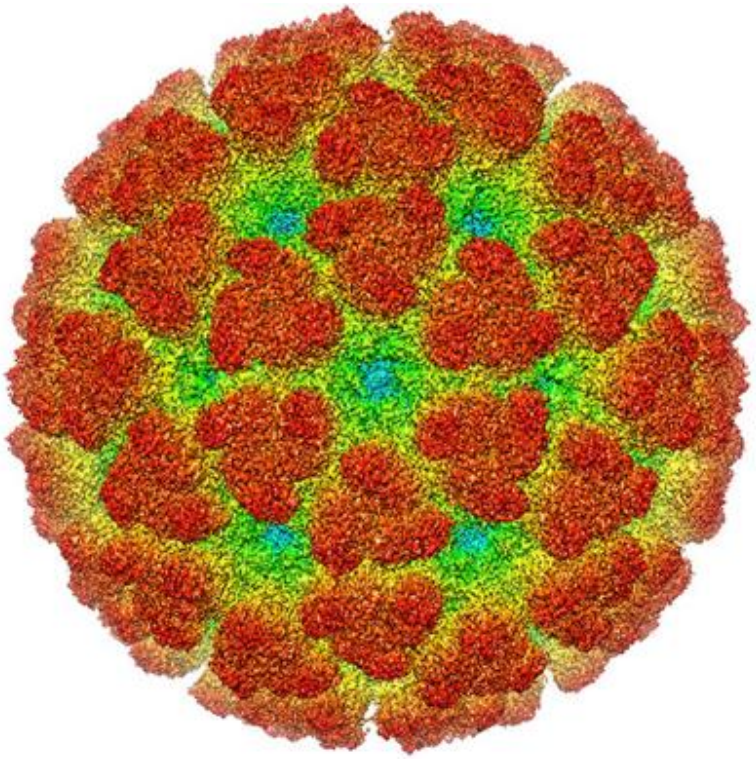
Chikungunya fever disease

Chikungunya fever is an arboviral disease caused by an alphavirus(CHIKV) belonging to the order unassigned, togaviridae family, genus alphavirus, and transmitted to humans mainly by infected mosquitoes of the Aedes alphavirus genus (*Aedes aegypti* and *Aedes albopictus*).

Figure 1 shows the Chikungunya virus (CHIKV)

Figure 1



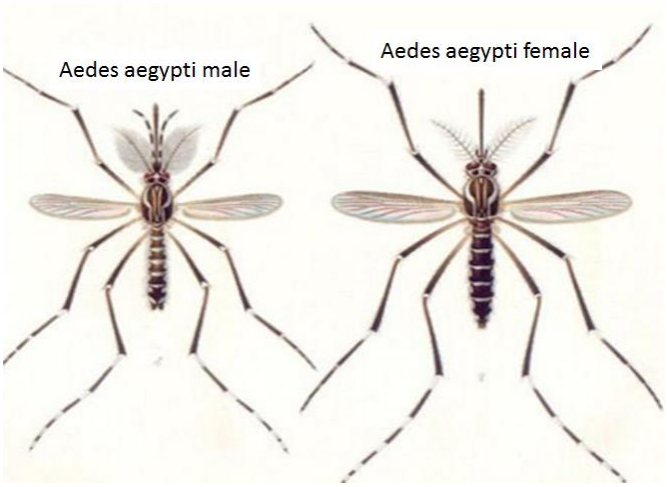
They also transmit dengue fever types 1 to 4, and zika virus. Chikungunya virus is transmitted to people through infected female mosquitoes bites of the Aedes species.

The virus is mainly "spread from person to person through mosquitoes. Mosquitoes become infected when they feed on a person already infected with the virus. Infected mosquitoes can then spread the virus to other people through bites. Chikungunya virus is most often spread to people by *Aedes aegypti* and *Aedes albopictus* mosquitoes. These are the same mosquitoes that transmit dengue virus. They bite mostly during the daytime. Chikungunya virus

(CHIKV) was first isolated from human serum during a febrile illness outbreak in Tanzania in 1953. The word chikungunya is derived from Makonde (Kimakonde), one of the languages spoken in southeastern Tanzania, and means “to bend over or become contorted”, referring to the posture adopted by the patient due to serious joint pain in severe infections caused by CHIKV.

Figures 2 and 3 show the *Aedes aegypti*

Figure 3



Viral disease is transmitted by the bite of infected female mosquitoes of the Aedes species

Rarely, the transmission is from mother to child. Chikungunya virus is transmitted rarely from mother to newborn around the time of birth. To date, no infants have been found to be infected with chikungunya virus through breastfeeding. Because of the benefits of breastfeeding, mothers are encouraged to breastfeed even in areas where chikungunya virus is circulating. Finally, rarely, through infected blood. In theory, the virus could be spread through a blood transfusion. To date, there are no known reports of this happening.

The entity is an acute febrile illness with an incubation period of 3-7 days. It affects all age groups and both sexes equally, with an attack rate (percentage of individuals who develop illness after infection) of 40%-85%. Patients present with abrupt onset of high-grade fever often reaching 102°-105°F, with shaking chills that last 2-3 days. The fever may return for 1-2 days after an afebrile period of 4-10 days, hence called a "saddle-back fever."

The figure 4 shows the world distribution of CHIKV transmission areas.

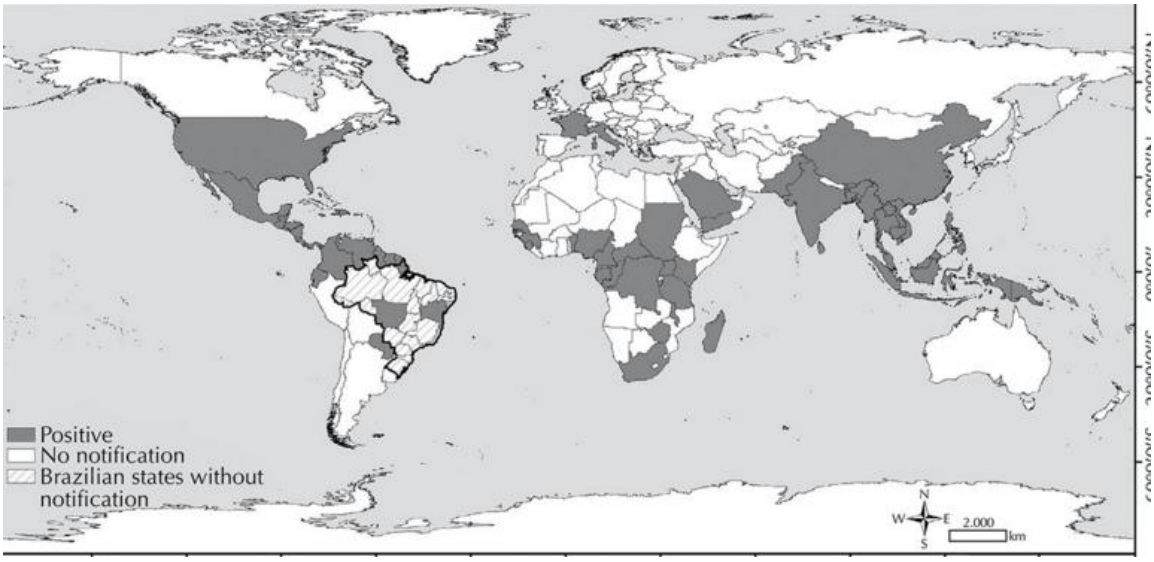


Figure 4 Areas with chikungunya virus transmission in the world.

Prodromal symptoms are uncommon. However, sore throat, headache, abdominal pain, constipation, and retro-orbital pain have been reported during the acute phase of the illness.

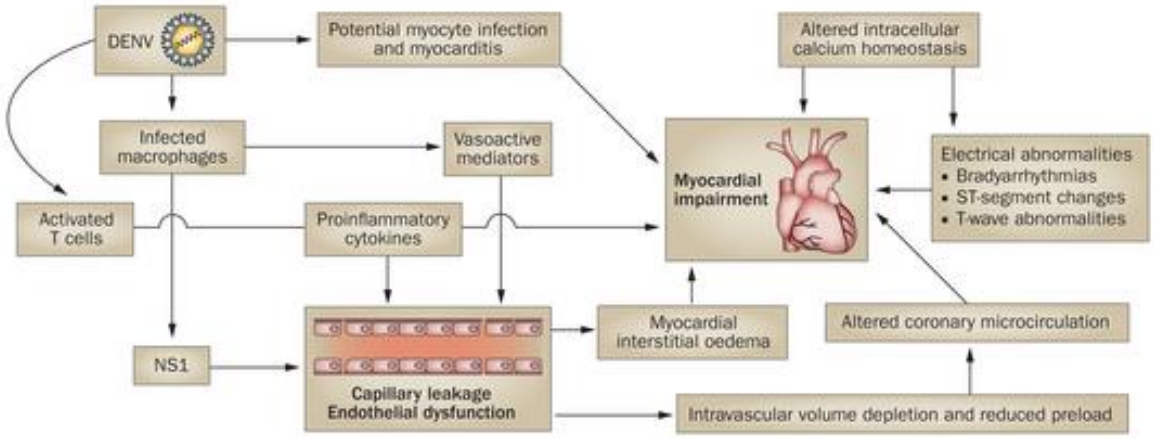
Physical Examination: Clinical examination reveals high-grade fevers (up to 105°F), pharyngitis, conjunctival suffusion, conjunctivitis, and photophobia. Cervical or generalized lymphadenopathy has also been reported in rare cases. Other frequent manifestations include severe arthralgias, myalgias, and rash.[4, 7, 8]

Arthralgia: The arthralgia are usually polyarticular and migratory and frequently involve the small joints of the hands, wrist, and ankle, with lesser involvement of the large joints such as the knee or shoulder with associated arthritis. More than 10 joint groups may be involved simultaneously, incapacitating the patient. Swollen tender joints with tenosynovitis and crippling arthritis are often evident at the time of presentation. Joint pain is worse in the morning, gradually improving with slow exercise and movement but exacerbated by strenuous exercise. Patients characteristically lie still in a flexed posture owing to the pain upon any movement. Rarely, sternoclavicular and temporomandibular joints are involved. Axial involvement is common, but hips are relatively spared. Inflammatory markers may be mildly elevated, but radiological findings are usually normal. Joint edema is seen, but effusion is uncommon. Although joint manifestations resolve completely within 1-2 weeks in most patients, about 10%-12% develop chronic joint symptoms that may last for months.[61, 64, 62, 65]

Cutaneous manifestations: Individuals with Chikungunya fever frequently present with a flushed appearance involving the face and trunk, followed by a diffuse erythematous maculopapular rash of the trunk and extremities, sometimes involving the palms and soles. The rash gradually fades; may evolve into petechiae, urticaria, xerosis, or hypermelanosis; or resolves with desquamation.[66, 67] A tourniquet test is positive in some patients, similar to dengue fever. In fact, some of the symptoms and signs of Chikungunya fever are almost indistinguishable from those of Dengue fever. As both illnesses are transmitted by the same vector, coinfection has been reported in the literature.

Neurological manifestations: In the acute phase of the illness (reported during the outbreak in the Indian Ocean in 2005-2006), 23 patients presented with neurological symptoms associated with abnormal CSF tests and positive CSF immunoglobulin M (IgM) or reverse-transcriptase polymerase chain reaction (RT-PCR) for Chikungunya virus. Clinical manifestations in this outbreak included altered mental status or behavior in 95%, headache in 30.4%, seizures in 26%, motor dysfunction in 4.3%, and sensorineural abnormalities in 8.7%.[68, 69, 70, 71, 72] Severe cases of chikungunya in children provide a stark reminder of the cardiac and neurological tropism of the virus and its hemorrhagic forms with potential mortality and morbidity. These cases underline the need for personal protection measures and for research to develop specific antiviral therapy and vaccines to prevent potentially lethal forms of the disease. Figure 4 shows the proposed viral and immune mechanisms involved in the cardiac and vascular manifestations of dengue and Chikungunya (Figure 5).

Figure 5



Others: Rare presentations include severe rheumatoid arthritis, neuroretinitis, uveitis, hearing loss, myocarditis, and cardiomyopathy.[73, 74, 75, 76, 77, 78, 79, 80, 81, 82]

Diagnostic Criteria for Chikungunya Fever: The case definition of Chikungunya fever as proposed by the World Health Organization (WHO) Regional Office for Southeast Asia is discussed below.[83]

I. **Suspected case:** A suspected case involves a patient presenting with acute onset of fever, usually with chills/rigors, that lasts for 3-5 days with pain in multiple joints/swelling of extremities that may continue for weeks to months.

II. **Probable case:** A probable case is characterized by conditions that support a suspected case along with one of the following conditions: History of travel or residence in areas reporting outbreaks, ability to exclude malaria, dengue, and any other known cause of fever with joint pains.

III. **Confirmed case:** Chikungunya fever is confirmed in the patient meets one or more of the following findings irrespective of the clinical presentation: Virus isolation in cell culture or animal inoculations from acute-phase, presence of viral ribonucleic acid (RNA) in acute-phase sera as determined with RT-PCR. Presence of virus-specific IgM antibodies in single serum sample in acute phase or 4-fold increase in virus-specific IgG antibody titer in samples collected at least 3 weeks apart

Diagnostic Considerations: Other diseases to be considered in the differential diagnoses depend on the country of residence, local epidemiology, travel history, and exposure. Table 1. Clinical and Laboratory Features of Chikungunya Virus Infections Compared with Dengue virus infections **(adapted from http://www.cdc.gov/chikungunya/)**

Table 1

Feature	Chikungunya Virus Infection	Dengue Virus Infection
Fever (>39°C)	+++	++
Arthralgia	+++	+/-
Arthritis	+	-
Headache	++	++
Rash	++	+
Myalgia	+	++
Hemorrhage	+/-	++
Shock	-	+
Lymphopenia	+++	++
Neutropenia	+	+++
Thrombocytopenia	+	+++
Hemoconcentration	-	++

Differentials

I. ***Viral infections*:** Dengue fever, west Nile fever, adenovirus infection O'nyong-nyong fever Ross River fever, Sindbis fever, Crimean-Congo fever, Bussuquara fever, Mayaro fever, Ebola fever, hantavirus infection, Kyasanur Forest disease, Lassa fever, Rubella, Parvovirus B 19 infection, hepatitis B, mumps, Infection with herpes viruses

II. ***Parasitic infections****; Falciparum infection,*

III. ***Bacterial infections:*** Leptospirosis, Rickettsial infections, gonococcemia, postinfectious reactive arthritis, group A streptococcal infection

Prognosis: The disease is rarely fatal, according to the World Health Organization, although in older people, the disease can contribute to the cause of death. As of July 11, 5,037 cases have been confirmed in the Caribbean with 21 deaths, according to the Pan American Health Organization. Most people will get better in about a week although some will need to be hospitalized. A small number of people will have joint pain that lasts for months. Newborns exposed during delivery, people 65 and older, and people with medical conditions like, diabetes, hypertension or heart disease are particularly vulnerable to infection.

Prevention and control: The proximity of mosquito vector breeding sites to human habitation is a significant risk factor for chikungunya as well as for other diseases that these species transmit. Prevention and control relies heavily on reducing the number of natural and artificial water-filled container habitats that support breeding of the mosquitoes. This requires mobilization of affected communities. During outbreaks, insecticides may be sprayed to kill flying mosquitoes, applied to surfaces in and around containers where the mosquitoes land, and used to treat water in containers to kill the immature larvae. For protection during outbreaks of chikungunya, clothing which minimizes skin exposure to the day-biting vectors is advised. Repellents can be applied to exposed skin or to clothing in strict accordance with product label instructions. Repellents should contain DEET (N, N-diethyl-3-methylbenzamide), IR3535 (3-[N-acetyl-N-butyl]-aminopropionic acid ethyl ester) or icaridin (1-piperidinecarboxylic acid, 2-(2-hydroxyethyl)-1-methylpropylester). For those who sleep during the daytime, particularly young children, or sick or older people, insecticide-treated mosquito nets afford good protection. Mosquito coils or other insecticide vaporizers may also reduce indoor biting.

Basic precautions should be taken by people travelling to risk areas and these include use of repellents, wearing long sleeves and pants and ensuring rooms are fitted with screens to prevent mosquitoes from entering.

Approach Considerations: Chikungunya infection is confirmed via serological tests, which take about 5-7 days into the illness to turn positive. Therefore, early diagnosis is based on a high index of clinical suspicion based on epidemiology and clinical presentation that includes the triad of high fever, rash, and associated rheumatologic manifestations.[84, 85, 86, 87]

Serological Testing: Chikungunya virus–specific IgM antibodies usually appear upon cessation of viremia, usually by day 5-7 into the illness, and stay positive for 3-6 months. Immunoglobulin G (IgG)–neutralizing antibodies appear after 7-10 days and may persist for several months. These antibodies are detected with an enzyme-linked immunoassay (ELISA) test that is available through the CDC and several state health departments.

Viral Culture: Chikungunya virus may be isolated in culture within the first 3 days of illness during the period of active viremia by inoculation of blood into mice or mosquitoes. Culture-based detection is also available through the CDC

Molecular Diagnostics: RT-PCR has been standardized using both structural and nonstructural domains of the Chikungunya virus genome and is available through the CDC. A genotyping assay has also been developed that would help in outbreak settings. The molecular assay detects viral RNA during the first 7-8 days of the illness.

During Pregnancy: Prenatal Testing

Screening Tests: A screening test is a procedure or test that is done to see if a woman or her baby might have certain problems. A screening test does not provide a specific diagnosis—that requires a diagnostic test. A screening test can sometimes give an abnormal result even when there is nothing wrong with the mother or her baby. Less often, a screening test result can be normal and miss a problem that does exist. During pregnancy, women are usually offered these screening tests to check for birth defects or other problems for the woman or her baby. Talk to your doctor about any concerns you have about prenatal testing.

First Trimester Screening: First trimester screening is a combination of tests completed between weeks 11 and 13 of pregnancy. It is used to look for certain birth defects related to the baby's heart or chromosomal disorders, such as Down syndrome. This screen includes a maternal blood test and an ultrasound.

- Maternal Blood Screen: The maternal blood screen is a simple blood test. It measures the levels of two proteins, human chorionic gonadotropin (hCG) and pregnancy associated plasma protein A (PAPP-A). If the protein levels are abnormally high or low, there could be a chromosomal disorder in the baby.

- Ultrasound: An ultrasound creates pictures of the baby. The ultrasound for the first trimester screen looks for extra fluid behind the baby's neck. If there is increased fluid found on the ultrasound, there could be a chromosomal disorder or heart defect in the baby.

Second Trimester Screening tests are completed between weeks 15 and 20 of pregnancy. They are used to look for certain birth defects in the baby. Second trimester screening tests include a maternal serum screen and a comprehensive ultrasound evaluation of the baby looking for the presence of structural anomalies (also known as an anomaly ultrasound).

- Maternal Serum Screen: The maternal serum screen is a simple blood test used to identify if a woman is at increased risk for having a baby with certain birth defects, such as neural tube defects or chromosomal disorders such as Down syndrome. It is also known as a "triple screen" or "quad screen" depending on the number of proteins measured in the mother's blood. For example, a quad screen tests the levels of 4 proteins AFP (alpha-fetoprotein), hCG, estriol, and inhibin-A. Generally, the maternal serum screen is completed during the second trimester.

- Anomaly Ultrasound An ultrasound creates pictures of the baby. This test is usually completed around 18–20 weeks of pregnancy. The ultrasound is used to check the size of the baby and looks for birth defects or other problems with the baby.

Diagnostic Tests

If the result of a screening test is abnormal, doctors usually offer further diagnostic tests to determine if birth defects or other possible problems with the baby are present. These diagnostic tests are also offered to women with higher risk pregnancies, which may include women who are 35 years of age or older; women who have had a previous pregnancy affected by a birth defect; women who have chronic diseases such as lupus, high blood pressure, diabetes, or epilepsy; or women who use certain medications.

High resolution Ultrasound: An ultrasound creates pictures of the baby. This ultrasound, also known as a level II ultrasound, is used to look in more detail for possible birth defects or other problems with the baby that were suggested in the previous screening tests. It is usually completed between weeks 18 and 22 of pregnancy.

Chorionic Villus Sampling (CVS) is a test where the doctor collects a tiny piece of the placenta, called chorionic villus, which is then tested to check for chromosomal or genetic disorders in the baby. Generally, a CVS test is offered to women who received an abnormal result on a first trimester screening test or to women who could be at higher risk. It is completed between 10 and 12 weeks of pregnancy, earlier than an amniocentesis.

Amniocentesis: is test where the doctor collects a small amount of amniotic fluid from the area surrounding the baby. The fluid is then tested to measure the baby's protein levels, which might indicate certain birth defects. Cells in the amniotic fluid can be tested for chromosomal disorders, such as Down syndrome, and genetic problems, such as cystic fibrosis or Tay-Sachs disease. Generally, an amniocentesis is offered to women who received an abnormal result on a screening test or to women who might be at higher risk. It is completed between 15 and 18 weeks of pregnancy. Below are some of the proteins for which an amniocentesis tests. AFP stands for alpha-fetoprotein, a protein the unborn baby produces. A high level of AFP in the amniotic fluid might mean that the baby has a defect indicating an opening in the tissue, such as a neural tube defect (anencephaly or spina bifida), or a body wall defect, such as omphalocele or gastroschisis.

AChE stands for acetylcholinesterase, an enzyme that the unborn baby produces. This enzyme can pass from the unborn baby to the fluid surrounding the baby if there is an opening in the neural tube.

After the Baby is Born Certain birth defects might not be diagnosed until after the baby is born. Sometimes, the birth defect is immediately seen at birth. For other birth defects including some heart defects, the birth defect might not be diagnosed until later in life.

When there is a health problem with a child, the primary care provider might look for birth defects by taking a medical and family history, doing a physical exam, and sometimes recommending further tests. If a diagnosis cannot be made after the exam, the primary care

provider might refer the child to a specialist in birth defects and genetics. A clinical geneticist is a doctor with special training to evaluate patients who may have genetic conditions or birth defects. Even if a child sees a specialist, an exact diagnosis might not be reached.

Prevention

Vector control plays a key role in preventing the spread of Chikungunya virus. Humans traveling to endemic/epidemic areas are recommended to use mosquito repellents, to wear long-sleeve shirts and long pants, and to use air-conditioned rooms or rooms with window and door screens.

People with suspected Chikungunya fever should avoid mosquito exposure during the first week of viremia to prevent local transmission of the illness.

Appropriate education of the community and public health officials on eliminating mosquito breeding sites (stagnant water, weeds and tall grass) and spraying insecticides is essential for optimal vector control and for interrupting transmission of the disease.

Humans at risk for severe disease must avoid travel to areas with ongoing outbreaks.

Approach

No specific antiviral treatment is available for Chikungunya fever.

It is important to exclude other serious infections similar to Chikungunya fever such as dengue, malaria, or bacterial infections.

Once other infections are excluded, management includes hydration, monitoring of hemodynamic status, collection of blood specimens for diagnosis, and antipyretic therapy. Severe arthralgia may be managed with nonsteroidal anti-inflammatory drugs (NSAIDS) (once dengue is excluded) and physiotherapy.

Published evidence does not recommend the use of corticosteroids or antiviral agents.

Conservative treatment includes management of electrolyte imbalance, prerenal azotemia, and hemodynamic monitoring based on severity of illness. Indiscriminate use of

corticosteroids, NSAIDS (especially aspirin), and other antibiotics could contribute to thrombocytopenia, gastrointestinal bleeding, gastritis, and renal failure and could indirectly contribute to mortality.

Future Perspectives

Research into development of a live-virus and attenuated-virus vaccine against Chikungunya virus is ongoing. However, no vaccines are available at this time.[88, 89, 90] A phase-II vaccine trial used a live, attenuated virus, to develop viral resistance in 98% of those tested after 28 days and 85% still showed resistance after one year. However, 8% of people reported transient joint pain, and attenuation was found to be due to only two mutations in the E2 glycoprotein. Alternative vaccine strategies have been developed, and show efficacy in mouse models, but have so far not reached clinical trials. In August 2014 researchers at the National Institute of Allergy and Infectious Diseases in the USA were testing an experimental vaccine. Even with a vaccine, mosquito population control and bite prevention will be necessary to control chikungunya disease.

Chikungunya fever is an emerging global disease with several intriguing and unanswered questions such as the reason for sudden major rapid outbreaks with disease-free intervals, mode of survival or maintenance of the virus in nature between epidemics, factors that trigger the outbreaks, and strain replacements during outbreaks.[91]

More research is needed to understand the epidemiology and natural history of this disease. Until then, prevention and vector control at personal and community level should be implemented.

Consultations: may include the following: Infectious disease specialist**,** Rheumatologist**, i**ntensive care specialist**, n**eurologist

Long-Term Monitoring: Arthralgias resolve spontaneously within 3 weeks in about 70% of patients. However, they can persist for 3-6 months in 30% of patients, for 20 months in 15%, and for 3-5 years in 12%. Elderly patients and patients with prior rheumatologic conditions are at higher risk for chronic polyarthritis, tenosynovitis, and bursitis. Bouquillard et al have reported the possible unmasking or occurrence of rheumatoid arthritis in patients

infected with Chikungunya virus. Patients with chronic arthritis may need long-term follow-up with both infectious disease and rheumatology experts.[75]

Medication Summary: NSAIDS play a major role in the treatment of Chikungunya infection. Aspirin must be avoided owing to bleeding risk. No specific antiviral therapy is available. Antibiotics and corticosteroids are not indicated.


CHIKUNGUNYA FEVER
Viral disease transmitted by the bite of infected female mosquitoes of the Aedes species.
Symptoms include fever, headache, fatigue, nausea, vomiting, muscle pain and rash (but no related haemorrhaging).
Severe and sometimes persistent joint pain. Many symptoms similar to dengue except for prolonged joint pain.
Fever lasts from a few days to a couple of weeks.
Some patients have prolonged fatigue lasting several weeks.
Incubation period can be two to 12 days but normally it is three to seven days.
Recovery is expected but elderly folks take longer and some may take a year or more.
No death has been conclusively proven.
Infection happens when a mosquito spreads it after biting an already infected person in the daytime.
Monkeys and possibly other animals may also serve as reservoirs.
There is no vaccine or antiviral treatment.
Treatment is rest, taking fluids and medication for mitigating pain and fever. Avoid aspirin.
Patient's movements should be restricted so that exposure to mosquitoes is limited to prevent further spreading the virus.
Prevention includes using insect repellents, mosquito coils/mats/nets and proper clothing that cover your body.
Cover or drain any place or receptacle which has still water because they breed in clean stagnant water. Also properly dispose of used containers which can collect water.
GRAPHICS © 2008
Source: The Centers for Disease Control and Prevention and WHO.

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