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An Update on Chikungunya Fever and Homoeopathic Management

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Introduction:

Chikungunya fever is a viral disease transmitted to humans by the bite of infected mosquitoes. Chikungunya virus (**CHIKV**) is a member of the genus *Alpha virus*, in the family *Togaviridae*. Chikungunya Virus is also known as Buggy Creek Virus. **CHIKV** was first isolated from the blood of a febrile patient in Tanzania in 1952. (1)

Chikungunya is derived from the Swahili / Makonde word for "that which twists or bends up". It is a febrile arthritis occurring in sporadic cases and in epidemics. (2)

The first outbreak of the disease was seen in the year 1952, in the Makonde plateau, along the border between Tanzania and Mozambique.

The disease was first described by Marion Robinson and W.H.R. Lumsden in 1955 . (3)

International Classification of Disease Codes for Chikungunya Fever is ICD-10 A92.0 (4)

Epidemiology:

Chikungunya is endemic in sub-Sahara Africa, India, the Philippines and Southeast Asia. Outbreaks typically occur after heavy rains. In urban settings, outbreaks are explosive. In a 1964 epidemic in Bangkok, Thailand, an estimated 40,000 patients of an urban area of 2 million were infected.

In endemic areas seroprevalence rates may be as high as 90%, suggesting that time required for loss of herd immunity is the reason for prolonged absence of cases in a region after an outbreak. Globalization may contribute to increasing risk of spread.

An outbreak in Malaysia from 1998 to 1999 was attributed to migrant workers from endemic areas. After inoculation, the incubation period is typically 2 to 3 days but ranges from 1-12 days. (5)

Reunion Island, a french overseas departement with 780,000 inhabitants, is currently suffering an explosive Chikungunya fever epidemic: on mid-january 06, about 10,000 cases had been officialy recorded (unofficially 40,000), which makes it a major public-health issue.

Aedes albopictus is the suspected vector of the current outbreak of Chikungunya virus on Reunion island.

An outbreak of chikungunya was discovered in Port Klang in Malaysia in 1999 affecting 27 people.

Update January 26 According to InVS, Chikungunya epidemic is now officialy around 30,000. It is an estimate based on a mathematical model. The number of new cases is increasing very rapidly and is estimated to around 5000 cases for the second week of January 2006. It would not have yet reached a peak. To date, no direct fatal cases have been reported. However, the epidemic seems to have a strong and very bad effect in people with chronic diseases.

Update February 4 The epidemic has risen to 50 000 cases, with an increase of 15 000 in the past week alone. The chikungunya disease was not previously thought to be lethal, but 25 indirect fatalities are officially reported, mostly in patients with chronic diseases.

Update February 17 As expected, the situation is getting worse. Chikungunya fever has now officially affected more than 110 000 people, with an increase of 22 000 over the past week. Chikungunya fever is cited as a more or less direct cause in 52 death certificates since January 2006. Death rate has increased in 2005, and is apparently increasing in 2006, and it may have to be imputated to the current epidemic.

Update March 11 The epidemic has now infected 204 000 people, with an increase of 13 000 during the last week. Chikungunya fever is now cited in 125 death certificates. The epidemic seems to be slowing down.

Update April 6 The number of people newly infected with chikungunya is decreasing from the high level seen at the beginning of the year (40000 cases a week), although it still remains very high (almost 8000 cases a week). So far, 230000 people have now been infected (29 % of the population) and chikungunya is now cited in 174 death certificates since january 06.

Update May 13 Although a decreasing trend is reported since mid February 2006, the epidemic is still very active. After 15 months, this outbreak involved 256000 people, and the incidence here remains high with 1500 people infected in the past week.

Update July 1st The situation is worrying. Latest estimated figures in Reunion show that the epidemic is still standing at a high level with 600 new cases in the past week. To date, 266000 people have been infected (34 % of the population), 238 fatalities have been reported (lethal rate is about 0.08%). Chikungunya fever epidemic is apparently deepening and accelerating in India. It seems that Chikungunya fever has reached a quasi-pandemic dimension with more than a million people infected during the past 24 months in a large geographic area encompassing the East-African equatorial coasts, the Indian Ocean islands and half of the Indian peninsula. (6)

Recent outbreaks in February 2005, an outbreak was recorded on the French island of Réunion in the Indian Ocean. As of February 25, 2006, 157,000 residents have been hit by the virus in the past year (out of a population of about 777,000 - 20%). Since October 2005, 52 deaths have been associated with chikungunya (French health minister Xavier Bertrand said 77 deaths in January 2006 may have been «directly or indirectly attributable» to the outbreak. France initiated a massive effort to eradicate mosquitos' nesting grounds involving over 4000 people, including 800 troops. In neighboring Mauritius, 3,500 islanders have been hit in 2005. There have also been cases in Madagascar, Mayotte and the Seychelles. In 2006 there was a big outbreak in the Andhrapradsh state in India. Nearly 200,000 people were affected by this disease in the districts of praksham and nellore in this state. (7)

In India :

The first outbreak in India's was in the year 1963, in Calcutta. Since the first reported case in India in 1963 there have been sporadic outbreaks in varies parts of India. However recently reports have been shown the re-emergence of the disease in India in 2005, specially in the southern states. Since the outbreak in December 2005 there have been more that 1,80,000 reported cases of Chikungunya in India. Beginning of 2006 between February to March there have been more than 2000 cases reported in Maharashtra. (8)

Nagpur: A large number of people in Nagpur have been affected by a crippling disease, identified as "Chikungunya" that is similar to that of the lethal dengue disease, and is marked by high fever, severe rashes, body ache, joint pains and nausea.

Though the disease is not considered to be fatal, in 2005-2006, 200 deaths have been associated with chikungunya on Reunion Island and a widespread outbreak in South India. (9)

Pune, July 28 (ANI): Nearly 2.25 lakh persons in Maharashtra have been affected by a crippling fever, the state government said on Friday. The fever, known as "Chikungunya", has spread across 26 districts of Maharashtra. Around 2.25 lakhs suspected cases of Chikungunya have been registered across 26 districts in Maharashtra. (10)

There has been reports of large scale outbreak of this virus in southern India. At least 80,000 people in Gulbarga, Tumkur, Bidar, Raichur, Bellary, Chitradurga, Davanagere, Kolar and Bijapur districts in Karnataka state are known to be affected since December 2005.

A separate outbreak of chikungunya fever was reported from Malegaon town in Nasik district, Maharashtra state, in the first two weeks of March 2006, resulting in over 2000 cases. In Orissa state, amost 5000 cases of fever with muscle aches and headache were reported between February 27 and March 5, 2006.

Morphology :

Chikungunya virus (**CHIKV**) is a member of the genus *Alpha virus*, in the family *Togaviridae*. Chikungunya Virus is also known as Buggy Creek Virus. It consists of enveloped single stranded RNA viruses, that are 60 to 70 nm in diameter. (11)

CHIKV is an enveloped, positive-strand RNA virus. To date, two CHIKV complete nucleotide sequences have been determined, for the strains Ross and S27 , both isolated from patients during the 1952 Tanzania outbreak. Another complete nucleotide sequence has been determined for a strain isolated in *A. furcifer* during the Senegal 1983 outbreak (accession no AY726732). Khan et al showed that the S27 genome was similar in its structure to that of other alpha viruses and that O'nyong-nyong virus (ONN) was the closest relative to CHIKV. In addition, phylogenetic analyses based on partial E1 sequences from African and Asian isolates revealed the existence of three distinct CHIKV phylogroups: one containing all isolates from West Africa, one containing isolates from Asia, and one corresponding to Eastern, Central, and Southern African isolates. Strains isolated in 1999–2000 in the Democratic Republic of Congo belonged to the latter phylogroup. (12)

Pasteur Institute virologists have worked out the genetic sequence of six samples of chikungunya virus taken from patients throughout the current outbreak, and the E1 coat protein from another 127 patients. The genome sequences analysis showed the Indian Ocean strains are most related to East-African strains. The analysis also revealed several distinct variants. For instance, the virus acquired a change at position 226 of the E1 coat protein (A226V mutation), that could allow the virus to more easily invade and multiply in mosquitoes. The researchers also identified three protein changes in non-structural proteins nsP1 (T301I), nsP2 (Y642N), and nsP3 (E460 deletion) that were present in a virus isolated from a neonatal encephalopathy case, but were missing from other classical forms of the disease. (13)

Brisse and colleagues determined the entire genetic sequence of six virus samples isolated from patients in different places (five from Reunion and one from the Seychelles) and different times (three from early 2005 and three from later in 2005) during the outbreak. They also sequenced one of the viral genes (called E1) from

virus samples taken from an additional 121 patients. The results show that the outbreak began with a strain related to East-African strains of the virus which subsequently developed into several distinct variants. All of the Indian Ocean sequences share unique molecular features that differ from strains of the virus involved in earlier outbreaks and suggest how the virus could have become more «aggressive». (14)

Unique molecular features of the outbreak isolates were identified. Notably, in the region coding for the non-structural proteins, ten amino acid changes were found, four of which were located in alpha virus-conserved positions of nsP2 (which contains helicase, protease, and RNA triphosphatase activities) and of the polymerase nsP4. The sole isolate obtained from the cerebrospinal fluid showed unique changes in nsP1 (T301I), nsP2 (Y642N), and nsP3 (E460 deletion), not obtained from isolates from sera. In the structural proteins region, two noteworthy changes (A226V and D284E) were observed in the membrane fusion glycoprotein E1. Homology 3D modeling allowed mapping of these two changes to regions that are important for membrane fusion and virion assembly. (15)

Transmission:

Chikungunya is spread by the bite of female Aedes mosquitoes, primarily Aedes Aegypti. Humans are considered to be the major sources of reservoir of chikungunya virus for mosquitoes. The mosquitoes usually transmit the disease by biting infected persons and then biting others. The infected persons cannot spread the infection directly to other person (i.e. it is not contagious disease). Chikungunya typically results in a large number of cases but deaths are rarely encountered. The disease is mostly present in urban and peri-urban areas.

Aedes aegypti mosquitoes bite during the day and breed in a wide variety of man-made containers which are common around human dwellings. These containers such as discarded tyres, flower pots, old water drums, family water trough, water storage vessels and plastic food containers collect rain water. (16)

It may be transmitted by Mansonia africana and other genera. Known reservoirs are monkeys, baboons and in Senegal, scotophilus bat species. During outbreaks, humans are the major reservoirs. (17)

In Africa, the virus is maintained through a sylvatic transmission cycle between wild primates and mosquitoes such as *Aedes luteocephalus, A. furcifer,* or *A. taylori* . In Asia, CHIKV is transmitted from human to human mainly by *A. aegypti* and, to a lesser extent, by *A. albopictus* through an urban transmission cycle. (18)

Pathogenesis:

Intense viremia occurs within 48 hrs of the mosquito bite and wanes 2 to 3 days later. Onset of haemagglutination inhibition and neutralizing antibodies clears the viremia. Superficial capillaries in rash-involved skin demonstrate erythrocyte extravasations and perivascular cuffing. The virus adsorbs to the human platelets, causing aggregation. Synovitis probably results from direct chikungunya viral infection of synovium.

clinical features :

1. Explosive onset of fever and severe arthralgia.
2. Constitutional symptoms:

   High rise of temperature (40°C)

   Rigors

   Headache

   Photophobia

   Retro-orbital pain

Conjunctival injection

Pharyngitis

Anorexia

Nausea

Vomiting

Abdominal pain

Tense lymphadenopathy

Myalgia

Facial flush is common initially

Maculo-papular rash located on the torso extremities and occasionally in the face, palms, soles occur in most patients 1 to 10 days of onset of illness.

Rash may recur with fever and may be pruritic.

Isolated patechial and mucosal bleeding may occur but significant haemorrahge is rare.

Desquamation may occur with rash resolution.

The initially acute illness may last 2 to 3 days (ranges from 1 to 7 days). Fever may recrudesce after 1 to 2 days hiatus. Poly arhtralgia is migratory and predominantly affects the small joints of hand, wrist, feet and ankles with less prominent involvement of large joints. Previously injured joints more severely affected. Stiffness and swelling may occur but large effusions are uncommon.

In most cases mild joint symptoms may last months. Destructive arthropathy is rare and may be associated with low titer rheumatoid factor, suggesting an unrelated underlying inflammatory arthritis.

Approximately 10% of patients have joint symptoms 1 year after infection. Symptoms in children tends to be milder, arthralgia and arthritis are milder and briefer in duration. Synovial fluid shows decreased viscosity with poor mucin clots and 2000 – 5000 white blood cells / mm^3.

Diagnosis:

- The virus can be isolated from blood during the initial 2 – 4 days of illness.
- In some patients, viral antigen may be detected in acute sera by haemagglutination assay due to the intensity of the viremia.
- Specific IgM antibody tests are available. Specific IgM may be detected for 6 months or longer.
- Haemagglutination inhibition and neutralization antibodies develop as viremia is cleared.
- Complement fixation antibodies are positive by the third week and slowly decrease over the subsequent year.
- RT-PCR offers an approach to diagnose more rapidly than the viral culture or antibody testing. (19)
- ELISA is available.
- An IgM capture ELISA is necessary to distinguish the disease from dengue fever. (20)

Treatment and prognosis:

During the acute arthritis range of motion exercises lessen stiffness. In other mode of treatments a vaccine is not available, no specific therapies are available and the symptoms are treated, e.g. with analgesics and anticonvulsants. Chloroquine phosphate has been used when NSAIDs failed. (21)

Decontamination: The virus is killed by common disinfectants, moist heat and drying. The vector (a mosquito) also needs to be controlled with

insecticides. (22)

Homoeopathic approach in the treatment Chikungunya fever:

The medicine can be prescribed according to the signs and symptoms of the patients. Some indicated and reliable therapeutics are given below:

1. **Eupatorium per. :**
   - Perspiration relieves all the symptoms except headache.
   - Chill between 7 and 9 a.m.
   - Preceded by thirst with great soreness and aching of bones.
   - Nausea, vomiting of bile at close of chill or hot stage.
   - Throbbing headache; sensation as if a cap of head pressed over the whole skull.
   - Knows chill is coming on because he cannot drink enough.
   - Aching in bones of extremities with soreness of flesh.
2. **Rhus tox.:**
   - Great restlessness.
   - During heat urticaria.
   - Rheumatic pain spread over a large surface at nape of neck, loins and extremities, better motion.
   - Occipital headache with heaviness of head.
   - Photophobia with pustular inflammation.
   - Chill with dry cough and restlessness.
   - Great thirst with dry mouth and throat.
3. **Ars. alb.:**
   - High temperature, great heat about 3 a.m.
   - Periodicity is marked with adynamia.
   - Paroxysms incomplete with marked exhaustion.
   - Cold sweat with unquenchable thirst.
   - Worse after midnight.
   - Delirium.
   - Great restlessness with burning pain, trembling and weakness in extremities.
   - Intense photophobia with burning in eyes.
   - Headache relieved by cold, other symptoms worse.
   - Great anguish and restlessness.
4. **Bryonia:**
   - Pulse full, hard, tense and quick.
   - Chill with external coldness and internal heat.
   - Easy, profuse perspiration.
   - Delirium.
   - Joints red, swollen and hot with stitches and tearing; < on least motion.
   - Dryness of mouth tongue and throat with excessive thirst.
   - Vertigo, nausea, faintness on rising with headache.
5. **Belladonna:**
   - A high feverish state.
   - Feet icy cold.

- Perspiration dry only on head.
- No thirst with fever.
- Throbbing headache.
- Delirium, loss of consciousness.

6. Ledum pul.:

- Coldness.
- Sensation as of cold water over parts.
- General coldness with heat of face.
- Ankles swollen, soles painful.

7. Gelsemium:

- Wants to be held because he shakes so.
- Pulse slow, full, soft.
- Chilliness up and down back, nervous chills.
- Heat and sweat stages, long and exhaustive.
- Muscular soreness and weakness, great prostration and violent headaches.
- Fever, with stupor, dizziness, faintness, thirstless.

8. Pyrogenium:

- Coldness and chilliness, chill begins in back.
- Temperature rises rapidly.
- Great heat with profuse hot sweat, but sweating does not cause a fall in temperature.
- Aching in all limbs and bones, bed feels too hard.
- Bursting headache with restlessness.
- Nausea and vomiting, taste terribly fetid.
- Sore, cutting pain in abdomen. (23)

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