



衛生防護中心
Centre for Health Protection

Scientific Committee on Vector-borne Diseases

Epidemiology and Prevention of Chikungunya Fever in Hong Kong

Purpose

This paper provides an overview of chikungunya fever, the global and local situation, current health protection measures, and recommendations for further prevention and control of the disease.

The Causative Agent and Vector

Chikungunya Virus (1,2)

2. Chikungunya fever is an acute viral disease caused by the chikungunya virus which is an enveloped, positive strand, RNA virus belonging to the genus *Alphavirus*, in the family *Togaviridae*. According to the genomic analysis, three distinct chikungunya virus phylogroups namely the West African, Central/East African, and Asian groups are currently circulated in their respective geographical region. Like other alphaviruses, chikungunya virus is readily inactivated by physical factors and chemical agents like heat, lipid solvent, acid PH, detergents, bleach, phenol, 70% alcohol and formaldehyde.

The Vector and Transmission Cycle

3. Chikungunya fever is known to primarily affect both human and non-human primates, e.g. monkeys and baboons. Monkeys are the common reservoirs.(1) Other animals like bushbabies, bats and rodents have been found to develop substantial viremia after chikungunya infection, but they are not considered as important hosts in virus maintenance.(3) *Aedes* mosquitoes are the principal vectors for



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both human and non-human primate infection.(4) For human infection, *A. aegypti* is main vector responsible for the epidemics. During the outbreaks occurred in Indian Ocean and Italy in the past 3 years, *A. albopictus* has been confirmed to be a competent and capable vector for chikungunya virus.(5,6) Other *Aedes* mosquitoes namely *A. furcifer-taylori* group, *A. luteocephalus*, and *A. africanus* are responsible for the non-human primate infection. Besides, *A. furcifer-taylori* group and *A. luteocephalus* have also been implicated in human outbreaks in Africa.(2,4,5,7)

4. Mosquitoes acquire lifelong infection when they feed on a viraemic person or animals infected with chikungunya virus.(7) Unlike dengue fever, transovarial transmission of this virus in mosquitoes has not been documented so far.(8) Human infection of chikungunya fever is caused by the bite of a mosquito which is infected with chikungunya virus.

5. Apart from being reported as a vector-borne disease, vertical transmission of chikungunya virus from infected pregnant women to the foetus has been documented in cases of the recent Indian Ocean epidemic. Besides, direct contact with viraemic blood was postulated as a possible mode of transmission in an autochthonous chikungunya fever case reported in France.(8,9)

Clinical Presentation and Treatment

Clinical Presentation (4,7)

6. Chikungunya infection can cause a debilitating illness, most often characterized by acute onset of high fever, severe arthralgia and rash. The fever can reach up to 40°C and is often associated with chills. It usually lasts for two to three days. However, in some cases, the fever may be biphasic and remit for 1-2 days after a remission period of 4-10 days.

7. Arthralgia is a characteristic symptom of the chikungunya fever. It is typically polyarticular and predominantly affects the small joints of hands and feet, wrists, ankles and previously injured sites. The joints are tender to touch. The arthralgia can be so severe that person prevent any movement and maintain still in a flexed posture during the acute stage. In fact the term of “chikungunya”, derived from a Makonde language of an African ethnic group, means “to dry up or become contorted” that described the characteristic posture of the affected person.

8. The rash, usually appears on the first day, evolves from a flush over the face and trunk to become maculopapular or macular forms which may be pruritic. The maculopapular rash commonly appears on the trunk and limbs, but face, palms and soles can also be involved. Petechial skin lesions may also be present.

9. Other symptoms like headache, fatigue, nausea, vomiting, muscle pain, photophobia, and retro-orbital pain may be present. In addition, signs of pharyngitis, conjunctivitis and lymphadenopathy may be observed. Haemorrhagic features including haematemesis and melaena have been documented in Southeast Asia and are more frequently reported in India.(1,2) Rare complications including meningo-encephalitis, Guillain Barre syndrome, fulminant hepatitis, myocarditis and pericarditis have been reported in cases of Indian Ocean epidemic in 2005-6. Severe infection can occur in infants, elderly and immunocompromised people.(10)

10. Patients with chikungunya fever may have prolonged illness especially fatigue lasting several weeks. Some patients have reported incapacitating joint pain, or arthritis which may last for weeks or months. Although chikungunya fever has been regarded as self-limiting and non-life threatening, deaths associated with the disease have been reported in the Indian Ocean epidemics in 2006.(11) Chikungunya infection (whether clinical or sub-clinical) is thought to confer life-long immunity. There is no evidence supporting that the genotypes of chikungunya fever behave similarly to the serotype of dengue fever in causing sequential infections.

11. Asymptomatic chikungunya fever infections can occur, but its prevalence is not known.(1,12,13) The incubation period ranges from 1-12 days and the patient usually develops symptoms in 3 – 7 days after infection.

12. Differential diagnosis of chikungunya fever includes dengue fever, West Nile fever, and Onyong – onyong virus infection. Other common infections like parvovirus infection, rubella, malaria, etc, may also present with similar symptoms.(1,4,7,14) Compared with dengue fever, the prolonged joint pain is a characteristic in chikungunya fever, whereas the haemorrhagic manifestations are considered rare. The similarities and differences of the epidemiological and clinical characteristics of chikungunya and dengue fever infection are listed in the Annex.

Laboratory Diagnosis (6,7)

13. Chikungunya fever can be diagnosed by isolation of chikungunya virus or detection of chikungunya virus genomic sequences by polymerase chain reaction (PCR) in clinical specimen. The virus and genomic sequences can be detected during the viraemic phase from day 1 to day 5 after onset of symptoms, up to day 8.(15) Alternatively, the diagnosis can be confirmed by a four-fold or greater rise in antibody titres to chikungunya virus antigen in paired serum samples. Also, presence of chikungunya virus IgM antibody, which is usually detectable in serum collected from day 5 after onset, provides a presumptive diagnosis. All these tests are available in Public Health Laboratory Services Branch of the Centre for Health Protection (CHP).

Clinical Management and Infection Control (1,7)

14. There is no specific antiviral treatment for chikungunya fever. Treatment is mainly supportive such as bed rest, adequate fluids, and symptomatic relief by using analgesics, antipyretics like paracetamol or anti-inflammatory drugs like ibuprofen and naproxen for the control of fever and joint pain. However, aspirin should be avoided because of its adverse effect on the platelet and possible haemorrhagic symptoms of the disease.(2,14) Persons who have persistent joint pain may require analgesic or long-term anti-inflammatory therapy. Chloroquine and hydroxychloroquine has been used in the treatment of chronic chikungunya arthritis that has limited response to non-steroidal anti-inflammatory drugs.(1,2,14)

15. Infected persons should be protected from further mosquito exposure by staying indoors with mosquito prevention measures like window screen and mosquito net until the end of viraemic phase, so as to break the human-mosquito-human transmission cycle. Since transmission may be possible by direct contact with blood, standard precaution should be applied for caring the patient. Owing to the risk of maternal-fetal chikungunya transmission and the observation of severe complications among infected newborn babies, it is recommended to retain the exposed asymptomatic neonates in maternity care for a week for close monitoring of symptoms.(9)

Vaccination (2)

16. The Walter Reed Army Medical Centre of the United States had performed extensive researches in the development of human chikungunya virus vaccine. A live attenuated chikungunya virus vaccine was developed which was found to be safe and efficacious in phase 2 clinical trial. However, further trials were withheld due to limited resources and lack of commercial potential.

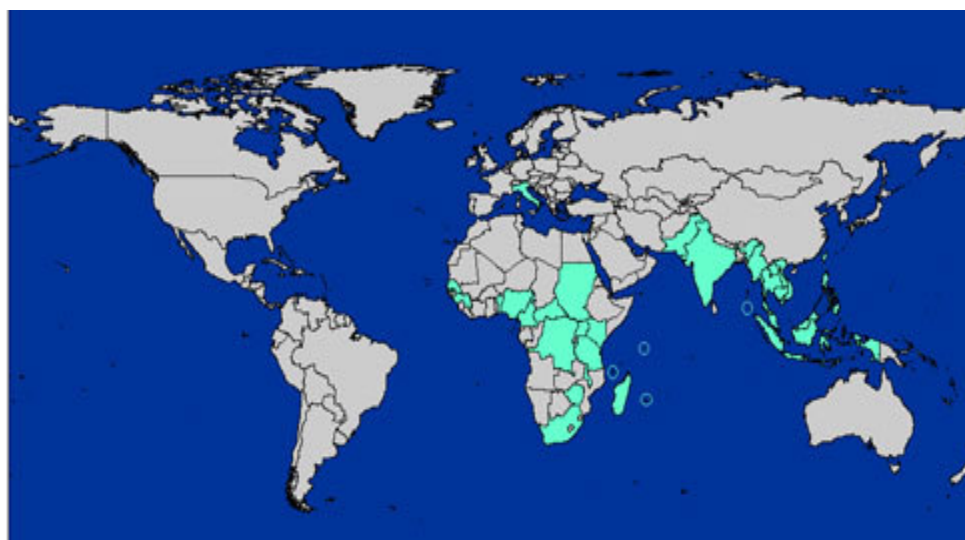
Global Epidemiology (6,16)

Overview

17. Epidemics of fever-rash-arthralgia syndrome resembling chikungunya fever had occurred as early as 1779 in Indonesia and elsewhere.(5) However, the virus was first isolated between 1952-1953 from both man and mosquitoes during an epidemic of fever that was considered clinically indistinguishable from dengue fever in Tanzania. Between 1960 and 1982, outbreaks of chikungunya fever were reported from Africa and Asia. In Asia, virus has been isolated in Bangkok, India, Sri Lanka, Vietnam, Myanmar and Indonesia during this period. Geographically, chikungunya fever occurs in many areas where dengue fever is also endemic. Dual infection with

chikungunya fever and dengue fever had also been reported in India where concurrent dengue fever and chikungunya outbreaks occurred.(17) Therefore, undiagnosed chikungunya infection and misdiagnosis as dengue fever may have happened so that the incidence of chikungunya fever could be much higher than that which has been previously reported. Figure 1 showed the countries with cases of chikungunya fever ever reported as of 2007.

Figure 1: Countries (highlighted in light blue) with cases of chikungunya fever ever reported as of 2007(18)



18. Chikungunya fever cause epidemics cyclically. The usual inter-epidemic period ranges from 7 to 8 years and sometimes as long as 20 years. Since 1986, chikungunya outbreaks re-emerged in African countries including Democratic Republic of Congo, Ivory Coast and Senegal, and in Asian countries including India, Indonesia, Malaysia and Sri Lanka.(2)

Recent Major Epidemics in Indian Ocean, India and Sri Lanka

19. In recent 3 years, most important epidemics occurred in various Indian Ocean islands, India and Sri Lanka. In 2005-6, major chikungunya epidemics occurred in various Indian Ocean islands including Comoros, Madagascar, Mayotte, Mauritius, Reunion and Seychelles. Over 280,000 persons were estimated to be affected during this period with over 95% of cases contributed by Reunion which amounted to one third of their total population. In Reunion, chikungunya fever continued to circulate at a much reduced level in 2007.

20. In 2006, India and Sri Lanka, where the chikungunya activity had not been detected for over 30 years, also experienced epidemics. In India, over 1.39 million cases from 15 states were reported in 2006 with attack rates reaching up to 45% in some areas. In 2007, the activity of chikungunya fever continued in the Indian subcontinent in a reduced magnitude that about 43,000

cases were reported from 17 states. No death was reported in both 2006 and 2007.(19) In Sri Lanka, over 37,000 cases were reported during the period of October 2006 to August 2007.

21. During the chikungunya epidemics in Indian Ocean Islands, India and Sri Lanka, about 960 imported cases were reported from 14 areas in Europe, the Americas, Australia, and Asia.(2) Although these imported cases constituted a potential threat of introducing the disease into places where competent mosquito vectors were present, there was no report of indigenous cases from these areas at that time.

Re-emergence of Chikungunya Fever in Southeast Asia

22. In Southeast Asia, Indonesia and Malaysia also experienced re-emergence of chikungunya fever. In Indonesia, chikungunya fever has remained active since its reappearance in 2001 after a silent period of 20 years. During the period from January 2001 to April 2007, a series of outbreaks occurred in 7 provinces and had affected about 15,000 persons. In Malaysia, an outbreak of chikungunya fever occurred in 2006 affecting about 200 persons.(20)

Indigenous Outbreaks in Italy and Singapore

23. Italy and Singapore reported their first local outbreak of chikungunya fever in 2007 and 2008 respectively. The disease was suspected to be introduced into Italy by an infected person returning from India while the outbreak in Singapore appeared to arise indigenously.

24. In August 2007, an outbreak of chikungunya was reported in the province of Ravenna in north-eastern Italy. Over a period of 15 weeks, a total of 204 cases were affected. The outbreak was found to be related a foreign visitor stopping in the country after visiting an affected area in Indian subcontinent. The cases were confirmed by serological testing and PCR. Vector studies by PCR found chikungunya virus in *A. albopictus*. This outbreak marks the first recorded occasion that chikungunya virus has been locally transmitted by mosquitoes within Europe. It also suggested that *A. albopictus* can be an efficient vector. High concentration of *A. albopictus* and their exposure to a highly viraemic person may be the possible contributing factors for the success of local transmission of the disease. The outbreaks were controlled by timely and intensive vector control measures including control of breeding sites and use of insecticides, and enhanced surveillance with active case finding.(7,21)

25. In January 2008, Singapore reported their first indigenous case of chikungunya fever. The first case was reported on January 14 in a 27-year-old foreign national who had no travel history prior to disease onset. The

Singaporean Ministry of Health conducted extensive investigations after the first case was reported. By early February (i.e., 22 days after the first case), a total of 13 local people with serological evidence of chikungunya fever were identified. All cases recovered. A cluster of ten cases was identified in the city area of Clive Street in Little India while the remaining three cases were identified in the nearby areas. Intensive vector control on the Singaporean prevalent vector, the *A. aegypti*, was implemented at and around the affected areas. No further clinical case related to this cluster was reported in 3 weeks after identification of the first case.(22) Later in June and August 2008, more local cases of chikungunya fever were diagnosed from Teacher Housing Estate (2 cases), Farrer Road (1 case), Jalan Jelita (1 case) and Kranji Way (3 cases). (23-26)

Local Situation

26. There were five cases of chikungunya fever reported so far to the Centre for Health Protection (CHP) from March 2006 through end of July 2008. All of them reported a history of traveling to endemic areas. Three cases were reported in 2006 and two cases in 2008. All of them are adults (median age 47 years, range 34 to 69 years). There are three males and two females. Two were reported in September, two in March and one in January.

27. As for the clinical features, all of them had fever, bone and/or joint pain. Four patients developed skin rash and two had prolonged joint pain lasting from 3 weeks to 3 months after onset. Four cases were confirmed by positive PCR test for chikungunya virus genome or a four-fold rise in chikungunya antibody in paired sera. The diagnosis of the remaining one case was made by detection of chikungunya IgM antibody in the patient's serum collected three months after onset of symptoms.

28. Regarding the travel history, three visited Asian countries namely India, Indonesia, and Sri Lanka and two visited Indian Ocean countries namely Mauritius and Madagascar during the incubation period. Table 1 summarizes the details of these five cases.

29. In Hong Kong, *A. albopitius* is common and widely distributed and can be a potential vector. *A. aegypti*, the other efficient vector for both chikungunya and dengue fever, has not been found in Hong Kong since the mid-1950s.

Table 1: Summary of chikungunya fever cases reported to CHP in Hong Kong

	Case 1	Case 2	Case 3	Case 4	Case 5
Date of notification	29 Mar 2006	4 Sep 2006	4 Sep 2006	22 Jan 2008	18 Mar 2008
Sex / Age	M/66	F/34	M/47	F/34	M/69
Ethnicity	Chinese	Indian	Chinese	British	Chinese

Imported country	Mauritius	India	Madagascar	Sri Lanka	Indonesia
Clinical presentation	Fever, chills and rigors, arthralgia, myalgia, petechiae in legs, generalized erythematous rash	Fever, bone pain, rash over legs and arms	Fever, bone and joint pain, stiffness of finger joint, rash	Fever, severe joint pain, rash	Fever, chills, headache, bone and joint pain
Laboratory confirmation	PCR test positive for chikungunya virus (Day 3 after onset)	PCR test positive for chikungunya virus (Day 8 after onset)	Serum positive for chikungunya IgM Ab (3 months after onset)	Four fold rise for chikungunya antibody detected in paired sera	Four fold rise for chikungunya antibody detected in paired sera
Outcome	Recovered	Recovered	Stable with persistent joint pain	Stable with persistent joint pain	Stable

Public Health Implications and Control Strategies of Chikungunya Fever

30. Chikungunya fever is generally believed to cause a much milder illness as compared with dengue fever, West Nile fever, or other arboviral infections. However, the disease can cause severe symptoms especially joint pain and prolonged fatigue in previously healthy persons. Complications can still occur although relatively less common. Infants, elderly and immunocompromised persons may be at risk of severe diseases. From the public health perspective, the disease may cause diagnostic difficulties especially in places where dengue fever is also prevalent. The outbreak in Italy last year demonstrates the feasibility of *A. albopictus* as an efficient vector for spreading the disease. Last but not least, both the healthcare providers and the public, especially travelers, should be updated with the rapidly changing geographical distribution of the diseases. In the following, we examine the various aspects of public health measures and identify areas for enhancement. Control strategies rest on early disease reporting and case investigation, vector surveillance and control, and public health education.

Disease Reporting and Case Investigation

31. Chikungunya fever has been placed under case-based surveillance of CHP since 2006. When physicians report a suspected case, the CHP will conduct epidemiological investigation and arrange for laboratory studies. The exposure and travel history would be explored to determine the

source of infection. Aggressive mosquito control will be implemented with the efforts of Food and Environmental Hygiene Department (FEHD) along the places where the patients have stayed during the infective period so as to prevent secondary spread in Hong Kong.

Vector Surveillance and Control

32. FEHD conducts regular mosquito survey in Hong Kong for guiding mosquito control efforts. The distribution and breeding of *A. albopictus* and *A. aegypti* is studied by using oviposition traps set in 38 areas over the territories, International Airport and port areas in Hong Kong. The percentage of the oviposition trap found positive with breeding of these mosquitoes gives the Ovitrap Index which indicates the extensiveness of the breeding of the vectors. The breeding activity is generally increased from spring, reached the peak in summer and decreased to the low levels in late autumn and winter times.(27)

33. The FEHD leads an annual inter-departmental anti-mosquito campaign to solicit community support to prevent and control mosquito-borne diseases in Hong Kong. This campaign aims at heightening public awareness on potential risk of mosquito-borne diseases, encouraging community participation in anti-mosquito work, and eliminating potential mosquito breeding sites, in particular improperly disposed containers. Legal action would be taken against those who allow mosquitoes to breed on their premises.

34. An Anti-mosquito Steering Committee chaired by the Permanent Secretary for Food and Health (Health) is also in place to co-ordinate the anti-mosquito measures from various government departments. The Committee holds regular and *ad hoc* meetings in response of the high Ovitrap Index to discuss the appropriate measures needed to be taken.

Public Health Education

35. Currently, no vaccine is available against chikungunya infection. Prevention mainly depends on steps to avoid mosquito bites and elimination of mosquito breeding sites. Health advice has been given to members of the public through various sources including fact sheets on chikungunya disease on CHP and Travel Health Service websites of the Department of Health. FEHD also targets the public on anti-mosquito measures through webpage, their health education exhibition and resource centre, the mobile education centre, Announcement of Public Interest, health talk, health education materials including leaflets and posters. A dedicated hotline has also been set to deal with public enquiry on anti-mosquito measures and complaint on mosquito breeding sites.

Conclusion and Recommendations

36. Chikungunya fever is a potential threat in Hong Kong for the following reasons:

- (a) A competent mosquito vector, *A. albopictus*, is widely available throughout the Hong Kong territory;
- (b) Hong Kong comprise a dense population with naïve immunity to the infection;
- (c) There is busy international traffic with numerous visitors from over the world including chikungunya endemic areas.

37. The robust mechanism in Hong Kong for detection and responding to infectious diseases and the ongoing efforts in minimizing mosquito vectors for dengue fever have been playing a crucial role in guarding against importation of the infection from endemic areas.

38. At present, the key to preventing the disease in Hong Kong is to identify cases early so that prompt vector control can be done, before any secondary spread occurs through infected persons. This relies on effective surveillance systems, early detection and diagnosis of case, and stringent mosquito surveillance and control. The followings are the recommendations on strengthening the prevention and control measures of chikungunya fever in Hong Kong:

- (i) To continue updating the global epidemiology of the disease by close monitoring of the chikungunya fever situation in endemic and emerging areas. Such information should be disseminated to the public and clinicians to raise their alertness.
- (ii) To enhance alertness among local physicians of the disease by informing the latest epidemiology, availability of diagnostic tests and public health management of the disease and to make the disease notifiable in due course.
- (iii) To secure the laboratory capacity and ensure diagnostic test of chikungunya fever is readily accessible by the referring clinician. Diagnostic test should be considered for patient who has compatible symptoms and returning from endemic areas of chikungunya fever. It is especially true for patient whose test for dengue fever is negative because the disease may be clinically indistinguishable.
- (iv) To maintain regular mosquito surveillance program for

monitoring of chikungunya vectors, which are also dengue fever vectors, and conduct mosquito survey in response to case investigation to prevent secondary spread.

- (v) To enhance awareness among the public especially travelers through various channels. Health advice would be provided to the travellers going to endemic areas.

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Annex: Comparison of Epidemiological and Clinical characteristics of Chikungunya and Dengue Fever Infection(4,5,28,29)

	Chikungunya Fever	Dengue Fever
Causative agent	Chikungunya virus: an alphavirus (family Togaviridae)	Dengue virus: a flavivirus of which there are 4 serotypes (1, 2, 3 and 4)
Major vectors	<i>Aedes aegypti</i> , <i>Aedes albopictus</i>	<i>Aedes aegypti</i> , <i>Aedes albopictus</i>
Reservoirs	Humans and non-human primates	Humans and non-human primates
Geographic distributions	Sub-Saharan Africa, South-East Asia, tropical areas of the Indian subcontinent, islands in the south-western Indian Ocean and north-eastern Italy.	Tropical and subtropical regions of central and South America, South and South-East Asia, and Africa.
Incubation period	1 – 12 days, usually 3 – 7 days	3 – 14 days, usually 4 – 7 days
Symptoms	<p>Can be asymptomatic or presented as an acute febrile illness, i.e. chikungunya fever:</p> <ul style="list-style-type: none"> • Sudden onset of fever (sometimes biphasic) • Severe joint pains, particularly affecting the hands, wrists, ankles and feet; generalized myalgia • Generalized symptoms (chills, headache, fatigue, nausea, vomiting, photophobia, retro-orbital pain) • Rash, usually macular or maculopapular and occasionally petechial skin lesions • Sometimes signs of pharyngitis, conjunctivitis, leukopenia and hepatomegaly may be present. • Rare manifestations or complications: haemorrhagic manifestations including haematemesis, melaena and epistaxis, meningo-encephalitis, Guillain-Barré syndrome, fulminant hepatitis, 	<p>Three main clinical forms:</p> <ol style="list-style-type: none"> 1. Dengue fever (DF): <ul style="list-style-type: none"> • Sudden onset of fever (may be biphasic) • Generalized symptoms (headache, anorexia, nausea, vomiting) • Severe muscle, joint and bone pains • Sometimes a macular skin rash, retro-orbital pain, and minor bleeding phenomena like petechiae, epistaxis or gum bleeding 2. Dengue haemorrhagic fever (DHF) – sudden onset of fever, and symptoms resulting from thrombocytopenia, increased vascular permeability and haemorrhagic manifestations. 3. Dengue shock syndrome (DSS) – supervenes in a small proportion of cases. Severe hypotension develops, requiring urgent medical treatment to correct hypovolaemia.

	myocarditis and pericarditis	
Laboratory diagnosis	<ul style="list-style-type: none"> • Positive chikungunya virus IgM antibody • \geqFour-fold rise in antibody titres to chikungunya virus antigen in paired serum • Isolation of chikungunya virus from clinical specimens • Detection of chikungunya virus genomic sequences by polymerase chain reaction (PCR) in clinical specimen 	<ul style="list-style-type: none"> • Positive dengue virus IgM antibody • \geqFour-fold rise in antibody titres to dengue virus antigen in paired serum • Isolation of dengue virus from clinical specimens • Detection of dengue virus genomic sequences by polymerase chain reaction (PCR) in clinical specimen
Prognosis	<p>Most patients recover after a few days. Persistent joint pain lasting for weeks, months or even longer in some cases is a distinctive feature from DF. Older patients may experience joint stiffness, chronic pain and recurrent joint effusions for months to years, especially in individuals with HLA-B27 genotype. Mortality associated with chikungunya reported in the 2005 – 6 Indian Ocean epidemics.</p>	<p>Most patients recover after a few days. For DSS cases, mortality rate reduced from 40–50% to 1% or less with timely therapy.</p>

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