Chikungunya - Need of the Hour to Save Human Beings

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Chikungunya infection is a generalised viral infection. There is no specific antiviral drug available to treat this infection. This infection needs supportive and symptomatic treatment. Analgesics, antipyretics and fluid supplementation are important aspects in managing this infection. Further, treatment and future action require on the subject are presented in common man's language since every one needs to understand this.

Key words: Chikungunya, Viral infection, Human Beings.

Chikungunya is caused by Chikungunya Virus or CHIK Virus (CHIKV) and it belongs to the alphavirus family. 27 different types of alpha viruses cause diseases in humans and other mammals. Chikungunya virus is just one of them. The structure has a diameter of about 50nm to 70nm in diameter, with an icosahedral nucleocapsid enclosed in a lipid-protein envelope. Alphavirus RNA is a single 42S strand of approximately 4×10^6 daltons that is capped and polyadenylated. Alphavirus genomes that have been sequenced in their entirety are approximately 11.7 kilobases long. Virion RNA is positive sense: it can function intracellularly as mRNA, and the RNA alone has been shown experimentally to be infectious. The single capsid protein (C protein)

has a molecular weight of approximately 30,000 daltons. The alphavirus envelope consists of a lipid bilayer derived from the host cell plasma membrane and contains two viral glycoproteins (E1 and E2) of molecular weights of 48,000 to 52,000 daltons. A small third protein (E3) of molecular weight 10,000 to 12,000 daltons remains virion-associated in Semliki Forest virus but is dispatched as a soluble protein in most other alphaviruses. The only proteins in the envelopes of alphaviruses are the viral glycoproteins, each anchored in the lipid at or near their C-terminus. On the virion surface, E1 and E2 are closely paired, and together form trimers that appear as "spikes" in an orderly array.



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Meaning of chikungunya

The disease was first described by Marion Robinson (1)and W.H.R Lumsden(2); following an outbreak on the Makonde plateau, along the border between Tanganyika and Mozambique, in 1952. According to Lumsden's initial 1955 report about the epidemiology of the disease, the term chikungunya is derived from the Makonde root verb Kungunyala, meaning to dry up or become contorted. In concurrent research, Robinson glossed the Makonde term more specifically as "that which bends up" the term derived from Swahili.

Life cycle of Alpha virus

The Life cycle of an alphavirus starts with its attachment to the host receptors through E2 glycoprotein. The virion endocytoses into the vesicles of the host cell by membrane fusion between the virus and the host vesicle, releasing the nucleocapsid into the cytoplasm. Soon uncoating occurs with the release of RNA genome for the synthesis of the new RNA genome. Further, the process of replication follows with the translation of the positive-sense genomic SSRNA acting as the messenger RNA for the synthesis of non structural proteins(P270 and P230 polyproteins) and the negative-sense complementary SSRNA that serves as a template. A subgenomic RNA (26SRNA) constituting the last third of the genome translates into the capsid protein(P130 polyprotein) and four distinct membrane embedded proteins(E3,E2, 6K, E1)



Epidemiology

The Chikungunya virus was first isolated between 1952-1953 in Tanzania where the disease was first reported. However, a similar outbreak could have happened as early as 1824 in India and elsewhere. This disease is seasonal and may disappear for 7-8 years or as long as 20 years before reappearing elsewhere. It appear in Bangkok in the 1960s; in Sri Lanka in 1969;

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Vietnam in 1975; Myanmar in 1975; Indonesia in 1982 and 1999; and in various parts of India including Vellore, Calcutta and Maharastha in 1964 and2006.

MathematicalModeling

A compartmental human-mosquito interaction model (3) was used to simulate the temporal evolution of Chikungunya in a locality. A schematic diagram of the model is shown in Figure.



Fig. Schematic diagram of the compartmental human-mosquito interaction model. The

human population was divided into susceptible, infected, and recovered classes, whereas the mosquitoes were either susceptible or infected

Denoting the human and mosquito population sizes by Nh and Nv respectively, the number of susceptible humans by Sh, and the number of infected humans and mosquitoes by Ih and Iv respectively, the following differential equations describe the time evolution of Sh, Ih and Iv:

$$\frac{dS_k}{dt} = \gamma N_k - \left(\gamma + C \frac{I_v}{N_k}\right) S_k$$
$$\frac{dI_k}{dt} = C \frac{I_v}{N_k} S_k - (\gamma + \beta) I_k$$
$$\frac{dI_v}{dt} = C \frac{I_k}{N_k} (N_v - I_v) - \eta I_v.$$

Infected humans and infected mosquitoes were assumed to be infectious. The lifetime of a human was $1/\gamma$, that of a mosquito was $1/\eta$, and the human infectious period was 1/β. It was assumed that infected mosquitoes and susceptible mosquitoes had the same biting rate and that the probability of the virus transmission from an infected mosquito to a susceptible human during a bite was the same as that from an infected human to a susceptible mosquito. The product of the mosquito biting rate and the probability of the transmission of the virus was denoted by C. It was further assumed that Aedes albopictus mosquitoes had a flight range of one kilometer (4) and that, because of the random mixing assumption of the model, the populations Nh and Nv represented population densities per sq. km.

The model was integrated to compute the evolution of the outbreak for a period of 60 days in a theoretical locality with a human population of density 3000 per sq. km and with initially one infected human but an otherwise susceptible human and mosquito population. The lifetimes of humans and mosquitoes were respectively taken to be 70 years and 30 days. During the outbreak it was assumed that the human population was constant and that the mosquito population had attained its carrying capacity during that time and was therefore constant and that both these populations were homogeneously spatially distributed over the locality. Further assumptions included the following: the mosquito biting rate was once weekly, the probability of the virus transmission during a bite was 0.9, the human infectious period was 3 days and the mosquito population was four times greater than the human population.

The behavior of a follow-up outbreak in the theoretical locality was investigated by computing the evolution of the disease with the number of humans affected in the previous outbreaks as having acquired immunity, but with otherwise the same initial conditions. In a mosquito-control scenario for the theoretical locality, the evolution of the epidemic was computed with the number of infected adult mosquitoes controlled to one per sq. km every seven days.

Transmission

Chikungunya is generally spread through bites from *Aedes aegypti* mosquitoes, but recent research by the Pasteur Institute in Paris has suggested that Chikungunya virus strains in 2005-2006. Reunion Island outbreak incurred a mutation that facilitated transmission by *Aedes albopictus* (Tiger mosquito)⁵. Concurrent studies by arbovirologists at the University of Texas Medical Branch in Galveston, Texas, confirmed definitively that enhanced chikungunya virus infection of *A. albopictus* was caused by a point mutation in one of the viral envelope genes (E1).^{6,7}



During pregnancy

Gabriele and Domenique of the perinatal Network, observed cases of Mother - to - fetus infection which occurred between 3 and 4 months into pregnancy. Before and after that period in pregnancy, they have not seen any infection. However, there is a 48% risk of infection at birth if the virus is still present in the mother's blood.

The incubation period of the chikungunya virus is about 2 to 4 days, according to the Regional Department of Health and Social affairs of La Reunion. ImmunoglobulinM(IgM), an antibody, generally appears between 4 to 7 days after the onset of clinical signs. IgM, however, does not pass through the placental barrier. The body starts producing Immunoglobulin G(IgG) around Day 15 and does pass it through the placenta and confer immunity to the featus.

On 28 May 2009 in Changwat Trang of Thailand where the virus is endemic, the provincial hospital decided to deliver by Caesarean section a male baby from his Chikungunya-infected mother-Khwanruethai Sutmueang, 28, a Trang native-in order to prevent mother-foetus virus transmission. However, after delivering the baby, the physicians discovered that the baby was infected with Chikungunya virus, and put him into intensive care because the infection had left the baby unable to breathe by himself or to drink milk. The physicians presumed that Chikungunya virus might be able to be transmitted from a mother to her foetus; however, there is no laboratory confirmation for this presumption.

Signs and symptoms

The incubation period of Chikungunya disease is from two to four days. Symptoms of the disease include a fever up to 40 °C (104 °F), a petechial or maculopapular rash of the trunk and occasionally the limbs, and arthralgia or arthritis affecting multiple joints⁸. Other nonspecific symptoms can include headache, conjunctival infection, and slight photophobia. Typically, the fever lasts for two days and then ends abruptly. However, other symptoms—namely joint pain, intense headache, insomnia and an extreme degree of prostration—last for a variable period; usually for about 5 to 7 days.⁸ Patients have complained of joint pains for much longer time periods depending on their age^{9,10}.

Diagnosis

Laboratory investigation

Blood count

- I low white cell count with raise lymphocytes count (common inviral infection) Raise ESR, CRP (nonspecific) Virusisolation Ig Mdetection (ELISA) Haemagglutination Inhibition (HI) antibodies – positive by day 5-7 Common laboratory tests for chikungunya include RT-PCR, virus isolation, and serological tests.
- Virus isolation provides the most definitive diagnosis but takes 1-2 weeks for completion and must be carried out in Biosafety level 3 laboratories. The technique involves exposing specific cell lines to samples from whole blood and identifying chikungunya virus-specific

responses.

- RT-PCR using nested primer pairs to amplify several Chikungunya-specific genes from whole blood. Results can be determined in 1–2 days.
- Serological diagnosis requires a larger amount of blood than the other methods and uses an ELISA assay to measure Chikungunya-specific IgM levels. Results require 2–3 days and false positives can occur with infection via other related viruses such as O'nyong'nyong virus and Semliki Forest Virus.

Treatment

There are no specific treatments for Chikungunya. There is no vaccine currently available. A Phase II vaccine trial, sponsored by the US Government and published in the American Journal of Tropical Medicine and Hygiene in 2000, used a live, attenuated virus, developing viral resistance in 98% of those tested after 28 days and 85% still showed resistance after one year¹¹.

Chloroquine is gaining ground as a possible treatment for the symptoms associated with Chikungunya, and as an anti-inflammatory agent to combat the arthritis associated with Chikungunya virus. A University of Malaya study found that for arthritis-like symptoms that are not relieved by aspirin and non-steroidal antiinflammatory drugs (NSAID), chloroquine phosphate (250 mg/day) has given promising results.

Ayurvedic Treatment

There is no drug prescribed for chikungunya from the world helth organization until now. Doctors are using aspirin, ibuprofen, combiflam, paracetamol, etc. to reduce the pains and the fever, but there is no universally acceptable treatment in allopathic medicine yet. Some people are benefited by some medication, while others are not. Some chickungunya people get healed on their own after a few days. Hence, medical science is not trusted enough where chickungunya is concerned.

This led many people with chickungunya to turen to Ayurveda for seeking out treatment. Ayurveda may not be able to treat the condition of chickungunya completely, but it provides the

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necessary resistance for the body to combat with the disease.

There are certain Ayurvedic herbs that have a potential to reduce the symptoms of chickungunya. The following is a list of some herbs with their action on the human body.

Ayurvedic name of the herb	Biological Name of the herb	Common English Name of the herb	Action on the human body	
Angoor	All belong to the family <i>vitaceae</i>	Grapes	Grapes are taken along with some of the severe chickungunya symptoms. The grapes must be drv and seedless.	
Gaajar	Daucus carota	Carrot	Carrots eaten either raw or in the form of salads are beneficial in increasing the resistance of people suffering from chickungunya and in protecting them from major complications	
Tulsi	Ocimum sanctum	Sacred Basil	Tulsi leaves are used for chickungunya patients as they are effective in reducing the fever.	

The following Ayurvedic preparations have been found to be effective against the symptoms of chickungunya.

Sudarshan choorna	-	Two tablespoons of this
		chooma must be taken
		per day
Yogiraj guggulu	-	Two tables per day are
		to be taken.

- Apply vitamin E oil on the eruptions. For rashes, calamine lotion is a good remedy. But it will take months for curing the eruptions and rashes. Olive oil and lime juice and apply over the affected areas. The skin rashes will go.
- Grind fresh neem leaves and apply on skin.Boil water with neem leaves or red sandal and wash the areas with the same.

Here it is important mention that there is currently a debate going on about the effectiveness of Ayurvedic medicines in the treatment of Chickungunya.

Homeopathy Treatment

Homeopathy offers many medicines which may help in Chikungunya. These include medicines like Eupatorium-perf, Pyroginum, Rhus-tox, Cedron, Influenzinum, China, Arnica, Belladona, Bryonia etc. Many homeopaths consider Eupatorium perf. as a preventive medicine for Chikungunya. The most commonly suggested potency as prophylaxis is 200C of Eupatorium perf. Eupatorium Perfoliatum Q (tincture, 3 to 5 drop dose)will remove the debilitating joint pains and cut short the intensity and duration of the disease.

Vaccine and antiviral development

Due to the significant infection rates during outbreaks, the extensive geographical distribution of this virus, and the severe morbidity associated with clinical disease, a CHIKV vaccine is highly desirable. Given the numerous documented cases of laboratory acquired infections (Biosafety in Microbiological and Biomedical Laboratories 5th Edition), a vaccine would also be beneficial to personnel with occupational risk. However, while there has been extensive work in vaccinology for several other alphaviruses¹², the history of vaccine development for CHIKV is short and none of these efforts have yet resulted in a licensed vaccine. The most extensive work performed in the development of a human CHIKV vaccine was initiated by investigators at Walter Reed(USA). Virus from the original outbreak was formalin inactivated and potency tests using this product generated variable results depending upon dose, route of inoculation and vaccine concentration. One of the preparations harvested from green monkey kidney cells (GMKC) was found to induce high levels of antibodies, it was protective against intracranial challenge with homologous virus, it produced no detectable viraemia and it resulted in good protection in monkeys after challenge with four strains of CHIKV¹³.

The lack of specific treatment for CHIKV infection has resulted in several laboratory studies to identify antiviral agents effective against this virus. Compounds including ribavirin, sulfated polysaccharides (iotacarrageenan, fucoidan and dextran sulfate), 6-azauridine, glycyrrhizin and interferon- have been evaluated for their ability to inhibit replication of CHIKV in cell culture. With the exception of the polysaccharides, all were found to have both potent and selective antiviral activity¹⁴.

CONCLUSION

CHIKV has been responsible for significant human morbidity for (probably) several hundred years; yet in spite of its prevalence, CHIKV epidemiology and mechanisms of virulence and pathogenesis are poorly understood. Simple mathematical models can provide valuable insight into epidemicoutbreak initial conditions and development.

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