally good, with most patients recovering good vision. There is no significant sex predilection and causes illness in almost all age groups.

Laboratory Criteria

Laboratory criteria: Residing or having visited epidemic Confirmed case

### Clinical criteria

- A patient meeting the laboratory criteria, Probable case

Clinical criteria

- At least one of the following tests in the acute phase
- Virus isolation
- Presence of viral RNA by RT-PCR
- Presence of virus-specific IgM antibodies in single serum sample collected in acute or convalescent stage
- Increase in IgG values in samples collected at least 3-week apart.

Case Definition

Although case diagnosis can only be made by laboratory means, chikungunya should be suspected when epidemic occurs with the characteristic triad of fever, rash and joint manifestations.

To suspect a case, it does not have to be an epidemic situation. If a given case satisfies the case definition for "suspect case"; i.e. acute onset of fever of greater than or equal to 38.5°C associated with severe arthralgia/arthritis not explained by any other medical conditions in a patient residing in or visited within 15 days prior to the onset of symptoms a geographic area where both the vector and the virus are prevalent, he or she should be labeled as a "suspect case" and tested for the presence of viremia [tissue culture or reverse transcription-PCR (RT-PCR)] or IgM antibodies or for the 4-fold rise in CHIK-specific IgG titer. In an epidemic situation, i.e. with a history of exposure to the time and place of epidemic, such a patient automatically becomes a probable case and it would not be necessary to confirm the diagnosis in a laboratory to include him or her as one of the cases for reporting as CF.

The Chikungunya case definition here is adapted from that proposed by European Centre for Disease Prevention and Control (ECDC).3

- **Clinical criteria:** Acute onset of fever greater than 38.5°C and severe arthralgia/arthritis not explained by any other medical conditions
- **Epidemiological criteria:** Residing or having visited epidemic areas, having reported transmission within 15 days prior to the onset of symptoms
- **Laboratory criteria:** At least one of the following tests in the acute phase:
  - Virus isolation
  - Presence of viral RNA by RT-PCR
  - Presence of virus-specific IgM antibodies in single serum sample collected in acute or convalescent stage
  - Increase in IgG values in samples collected at least 3-week apart.

On this basis, cases are to be categorized as:

- **Possible case:** A patient meeting clinical criteria
- **Probable case:** A patient meeting both the clinical and epidemiological criteria
- **Confirmed case:** A patient meeting the laboratory criteria, irrespective of the clinical presentation.

It may be noted that during an epidemic, all patients need not be subjected to confirmatory tests as above. An epidemiologic link may be enough. Clinical management as of now does not differ between a probable case and a confirmed case.

Clinical Management

Clinical management should be instituted in all suspect cases without waiting for serological or viral confirmation. During an epidemic, it is not imperative that all cases should be subjected for virologic/serologic investigations. It may be stressed that all suspected cases should be kept under mosquito nets during the febrile period along with other control measures. All persons in the affected areas should be sensitized about the mosquito control measures to be adopted in hospital premises and houses. During acute stage of the disease, steroids are not usually indicated because of the adverse effects. Aspirin is preferably avoided for fear of gastrointestinal and other side effects like Reye’s syndrome.

Clinical management of CF is discussed at two stages:

- **Acute stage of the illness**
- **Sequela**

As CF produces illnesses in an epidemic pattern, large numbers of persons are likely to be affected simultaneously in the family and in the community. It may not be feasible to offer institutionalized care to all of them at the same time. Besides, many symptoms will disappear with good home care. It may also be imperative that early graded ambulation and mild exercises might benefit the persons after the acute phase.

Domiciliary (Home Based)

All cases of fever cared in their own homes should be advised the following:

- **Adequate rest in a warm environment; avoid damp surroundings**
- **Refrain from exertion**
- **Cold compresses may help in reducing joint damage**
- **Consume plenty of water with electrolytes (approximately 2 liters of home available fluids with salt in 24 hours).** If possible a measured urine output of more than a liter in 24 hours should be ensured.
- **Take paracetamol tablets during periods of fever (up to two 500 mg tablets four times daily) in an average sized adult.** In general, children’s dosages are based on a single dose of 10 mg paracetamol per kilogram body weight, which can be repeated 4–6 hourly, not exceeding four doses per 24 hours.
- **Avoid self-medication with aspirin or other pain killers.**

When to Seek Medical Help?

- **Fever persisting for more than 5 days**
- **Intractable pain**
- **Postural dizziness, cold extremities**
- **Decreased urine output**
- **Any bleeding under the skin or through any orifice**
- **Incessant vomiting**

The diagnoses of dengue fever, leptospirosis, malaria and other illnesses excluded by history, clinical examination and basic investigations should be carried out. The following points may be noted. Chikungunya fever may not have the typical manifestations or coexist with other infectious diseases like dengue fever or noninfectious diseases like rheumatoid arthritis.

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Infectious Diseases

- Leptospirosis: Severe myalgia localized to calf muscles with conjunctival congestion/subconjunctival hemorrhage with or without oliguria or jaundice in a person with history of contact with contaminated water might suggest leptospirosis.
- Dengue fever: Sever back pain with purpuras or active bleeding might suggest dengue fever.
- Malaria: Periodicity of fever and alteration of consciousness/seizures should prompt for malaria.
- Meningitis: High fever with neck stiffness or alteration of consciousness should prompt a thought about meningitis. All cases of meningococcal meningitis during an outbreak of CF must be suspected to have CF.
- Rheumatic fever: It is more common in children and presents with fleeting (migratory) polyarthritis predominantly affecting the large joints. Modified Jones criteria should be the basis for diagnosis. Raised anti-streptolysin O (ASO) titer and a history of recent infection are other points to be noted.

Collect blood samples for total leucocyte count, platelet count and for serology (IgM-ELISA). The total leucocyte count is usually on the lower side (below 5,000 cells/cmm). If it is more than 10,000/cmm, possibility of leptospirosis has to be thought of. A low platelet count (below 50,000/cmm) should alert the possibility of dengue fever. The peripheral smear has to be examined for malarial parasite as well at this level and if positive, treatment started as per national guidelines.

Treat symptomatically (paracetamol 1g three to four times a day for fever, headache and pain, and antihistamines for itching). Paracetamol must be used with caution in persons with pre-existing underlying serious illnesses. Children may be given 50–60 mg per kg body weight per day in divided doses. Tepid sponging can be suggested.

If the case has already been treated with paracetamol/other analgesics, start one of the nonsteroidal anti-inflammatory drugs (NSAIDs) as per standard recommendations. Monitor for any adverse side effects of NSAIDs. Cutaneous manifestations can be managed with topical or systemic drugs.

If the person has hemodynamic instability (frequent syncopal attacks, hypotension with a systolic blood pressure less than 100 mm Hg or a pulse pressure less than 30 mm Hg), oliguria (urine output less than 500 ml in 24 hours), altered sensorium or bleeding manifestations refer immediately to higher center. Refer persons not responding or having persistent joint pain or disabling arthritis even after 3 days of symptomatic treatment. It may be advisable to refer persons above 60 years and infants (below 1 year of age) as well.

Recommended mild exercises and physiotherapy in recovering persons. The persons may be encouraged to walk, use their hands for eating, writing and regular isotonic exercises. Cold compresses may be suggested depending on the response. Exposure to warm environments (morning and evening sun) may be suggested. Encourage active movements and advise regarding complications. Exercises like walking on level grounds, active hand movements and proper posturing of joints to avoid contractures must be suggested.

Refer the cases with any of the following to higher center (pregnancy, oliguria/anuria, refractory hypotension, bleeding disorders, altered sensorium, meningococcal meningitis, persistent fever of more than 1-week duration, extremes of age—persons above 60 years and infants (below 1 year of age).

Treat serious complications (bleeding disorders with blood components, hypotension with fluids/inotropics, acute renal failure with dialysis, contractures and deformities with physiotherapy/surgery, cutaneous manifestations with topical or systemic drugs, neuropsychiatric problems with specialist care and drugs).

Patients with bleeding diathesis, or with features of liver or kidney involvement need to be further investigated looking for other coexisting conditions even if the diagnosis of CF has been confirmed by laboratory investigation. Patients with myopericarditis or meningococcal meningitis may require intensive care with regular monitoring, inotropic support, ventilation, etc. In cases with ophthalmic complications, standard practice guidelines may be obtained from the ophthalmologists.

Use hydroxychloroquine 200 mg orally once daily or chloroquine phosphate 300 mg orally per day for a period of 4 weeks in cases where arthralgia is refractory to other drugs. Before using chloroquine or related compounds in these doses, the peripheral smear examination must be done at least twice to rule out malaria.

Chronic Sequelae

Osteoarticular Problems

Osteoarticular problems seen with CF usually subside in within 1–2 weeks. In approximately 20% cases, they disappear after a gap of few weeks. In less than 10% cases, they tend to persist for months. In about 10% cases, the swelling disappears. The pain subsides but only to reappear with every other febrile illness for many months. Each time the same joints show the tendency to swell up with or without effusion and symptoms persist for a week or two after subsidence of the fever. Compliment-mediated damage and persistence in intracellular sanctuaries for the virus have been implicated in occasional studies. Destroyed metatarsal head has been observed in patients with persistent joint swelling.

Proper and timely physiotherapy will help patients with contractures and deformities. Non-weight bearing exercises may be suggested, e.g. slowly touching the occiput (back of the head) with the palm, slow ankle exercises, pulley-assisted exercises, milder forms of yoga, etc. Surgery may be indicated in severe and disabling contractures. The management plan may be finalized in major hospitals, but the follow-up and long-term care must be done at a domiciliary or primary health center level.

Neurologic Problems

Various neurologic sequelae can occur with persistent CF. Approximately 40% of those with CF will complain of various neurological symptoms but hardly 10% will have persistent manifestations. Peripheral neuropathy with a predominant sensory component is the most common (5–8%). Paresthesias, pins and needles sensations, crawling of worms sensation and disturbing neuralgias have all been described by the patients in isolation or in combination. Worsening or precipitation of entrapment syndromes like carpal tunnel syndrome is reported in many patients. Motor neuropathy is rare. Occasional cases of ascending polyneuritis have been observed as a postinfective phenomenon, as seen with many viral illnesses. Seizures and loss of consciousness have been described occasionally; but a causal relationship is yet to be found. Antineuralgic drugs (amitriptyline, carbamazepine, gabapentin, pregabalin) may be used in standard doses in disturbing neuropathies.

Ocular involvement during the acute phase in less than 0.5% cases as described above may lead to defective vision and painful eye in a small percentage. Progressive defects in vision due to uveitis or retinitis may warrant treatment with steroids.

Dermatologic Problems

The skin manifestations of CF subside after the acute phase is over and rarely require long-term care. However, worsening of psoriatic lesions and atopic lesions may require specific management by a qualified specialist. Hyperpigmentation and papular eruptions may be managed with zinc oxide cream or calamine lotion. Persistent non-healing ulcers are rare. Scrotal and aphthous like ulcers on the
skin and intertriginous areas may be managed by saline compresses, topical or systemic antibiotics if secondarily infected.

**Emotional Problems**

Neuropsychiatric/emotional problems have been observed in up to 15% cases. These are more likely in persons with premorbid disorders and those with a family history of mood disorders. They may take different forms:

- When all family members are incapacitated with inability to walk even for their toilet needs—impairment in activities of daily living (ADL); nobody from the relations or neighborhood is free from the illness to help them.
- Even somebody who tries to offer help may be inhibited by the fears that arise from the panic prevalent at the time of the outbreak.
- The families and villages are starved from lack of job, lack of material supplies and from diversion of funds to clinical care and transport.
- Patients also present with confusion regarding the condition and this frequently leads to "doctor shopping" and negative thoughts like "nothing works", "nothing is making me feel better". This gives rise to feelings of helplessness, hopelessness and fear of being incapacitated for life. Some patients also have irrational fears (1 may die because of this condition). Also often seen is loss of interest in pleasurable activities and appetite.
- The sorrow and helplessness make persons lose sleep and this together with starvation, dehydration, metabolic disturbances and illness precipitates hidden premorbid mood disorders like depression to crop up.
- Alcohol withdrawal phenomena and effects of prolonged confinement may tilt the balance toward delirium or suicidal ideation. The emotional and psychosocial issues need individual assessment and have to be considered in the social context of the patient and community. Often patients have inadequate information regarding Chikungunya. The most common being "I will die because of this illness”. It is important to clarify these and similar misconceptions. Broadly, psychosocial support and reassurance may solve some of the problems. A well thought about plan for community support, occupational and social rehabilitation may hold the key for achieving a success in the remaining life.

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3. Meta-analysis of presentations from various parts of India— in the National workshop on emerging fevers with focus on Chikungunya held in Kochi on December 28, 2007.